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OPTIMIZATION OF TREATMENT OF LOCAL ENAMEL DEMINERALIZATION OF PERMANENT TEETH IN CHILDREN

Scientific specialty 3.1.7. Dentistry

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CONTENTS

INTRODUCTION

Relevance of the research topic. The problem of dental caries occupies one of the leading places in dentistry due to its high prevalence in all countries of the world [34, 48, 83, 137]. In the last decade, the concepts of etiology, pathogenesis and treatment of dental caries have changed, the principle of preventing the formation of carious cavities by identifying and effectively treating the early stages of the disease has come to the forefront [32,81]. Modern systems of caries diagnosis and evaluation, classifications that take into account the initial stages of carious lesions are more and more widely used [8,37,88,113]. However, there are still only sporadic reports on the prevalence and clinical features of initial caries in permanent teeth in children [33,54,206].

The first manifestation of the initial carious process is white spot lesion (WSL), which initially occurs in the subsurface enamel layer and is reversible [36,101,119,180]. In recent years, an active search and introduction of new methods of early caries diagnosis and carious process severity assessment has been carried out [10,147,175].

In practical dentistry, common additional methods of diagnosing WSL are vital staining and radiography. More objective and modern methods of diagnostics of initial caries include laser fluorescence (LF) diagnostics, Quantitative Light-induced Fluorescence (QLF) technologies and other hardware methods [3,38,64,140,182]. However, their effectiveness and feasibility of their application at mass dental appointments need to be confirmed.

With the development of ideas about the pathogenesis of the carious process, approaches to the treatment of initial forms of caries have changed [95]. The main task in the treatment of WSL is to reduce the effect of cariogenic factors and to use therapy aimed at restoring and remineralizing the affected enamel areas [56,106,171]. The first task is achieved by normalizing oral hygiene and controlling nutrition, including reducing the frequency of easily digestible carbohydrates [43,63,154]. A wide range of methods are currently available to restore areas of tooth enamel demineralization, among which noninvasive and microinvasive techniques are the most important [183,187].

One of the common methods of enamel caries treatment is the use of fluoride-containing preparations, the effectiveness and safety of which have been confirmed by 80 years of practical experience [32,121,163]. There are many fluoride products of different composition and fluoride concentration on the dental market, but there are no unambiguous recommendations for their selection and use in children. The use of toothpastes with higher fluoride content (2800-5000 ppmF^-) has been shown to increase enamel microhardness and reduce the permeability of local demineralization, compared to toothpastes with standard (1000-1500 ppmF^-) fluoride concentration. An in-vitro study by Wierichs R.J. et al., 2020, demonstrated an improvement in enamel remineralization due to the use of toothpastes with high (5000 ppm) fluoride concentration [199]. However, further studies are needed to confirm the clinical efficacy of fluoride- enhanced toothpastes in the treatment of WSLs in children.

Professional application of fluorides in the form of fluoride varnishes and gels is also an effective method for the treatment of caries in the initial stage [134]. Fernández-Ferrer L. et al., 2018 [118], showed that among remineralizing agents for WSL, only varnish based on 5% sodium fluoride has a positive effect. Increased remineralizing ability of fluorides when combined with casein-phosphopeptide-amorphous calcium phosphate (CPP- ACP) has been reported; however, evidence of this effect is insufficient, long-term randomized controlled trials are needed [71,146].

A modern method of treatment of initial carious lesions is the infiltration method [161], which allows treatment of WSL in one visit, one-stage. The use of the caries infiltration method has shown good results in children and adults [30,166]. However, this method of treatment is expensive, is not covered by the compulsory medical insurance (CMI) system, and does not prevent the development of new and secondary carious lesions.

The concept of stimulating the natural regeneration of demineralized enamel through the use of amelogenin peptides is new in the treatment of WSL [111,181]. Amelogenin peptide forms a fibrillar biomatrix, which acts as a three-dimensional framework that sorbs calcium and phosphates from saliva. The process occurring in enamel resembles amelogenin and contributes to the restoration of demineralized enamel.

However, the main studies of the preparation were conducted “in vitro”, and the data on the clinical effectiveness of this method are insufficient [7,127].

Thus, the relevance of the research topic is due to the high prevalence of dental caries in children and the need to substantiate the choice of the most clinically effective methods of treatment of focal enamel demineralization of permanent teeth.

The degree of the development of the research topic

The epidemiology of dental caries in children is well studied in the works of foreign and domestic researchers. However, there are only single data on the frequency of occurrence and features of the clinic of the initial forms of dental caries – local enamel demineralization in permanent teeth in children. Detection and monitoring of WSL is performed visually, using vital staining, laser fluorescence, QLF and other methods. Non-invasive methods using fluorides (toothpastes, varnishes, gels, etc.) are most commonly used to treat WSL. New microinvasive methods of WSL treatment are being conducted using caries infiltration and amelogenin peptides. However, data on the results of noninvasive and microinvasive treatment methods are contradictory. In this regard, the actual direction of scientific search is to conduct a comparative study to justify the choice of the most effective methods of treatment of WSL in permanent teeth in children.

The purpose of the study:

To optimize the treatment of enamel demineralization of permanent teeth in children by justifying the choice of the most effective non-invasive and micro-invasive treatment methods.

Research objectives:

1. To determine the prevalence of local enamel demineralization in children 7-16 years of age.

2. To determine the peculiarities of the clinical course of WSL of permanent teeth in children.

3. To carry out treatment of WSL of permanent teeth in children using non-invasive methods (fluoride varnish, toothpaste with increased concentration of fluoride) and to determine their clinical efficiency.

4. To carry out treatment of WSL of permanent teeth in children with the use of

microinvasive methods (caries infiltrant, amelogenin peptide) and to determine their clinical efficiency.

5. To conduct a comparative evaluation of the results of treatment of WSL by non-invasive and micro-invasive methods according to laser fluorescence.

Scientific novelty of the study

A comprehensive study of the problem of local demineralization of enamel of permanent teeth in children was conducted for the first time. The high prevalence and intensity of WSL of permanent teeth in children aged 7-16 years have been determined, a direct correlation between the WSL indicators and the age of children, the state of oral hygiene, the DMF level and the presence of bite pathology has been revealed. The clinical characteristics of WSL of permanent teeth in children are presented for the first time, the features of lesions localization and depth in different groups of teeth are determined.

For the first time, a comparative assessment of the clinical efficiency of noninvasive and microinvasive methods of treatment of local enamel demineralization of permanent teeth in children was carried out. High clinical efficiency of toothpastes with increased fluoride concentration, fluoride varnish and caries infiltration method in children with WSL has been proved. High efficiency of amelogenin peptide in the treatment of WSL of permanent teeth in children has been established for the first time in clinical conditions. For the first time the efficiency of treatment of WSL of permanent teeth in children depending on the depth of the lesion according to laser fluorescence has been determined, the advantage of the caries infiltration method over other methods of treatment of initial and deep enamel demineralization has been proved.

Practical value of the research results

The revealed high prevalence of WSL of permanent teeth in children substantiates the necessity of timely detection and treatment of initial caries in childhood. On the basis of the obtained data the most effective methods of treatment of WSL of permanent teeth in children were determined. The gradation of treatment efficiency (recovery, regression, stabilization, progress) according to LF data has been developed, which will allow timely correction of WSL treatment methods and determine the terms of dispensary observation of children.

Methodology and methods of the study

The work was conducted in compliance with the basic principles of bioethics. Permission from the local ethical committee to conduct the study was obtained. Written voluntary informed consents were obtained from parents of children under 15 years of age and adolescents of 15 years of age to participate in the study. Methods of cross-sectional dental examination of children, clinical dental examination, methods of laser fluorescence to assess the condition of hard tissues of teeth, noninvasive and microinvasive methods of treatment of local enamel demineralization of permanent teeth were applied in the work. Statistical processing of the data included methods of descriptive statistics, comparative and correlation analysis.

Degree of reliability of the study results

The high degree of reliability of the revealed results is due to the representative volume of the conducted research (538 children were examined, WSL was detected in 4412 teeth, treatment was performed in 451 teeth), adequate statistical processing and careful analysis of the obtained data.

Approbation of the research results

Materials of the study were reported and discussed at regional, all-Russian and international scientific and practical conferences and congresses: Nizhnevolzhsky Dental Forum (Volgograd, 2017, 2018), Volga Dental Summit (Volgograd, 2020), Congress of the European Organization for the Study of Caries (ORCA, Sardinia, Italy, 2020), XIII, XIV All-Russian Scientific and Practical Conferences “Stomatology of Childhood and Prevention of Dental Diseases” (St. Petersburg, 2017, 2018), XV All-Russian Dental Forum Dental-Revue 2018 “Dental Education. Science. Practice” (Moscow, 2018), Jubilee All-Russian Scientific and Practical Conference with international participation ‘Actual issues of primary health care’ (St. Petersburg, 2018), 12th International Conference ‘Advances in the development of electronic systems’ (Kazan, 2019), VI Belarusian International Dental Congress (Minsk, Belarus, 2019), I All-Russian Medical Forum “CONSILIUM MEDICUM” (Volgograd, 2019), Scientific and Practical Conference with international participation “Topical issues of dental care for children” (Krasnodar, 2023).

The results of the study were discussed at a joint meeting of the Departments of Pediatric Dentistry, Therapeutic Dentistry, and Propaedeutics of Dental Diseases of the Federal State Budgetary Educational Institution of Higher Education “Volgograd State Medical University” of the Ministry of Health of the Russian Federation (FSBEI HE VolgSMU of the Ministry of Health of Russia).

Publications

On the subject of the dissertation research 12 scientific papers have been published, 2 of them in journals cited in Scopus, 3 in scientific journals recommended by the Higher Attestation Commission at the Ministry of Science and Higher Education of the Russian Federation.

Implementation into practice

The results of the study are implemented in the educational process of the Department of Pediatric Dentistry of the Federal State Budgetary Educational Institution of Higher Education of VolgSMU of the Ministry of Health of Russia, in the practical work of pediatric dentists and general dentists of the State Autonomous Establishment “Children's Clinical Dental Polyclinic No. 2” and the State Autonomous Establishment “Dental Polyclinic No. 8”. A textbook was published based on the study materials [46].

Personal contribution of the author to the conducted research

The author independently performed all stages of the dissertation work: analysis of modern literature sources, dental examination of children, treatment of WSL of permanent teeth in children in the study groups, dynamic observation of the children, evaluation, generalization and analysis of the obtained results, formulation of the main provisions, conclusions and recommendations, manuscript preparation.

Compliance with the scientific topics of the university. The dissertation research was carried out in accordance with the plan of scientific activity of FSBEI HE “Volgograd State Medical University” of the Ministry of Health of Russia within the framework of the scientific theme of the Department of Pediatric Dentistry “Modern methods of prevention and treatment of congenital and acquired pathology of the maxillofacial region”, R&D number 12092600037-3.

Compliance with the passports of scientific specialties. The scientific provisions of the thesis correspond to the passport of specialty 3.1.7. Stomatology, item. 1, Study of etiology, pathogenesis, epidemiology, methods of prevention, diagnosis and treatment of lesions of hard tissues of teeth (caries, etc.), their complications.

Structure and volume of the thesis

The work is set out on 123 pages of computer text, includes an introduction, literature review, three chapters of own research, conclusion, conclusions, practical recommendations, list of references, 26 tables and 43 figures.

Scientific statements submitted to the defense

1. The high prevalence and intensity of WSL in permanent teeth in children aged 7-16 years have been revealed. The intensity of WSL of permanent teeth increased with increasing age of children, as well as in children with poor oral hygiene, high level of DMF and bite pathology. According to laser fluorescence data, initial and deep demineralization of the enamel of permanent teeth in children was more frequent than the spread of demineralization to dentin.

2. The high clinical efficiency of non-invasive and micro-invasive methods of treatment of WSL in permanent teeth of children has been established. The use of laser fluorescence makes it possible to identify differences in the results of WSL treatment at different depths of demineralization, which can be assessed as recovery, regression, stabilization and progression of demineralization.

3. In the treatment of initial and deep enamel demineralization, according to the laser fluorescence data, the microinvasive method of single infiltration of caries was more effective as it significantly promoted enamel restoration more often than other treatment methods. Non-invasive methods of course application of fluoride varnish and fluoride-rich toothpastes gave better results than single use of amelogenin peptide.

Main scientific results

1. A cross-sectional study of children aged 7-16 years revealed a high (87.9%) prevalence of WSL. The number of teeth with WSL increased with increasing age of children. A direct correlation between the number of foci of enamel demineralization and the state of oral hygiene, the level of DMF, and occlusal pathology was revealed [26, p.45] (the author's personal contribution is at least 80%).

2. The use of non-invasive methods of treatment of WSL has shown high clinical efficiency (100% prevention of carious cavity formation) during 18 months of observation [27, p.67], [29, p.60], [47, p.88,96] (the author's personal contribution is not less than 80%).

3. High clinical efficiency of the use of microinvasive methods of treatment of WSL has been revealed: prevention of carious cavity formation in 100% when using caries infiltration, 98.3% when using amelogenin peptide [22, p.85], [23, p.77], [28, p.85], [42, p.24], [47, p.88,96], [160, p.17] (the author's personal contribution is not less than 80%).

4. The method of laser fluorescence is expedient to use in the process of treatment of enamel demineralization of permanent teeth in children to control the state of WSL [21, p.16,26], [23, p.77], [24, p.18,32,47], [25, p.18,32], [44, p.18] (the author's personal contribution is not less than 80%).

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1. The high prevalence and intensity of permanent teeth WSL in children aged 7-16 have been revealed. The intensity of WSL of permanent teeth increased with increasing age of children, as well as in children with poor oral hygiene, malocclusion and high level of DMF. According to laser fluorescence data, initial and deep demineralization of the enamel of permanent teeth in children was more frequent than the spread of demineralization to dentin.

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CHAPTER 1. THE PROBLEM OF LOCAL ENAMEL DEMINERALIZATION

1.1. Prevalence and risk factors of local enamel demineralization

Dental caries is one of the most widespread diseases in the world [35,43,48,83,89,136,137,193]. In Russia, the prevalence of dental caries in children 6 years old is 13%, 12 years old 71%, 15 years old 82% [34].

Despite the large number of publications on the prevalence of caries according to the World Health Organization (WHO) criteria, there are very few data on the frequency of the initial stages of the disease in the form of WSL. Usually, in epidemiologic surveys to assess the intensity of caries of permanent teeth, the WHO-recommended DMF index is used to record caries at the cavity stage, and carious lesions at the initial stage are not taken into account. The use of indices that record the initial forms of caries is uncommon, as it requires more time for examination, completion of registration cards and subsequent analysis. Nevertheless, data on the prevalence of initial carious lesions determined by the ICDAS (International Caries Detection and Assessment System) index are appearing more frequently in the literature [64,108].

Many authors have reported a high prevalence of WSL in permanent teeth in children [54,125,178,206]. According to Zaazou M.H. et al., 2023, the prevalence of caries in adolescents 15-18 years of age was 69.56% according to the DMF index, while the ICDAS-II, which took into account initial caries, was 78.29%. Almost 10% of those examined had initial forms of caries without cavitation lesions and required measures to remineralize WSL and prevent the formation of carious cavities [206].

Gudipaneni R.K. et al., 2022, showed that more than half (57.2%) of children aged 7-9 years had initial forms of caries in the first permanent molars [125]. In the study by Rozakova L.S. et al., 2020, an increase in the prevalence of initial carious lesions of the first permanent molars from 27.16% at the age of 6 years to 60.27% at the age of 8 years was found in children living in the city of Samara [54].

According to Abramova N.E. and Silin A.V., 2021, in St. Petersburg, in children aged 5-6 years caries in the initial stage occurred in 24.67% of cases, 12 years 24.57%, 15 years 38.71% of children [1]. Kuzmina E.M. et al., 2022, reported that in adolescents 12-17 years of age in the structure of lesions of tooth surfaces (according to the ICDAS index) from 63% to 70% are initial carious lesions [33].

The violation of the dynamic balance of demineralization and remineralization processes towards demineralization play the main role in the development of WSL [36,116]. The main factors leading to the disturbance of mineral metabolism are: plaque bacteria, carbohydrates (primarily sugars), the time of action of acids produced by bacteria on tooth enamel, and the susceptibility of dental hard tissues to pathogenic influences [36,101,119,159,180].

Many authors have shown in their studies that WSL occurs in places where plaque accumulates. Poor oral hygiene leads to plaque accumulation, formation of dental biofilm containing acidogenic bacteria, the most important of which are Streptococcus mutans, Lactobacilli, Candida albicans. The production of bacterial acids and their prolonged exposure to teeth causes the development of enamel demineralization, in which hydrogen ions from acid replace calcium ions and phosphates in hydroxyapatite crystals [62,97,148].

According to Bavykina T.Y. and Ovchinnikov I.V., 2023, the delay in the mouth of easily digestible carbohydrates, which are the substrate for the production of acids in dental plaque, contributes to various factors, which can include: features of the anatomical structure of teeth and oral mucosa, consistency of carbohydrates, time (frequency and duration of carbohydrate intake), the level of oral hygiene (presence of dental plaque), concomitant somatic pathology (diabetes mellitus, etc.) [9].

During orthodontic treatment, patients with dentoalveolar anomalies have additional areas of plaque adsorption, which increases the likelihood of WSL [93,138,202]. Sundararaj D. et al., 2015, showed that during treatment with fixed orthodontic appliances, the incidence of new carious lesions in the initial stage increased by 48% [189].

The prevalence of initial carious lesions in patients undergoing orthodontic treatment varies from 2% to 97%. Obviously, such heterogeneity in the figures is related to the methods used during patient examination: the smallest number of lesions is detected visually, while the largest number of lesions is detected using hardware diagnostic methods [85,87,94].

Patients with poor oral hygiene are at the highest risk of WSL formation during orthodontic treatment [93]. The first clinical signs of WSL in patients with poor oral hygiene may appear as early as one week after the start of orthodontic treatment [184]. The highest number of WSLs is detected in patients with braces and the lowest in patients with eliners [102].

Another important factor involved in the pathogenesis of WSL development is the frequent and indiscriminate consumption of easily digestible carbohydrates [130,180]. Easily digestible carbohydrates (sucrose, glucose, etc.) are fermented in the mouth by plaque microflora, resulting in the formation of organic acids (lactic acid, pyruvic acid, formic acid, etc.). The increasing concentration of acids on the enamel surface, changing the pH potential to the acidic side, has a demineralizing effect [36,66,90].

The longer cariogenic factors act on the enamel surface, the more organic acids, primarily lactic acid, accumulate. As acids accumulate in the biofilm, the pH level decreases to a critical level at which the boundary layer between enamel and biofilm becomes unsaturated and the acid partially demineralizes the surface layer of the tooth. The loss of minerals leads to increased porosity, expansion of spaces between enamel prisms and softening of the surface, which facilitates the diffusion of acids deeper into the hard tissues, leading to deeper demineralization [36,115].

Clinically, WSL is characterized by chalky, opaque stains that can be localized both in natural pits, fissures, cracks, and on smooth surfaces of teeth. As the process of demineralization progresses, the structure of enamel is disturbed, which eventually leads to the formation of a carious cavity. Foci of enamel demineralization have a white color due to the optical phenomenon arising from the loss of minerals in both the surface and subsurface layers, which causes a change in the refractive index and increases light scattering in the affected area, resulting in visual opacity of enamel [12,72].

In-depth scientific studies of mineral metabolism processes in tooth enamel have led to the conclusion that caries at the stain stage is a reversible process. This allowed the development of noninvasive and microinvasive approaches to the treatment of initial caries, aimed at restoring the form, function, and aesthetics of teeth with minimal or no removal of demineralized tissues [40,117].

1.2. Diagnostic methods of local enamel demineralization

All methods of WSL diagnosis can be divided into traditional (visual inspection, tactile diagnosis and radiography) and new modern technologies that help to evaluate carious lesions not only qualitatively, but also quantitatively [70].

The most common and simplest method of detecting the initial forms of caries is the visual method, in which the surface under examination is cleaned, isolated from saliva, dried, and visually evaluated. This method is subjective and uninformative, but it is considered acceptable in everyday clinical practice [10,122,129].

For visual assessment of carious lesions, the ICDAS index, developed by a group of authors in 2002, is currently the most informative caries diagnostic system [108,113]. The ICDAS index is a two-digit coding, the first digit of which denotes the presence and condition of the restoration, and the second digit denotes the stage of the carious process. An examination of all tooth surfaces is performed. Assessment of the condition of dental hard tissues according to the ICDAS index includes three main steps: 1) detection of carious lesions; 2) assessment of the stage of the carious process; 3) assessment of caries activity. Local demineralization of enamel, according to ICDAS criteria, is defined by the following codes: 1 – the first visible changes in enamel (visible only after prolonged air drying or visible changes in enamel that do not extend beyond the fossa or fissure); 2 – obvious visible changes in enamel without the presence of a cavity. Also, this index takes into account the activity of the carious process and according to these two stages are identified: active – matt, chalky spots with a rough surface; stabilization stage – pigmented spots with a dense, shiny surface. However, in practical dentistry this index is used quite rarely. According to Butvilovsky A.V. et al., 2018, the use of binocular loupe increases the sensitivity, but not the specificity of this method, compared to conventional visual examination [14].

A special method used to diagnose caries in the initial stage was proposed by Aksamit L.A. in 1978 – the method of vital staining of enamel using a 2% aqueous solution of methylene blue. This method is based on the increase of permeability in the lesion focus and allows to judge not only the fact of the presence of WSL, but also the depth of the lesion. The intensity of staining is evaluated on a 10-point scale and, according to this, 3 degrees of staining can be distinguished: low, medium and high. The method of vital staining also allows differential diagnosis between caries and non-carious lesions (fluorosis, hypoplasia), which cannot be stained [13].

The gold standard of additional diagnostics is radiological examination, which can help detect initial foci of enamel demineralization on the contact surfaces of teeth that are inaccessible to the clinician's eye. However, WSL on the vestibular, oral, and occlusal surfaces will go unnoticed on radiographs [11,144,191].

More informative methods of WSL diagnostics are hardware methods, which have a number of advantages, as they allow detecting earlier stages of the disease, are objective and can control the dynamics of the disease [3,19,67,123]. However, modern hardware methods of WSL diagnosis are rarely used in dental practice [21].

Since 1970, the method of Fiber-Optic Trans-Illumination (FOTI), which is based on the change of light refraction in the affected tissues due to the reversal of their density, has been used in practice for the detection of WSL. The use of new digital technologies allowed to obtain an image of the lesion on the computer screen – the method of Digital Imaging Fiber-Optic Transillumination (DIFOTI). Instead of visible light, near infrared light can be used in transillumination technology – Near infrared digital imaging transillumination (NIDIT). In transillumination, the initial carious lesions have the appearance of dark foci, which allows to detect the presence and size of WSL. According to Pellicioni G.A. et al., 2021, NIDIT requires less examination time and gives more accurate results than the use of radiography [168]. However, fiber optic transillumination methods FOTI, DIFOTI, and NIDIT do not provide information about the depth of the lesion [68].

The QLF method – light-induced fluorescence – is based on the assessment of the fluorescence of the dental hard tissue using an LED activator. The method is based on the fluorescence of porphyrins (products of pathogenic microflora). The ratio of fluorescence intensity in the red and green regions of the spectrum is used to assess bacterial activity and the degree of enamel damage. Quantitative light-induced fluorescence allows estimating the amount of demineralization and monitoring the dynamics of WSL changes [67,164]. A study by Maslak E. et al., 2019, reports the successful application of QLF to assess the outcomes of treatment of initial caries of permanent teeth in children [160]. The successful application of QLF to evaluate the results of remineralization therapy is also reported by A.V. Akulovich et al., 2024 [5]. The informativeness and accuracy of the QLF method is significantly higher than visual examination and other methods of detecting initial caries [17,141,169,190,205].

When the balance of de- and remineralization is disturbed, the electrical conductivity (and resistance) in the lesion is also disturbed. This principle is the basis for the electrometric method of diagnosis using the Electronic Caries Monitor (ECM), which can be used to determine the depth of the carious process - initial caries, enamel caries and dentin caries. However, convincing evidence of the value of using ECM in real clinical conditions is insufficient [153]. According to Gran'ko S.A. et al., 2017, the method has low diagnostic informativeness [17].

Luminescence diagnostics is also used to detect WSL. Under the influence of ultraviolet light, the hard tissues of the tooth have the effect of luminescence. In this case, completely healthy enamel gives a bright blue glow when examined, while areas of initial caries are detected as darkening. The method of luminescence diagnostics allows only detecting lesions, but not assessing their depth [17].

Changing the infrared spectral range is at the heart of the laser fluorescence method. The diagnosis uses a pulsed light flux emitted by a laser diode, red light spectrum with a wavelength of 655 nm and a peak power of 1 mW. Using a light guide, the flux is delivered to the pre-cleaned and dried tooth hard tissues. Returning through the light guide to the photodetector on the appliance, they are analyzed by the electronics of the apparatus. Based on the fluorescence value, a score (from 0 to 99) is assigned to the focus, depending on the depth of the lesion. The laser fluorescence technique allows not only initial diagnosis of the affected enamel areas, but also dynamic observation of how the depth of the WSL area changes during treatment [6,17,24,25,67,98]. Numerical indicators of the scale from 0 to 14 correspond to normal enamel structure (including hypomineralized areas), from 15 to 25 - to caries within enamel, and indicators 21-90 - to caries within dentin [152]. However, the criteria for evaluating laser fluorescence values on different tooth surfaces may differ. It has been suggested that the values of the indices for healthy enamel should be evaluated as 0-4, 0-13, 0-14, or 0-15, enamel demineralization 14-20, 15-21, or 16-25, demineralization of the outer half of enamel 5-10, inner half of enamel 11-18, and dentin demineralization more than 18, 21, 22, or 25 [177]. Another study showed that laser fluorescence values for caries in the stain stage corresponded to 9.0±2.0, superficial caries to 15.0±3.0, and medium caries to 50.0±30.0 [20].

To assess the depth of demineralization of hard tissues on the vestibular surface of teeth, Almosa N.A. et al., 2014, suggested using the following laser fluorescence indices to evaluate the state of enamel: healthy enamel – 0-13, initial enamel demineralization - 14- 20, deep enamel demineralization – 21-29, enamel demineralization extended into dentin – 30 and more [75]. The difference in the numerical indices characterizing the state of tooth tissues in different authors is explained by the different degree of initial mineral maturity of the diagnosed tooth surfaces.

The use of laser fluorescence method had higher sensitivity and accuracy compared to other traditional methods of enamel caries detection (visual, intraoral video camera, tactile, radiographic) [208].

According to studies by Melekhov S.V. et al., 2015, laser fluorescence diagnostics was 25% more effective than vital staining of demineralization foci with 2% methylene blue [49]. In addition, laser fluorescence can be successfully used to assess remineralization of initial carious lesions [44,177].

Based on in-vitro data, Iranzo-Cortés J.E. et al., 2017, recommend combining ICDAS and laser fluorescence criteria for better diagnosis of WSL, as the laser fluorescence method has higher sensitivity and ICDAS has higher specificity [133].

Many new technologies for WSL diagnosis are under development and validation, which require further clinical validation: AC impedance spectroscopy, terahertz imaging method, ultrasonic caries detector, optical coherence tomography, infrared thermography, laser modulation photothermal radiometry, laser-induced breakdown spectroscopy, laser optical-acoustic spectroscopy, dye-enhanced QLF, and others [67,68,98].

Modern hardware methods may eventually utilize artificial intelligence to more accurately diagnose WSL [70].

Thus, dentists are currently faced with the task of selecting a diagnostic method for WSL from a wide range of options, including both traditional and innovative methods for diagnosing initial caries. At the same time, it should be remembered that hardware diagnostic methods can be a useful addition to visual methods of WSL diagnosis [46]. According to Mirsalikhova F.L. and Khamroeva D.Sh., 2022, the most effective is a comprehensive approach to the diagnosis of WSL, which consists of a combination of several diagnostic methods, including hardware methods [50]. In addition, according to Lopes P.C. et al., 2024, the method of WSL diagnosis does not affect the choice of treatment method, and treatment results do not depend on the method of diagnosis [150].

1.3. Methods and results of treatment of local enamel demineralization

Since the balance of de- and remineralization processes in the direction of demineralization is disturbed in WSL, the treatment is primarily aimed at creating conditions for changing the vector of enamel metabolic processes in the direction of remineralization. For this purpose, based on the ecological theory of caries development, cariogenic factors are eliminated. It is recommended to control the nutrition of children (limiting the use of easily digestible carbohydrates, providing the necessary number of vitamins and minerals) [77,130,132].

To eliminate the effects of cariogenic plaque bacteria, a complex of individual oral hygiene is prescribed (toothpastes, rinses should contain fluorides) and regular professional cleaning of teeth [131,143,145,157,158,195]. Normalization of oral hygiene is one of the most important components of WSL treatment [203].

Along with the elimination of cariogenic factors, therapy aimed at restoring (remineralization) the affected areas of enamel is used. The results of treatment will depend on many factors, including the patient's compliance with dietary and oral hygiene recommendations, the degree of caries intensity, and the level of tooth enamel resistance [4]. Currently, there is a huge range of WSL treatment methods available, which can be categorized into non-invasive and micro-invasive [10,57,150].

Non-invasive methods of WSL treatment include remineralization therapy with fluoride, calcium, phosphate, silver and other microelements, ozone, laser, etc. [16,39,56,60,71,139]. Microinvasive methods include caries infiltration and application of amelogenin peptides [11,30,63,65,74,91,96,135].

It is noted that the results of remineralizing therapy for WSL depend on the activity of the carious process [18,59]. In addition, the degree of enamel demineralization should be taken into account when choosing a drug for the treatment of WSL in unformed permanent teeth in children [59]. Butvilovsky A.V. et al., 2016, based on questionnaire data, found that the choice of treatment method for initial caries in children depends on the length of service of a dentist [14].

The use of fluorides is recommended for the prevention and treatment of dental caries by the World Health Organization and international dental organizations [52,163, 192]. Long-term experience in the use of fluorides has proven their clinical efficacy and safety [174,194,198,209]. Fluorides can be used in the form of toothpastes, varnishes, gels, solutions, foams, films and fluoride-releasing devices [52,53,61,121,173,198].

Fluoride toothpastes have been used for more than 80 years. More than 370 randomized clinical trials have been conducted to evaluate their clinical efficacy. The pastes may contain various fluoride compounds: sodium monofluorophosphate, sodium fluoride, aminofluorides, aluminum fluoride, tin fluoride and others. Most of the works prove the effectiveness of fluoride pastes in the prevention of carious lesions [2, 172,100,103,105]. Increasing the concentration of fluoride in toothpastes increases their anti-carious activity [195].

Under experimental conditions, it was shown that pastes with high fluoride content (2800 and 5000 ppm) promoted enamel remineralization and inhibited the demineralization process more effectively than pastes with 1450 ppm F, fluoride-free and calcium-containing toothpastes [107]. Staun Larsen L. et al., 2018, found that regular exposure to 5000 ppm fluoride increased the concentration of fluoride ions in saliva and biofilm 3.5 times more, compared to fluoride concentration of 1500 ppm [188].

Toothpaste with 5000 ppm fluoride concentration showed 16% and 35% better results in improving WSL after 3 and 6 months of use, compared to toothpaste containing 1100 ppmF- ($p<0.001$) [82]. Yeung A., 2014, obtained similar findings in a similar study when comparing the effects of toothpastes containing 5000 ppm and 1350 ppm fluoride ions [204]. However, clinical studies confirming the value of toothpastes with high fluoride concentration in the treatment of WSL are scarce [41].

Fluoride varnishes (2-4 applications per year) have proven effective in reducing the incidence of dental caries in both deciduous and permanent teeth [157,158,196]. According to a meta-analysis, the use of varnish containing 5% sodium fluoride led to remineralization of 63.6% of demineralization foci [121].

The advantages of fluoride varnishes over other topical fluorides are the protection of enamel in the absence of patient compliance and the continuous release of fluoride ions over a long period of time [79]. The advantage of using fluoride varnishes, compared to toothpastes, is to reduce the need for patient compliance. According to Zabokova-Bilbilova E. et al. 2014, the use of fluoride varnish resulted in a 44.3% decrease in enamel demineralization in patients undergoing orthodontic treatment [207]. However, the use of fluoride varnish was effective only if patients demonstrated excellent oral hygiene [170].

In a study by Restrepo M. et al., 2015, the advantage of fluoride varnish in the control of WSL was shown compared to the effect of a gel containing 2% chlorhexidine [179]. However, the use of rinsing and application of 0.01% chlorhexidine solution in addition to fluoride remineralizing therapy improves the results of treatment of WSL localized on the smooth surfaces of teeth by 27.5% [50].

According to Skripkina G.I. et al., 2024, twofold (with an interval of 2 weeks) application of fluoride varnish containing sodium fluoride, calcium fluoride and aminofluoride in children 6-12 years old for the treatment of WSL in unformed teeth after 6 months resulted in a 15.5% decrease in the electrical conductivity of enamel in the area of demineralization. When using a similar preparation for deep fluoridation (containing fluoride, copper, magnesium ions and calcium hydroxide), the electrical conductivity of enamel in the demineralization area decreased by 73%, and by 80% when using a three-component gel containing calcium, phosphate and fluoride ions [59].

Meanwhile, Güçlü Z.A. et al., 2016, in their study showed that four times weekly applications of 5% sodium fluoride solution did not lead to remineralization of the lesion site, as indicated by laser fluorescence values, whereas the application of fluoride varnish in combination with CPP-ACP led to restoration of the WSL site [124].

According to Höchli D. et al., 2017, fluoride varnish is the most effective in remineralizing WSL compared to other preparations, but further clinical studies are required to confirm this conclusion [128]. A review by Fernández-Ferrer L. et al., 2018, also states that only 5% fluoride varnish is effective in remineralizing WSL [118].

A number of authors have shown the effectiveness of deep fluoridation in remineralization of initial carious lesions. Performing the procedure every 2 weeks for a year led to the restoration of WSL sites in patients with good oral hygiene, while the results were much worse in patients with poor oral hygiene [61].

Despite the large number of works confirming the effectiveness of professionally applied fluorides in the treatment of WSL in permanent teeth, a number of authors believe that these preparations have no significant advantages over conventional oral hygiene with fluoride toothpaste [104].

Results of in vitro studies have shown positive results of toothpastes that contained arginine, enzyme, hydroxyapatite or other calcium preparations in addition to fluoride (1450ppm) for remineralization of carious changes in tooth enamel [80,84,165]. In an in-vitro study, toothpastes with hydroxyapatite and 500 ppm fluoride have been shown to be equally effective in remineralizing WSL [76]. However, clinical evidence of the efficacy of these toothpastes in the treatment of WSL is insufficient.

Proteins statherin and proline, being in saliva, bind and stabilize biologically available ions of calcium and phosphate, which support the process of remineralization of enamel. This is the basis of the principle of action of preparations based on milk casein – casein phosphopeptide amorphous calcium phosphate. Many studies have shown that topical application of CPP-ACP for the treatment of natural and postorthodontic foci of demineralization is effective, but current data on the clinical efficacy of the preparations are contradictory [76].

Flynn L.N. et al., 2022, found that applications of CPP-ACP-containing varnish every 4-6 weeks for a year did not prevent new WSLs in 43% of orthodontic patients [120]. According to the meta-analysis by AlBuraiki O.B. et al., 2024, the results of WSL treatment with this preparation did not have statistically significant differences compared to the control, so further studies are needed to confirm the clinical effect of CPP-ACP in restoring demineralized enamel areas [73]. The synergistic effect of fluoride and CPP-ACP is also currently controversial. Some authors have shown that daily twice-daily topical application of 10% CPP-ACP paste combined with fluoride-containing toothpaste for tooth brushing significantly improved the appearance and remineralization of demineralization foci [124].

Other authors found that the use of CPP-ACP in addition to twice daily brushing with fluoride toothpaste had no advantage in remineralizing lesions [185]. The conflicting results of the CPP-ACP studies may be due to differences in study design, different lesion severity, differences between post-orthodontic foci and so-called natural foci, and different study durations.

The use of probiotics is considered to be a promising method for the treatment of dental caries, including its initial stages, but clinical studies on this topic are scarce [117].

The use of enamel whitening has been suggested to address the problem of white spots. However, it is more about masking rather than treating WSL. Kim Y. et al., 2016, in an in-vitro study concluded that bleaching of artificially created foci of demineralization with 10% carbamide peroxide leveled the differences between healthy and affected enamel without deterioration of chemical and mechanical properties [142]. However, enamel bleaching is not used in children, and in adults, bleaching can be used to treat inactive lesions in the presence of good oral hygiene [126].

The use of different laser modifications for the treatment of WSL is discussed. It has been shown that laser irradiation improves the results of WSL treatment with the use of various remineralization preparations [69,156]. Other authors believe that laser application in addition to remineralizing fluoride toothpaste does not improve the restoration of the enamel demineralization site [114]. The use of laser for the treatment of WSL has no independent value.

Microabrasion is a more invasive method of treatment for WSL and has insufficient evidence for use in children [86,186].

There are reports on the successful use of ozone for the treatment of WSL, but its isolated application, without the use of remineralizing drugs, is not effective enough [51].

In 2007, scientists Meyer-Luckel H. and Paris S. developed the concept of microinvasive treatment - infiltration of initial carious lesions of teeth (Infiltration concept). It consists in removing the poorly permeable pseudointact enamel layer from the carious lesion surface using 15% hydrochloric acid, followed by its dehydration with ethanol and infiltration with a high-flow polymer [161]. According to the data of a controlled randomized clinical trial conducted by the authors of this technique, after three years of observation, only in one of 26 (4%) cases of WSL treatment, the progression of the carious process was observed radiographically, which indicates the effectiveness of this method.

Multilevel analysis of the enamel microstructure of demineralization foci confirmed the validity of the caries infiltration method [15].

Numerous clinical studies have confirmed the efficiency of the caries infiltration method in the treatment of WSL of primary and permanent teeth [31,42,55,155]. Caglar E. et al., 2015, showed the effectiveness of the infiltration method in the treatment of WSL: after four years of observation in 100% of cases there was no progression of the carious process [96].

A systematic review published by a group of authors Chatzimarkou S. et al., 2018, proves that the progression of proximal initial carious lesions in permanent teeth is less likely after infiltration treatment compared to oral hygiene instructions for 18 months to 3 years [99].

In vitro and in vivo studies have shown the ability of the infiltration method to mask WSL. The extent to which the white spots become less visible depends on the depth of the lesion. Treatment is more effective in the early stages and depends on a number of factors: time of appearance, localization and color of the lesion. Thus, the longer the stain exists, the less pronounced the aesthetic effect. Better aesthetics can be achieved by treating stains in the equatorial area than in the vestibular areas. The maximum visual effect is observed in the treatment of white spots as opposed to pigmented spots [58].

According to Puleio F. et al., 2022, the caries infiltration method is more effective and predictable in aesthetic improvement of carious lesions in the white spot stage than remineralization and microabrasion [176].

During odontogenesis, enamel formation is controlled by proteins that serve as a matrix for mineral adsorption. These proteins are completely reduced after the completion of histogenesis. This phenomenon is the basis for a method that involves artificially injecting proteins onto damaged enamel areas [7,109,149,197].

A study conducted by Alkilzy M., Tarabaih A., 2018, demonstrated the efficacy of P 11-4 peptide in combination with fluoride varnish as a non-invasive treatment for WSL [74].

Doberdoli D. et al, 2020, also in their study demonstrated the efficacy of peptides combined with fluoride varnish in the treatment of WSL [110]. A meta-analysis by Xie Z. et al., 2023, showed that caries infiltration or peptides combined with fluoride varnish was most effective in the treatment of WSL [200].

At the same time, a study by Attea M. et al, 2023, using ICDAS and laser fluorescence data, showed no significant advantages of using P11-4 peptide and nanosilver fluoride over 5% fluoride varnish in the treatment of patients with initial caries of permanent teeth [78].

A comparative study (meta-analysis) of the results of treatment of WSL with CPP-ACP, whitening, films, gels and varnishes with low and high fluoride concentrations, composite infiltration, toothpastes with bioactive glass, miswak and traditional oral hygiene revealed that the greatest effectiveness of treatment was with fluoride films and varnishes [128]. Nevertheless, further development of biomimetic preparations (based on peptides, milk casein, crustacean shell, etc.) for mineralization of demineralized enamel areas continues to develop and is considered a promising area of research [151]. New directions of research aimed at finding polymers, functional inorganic and organic materials that will improve the remineralization of WSL are presented in the review by Xu J. et al., 2022 [201]. Application of a gel containing xylitol and calcium, phosphorus, and magnesium compounds resulted, according to QLF data, in a 19-100% reduction of the white spot area with bacterial activity; the average loss of mineral components decreased from 18% to 6.8% [5].

Currently, a large number of natural preparations are available that can inhibit cariogenic microflora, inhibit demineralization and potentiate remineralization of WSL. These include preparations based on chitosan, bitter chocolate (theobromine), ginger, Chinese gall, honey, cinnamon, green tea [184]. However, their clinical efficacy requires confirmation.

There is also insufficient evidence of the effectiveness of WSL treatment using cold plasma, xylitol, bioactive calcium and glass preparations [184].

It should be noted that in real dental practice, doctors rarely use modern methods of treatment of WSL. According to our data, the caries infiltration method was used only in one third (31.8%) of dental clinics in a million-strong city, ozone treatment - in 6.8% of clinics, while fluorides in various forms were used in 93.1% of dental clinics [21].

Thus, a large number of different methods are currently proposed for the treatment of WSL, but the data on the results of their application are contradictory, which may be a barrier to their introduction into widespread dental practice.

All of the above substantiates the relevance of the topic of this study aimed at optimizing the treatment of focal enamel demineralization of permanent teeth in children.

CHAPTER 2. MATERIAL AND METHODS OF THE RESEARCH

2.1. Study design and material

The study is of an applied nature and is aimed at improving the efficiency of treatment of local enamel demineralization in children aged 10-16 years. The study design (Fig. 1) was agreed and approved by the Regional Ethical Committee; protocol No. 2098-2017 dated January 20, 2017. Written voluntary informed consent for participation in the study was obtained from children 15-16 years of age and from the legal representatives of children under 15 years of age.

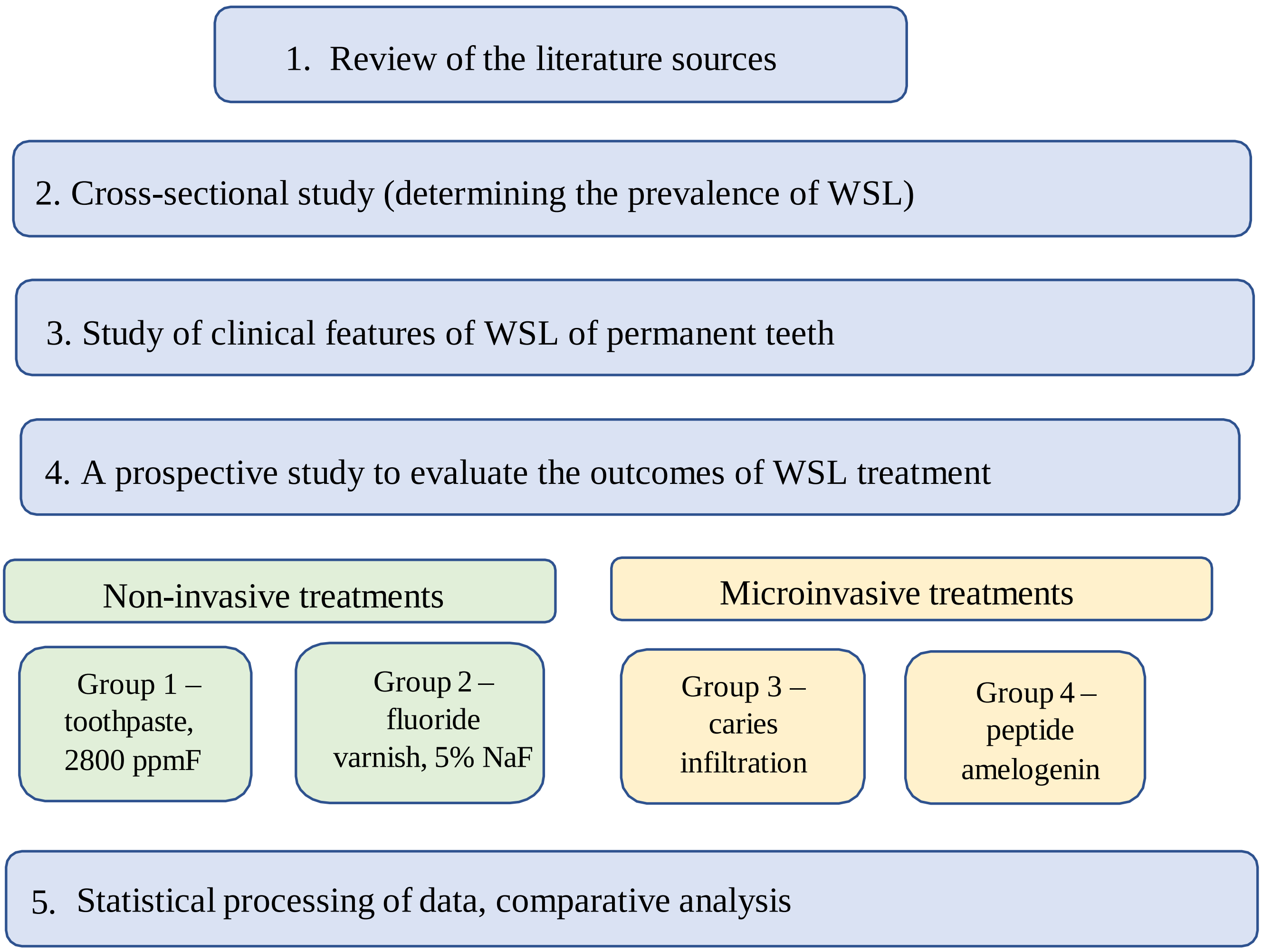

Figure 1 – Study design

The study was conducted in 5 stages. At the first stage, literature sources were analyzed to assess the current understanding of the problem of initial dental caries in children. The data of scientific literature on the prevalence of WSL, risk factors of development, methods of diagnosis and treatment, effectiveness of treatment of local enamel demineralization were considered.

Critical analysis of the literature data (209 sources) allowed us to identify unresolved problems in the chosen scientific direction and confirm the relevance of the research topic.

At the second stage, a cross-sectional study was conducted, which included dental examination of 528 children aged 7-16 years. The children were examined in school dental offices of two Municipal Educational Institution Secondary Schools (MEI SS) in Volgograd city (MEI SS No. 76 of the Krasnooktyabrsky District and MEI SS No. 14 of the Tractorozavodsky District). After the standard dental examination of children, the DMF, state of oral hygiene, and presence of malocclusions were recorded. WSL was detected visually after cleaning the teeth from plaque and drying the surface with an air jet. The prevalence of WSL (%) and the average number of teeth with WSL were determined. We evaluated the WSL indicators depending on the age of children, the level of DMF, oral hygiene and the presence of malocclusions. A total of 4412 teeth with WSL were examined.

The third stage of the study determined the clinical features of WSL of permanent teeth in children: the frequency of lesions in different groups of teeth of the upper and lower jaw, the distribution of demineralization foci according to the depth of lesions, and the determination of the average values of laser fluorescence depending on the localization of WSL.

During the fourth stage of the study, an open prospective randomized clinical trial was conducted to determine the efficiency of various methods of treatment of WSL. The clinical work was carried out on the basis of the Department of Pediatric Dentistry of FSBEI HE VolgSMU of the Ministry of Health of Russia in the State Autonomous Establishment “Children's Clinical Dental Polyclinic No. 2”. The study included 45 patients aged 10-16 years in parallel groups, in whom 451 teeth with WSL were treated. Inclusion criteria were the following:

- presence of local enamel demineralization in permanent teeth (clinically confirmed diagnosis: Caries enamel K02.0, ICDAS-II code 1.2);
- age 10-16 years;
- 1-3 general health group;
- written voluntary informed consent of the legal representative of a child aged 10-14 years / adolescent 15-16 years to participate in this study;

Non-inclusion criteria were:

- age below 10 and above 16 years of age;
- 4-5 groups of general health;
- non-carious lesions of teeth (amelogenesis disorders, molar-incisal hypomineralization, erosion, etc.);
- belonging to socially unprotected groups (orphans, children under guardianship, etc.);
- absence of written voluntary informed consent of the legal representative of a child aged 10-14 years / adolescent 15-16 years to participate in this study.

Exclusion criteria were:

- refusal of the patient (parents) to participate in this study at any stage;
- patient's failure to appear for the next examination.

All children in the study were taught oral hygiene and healthy eating habits, and all children were advised to brush their teeth daily 2 times a day with a toothpaste containing fluoride 1400-1500 ppmF^-.

Four groups were formed among the study participants, comparable in age and sex of children. In groups 1 and 2, noninvasive methods of treatment of WSL were applied: toothpastes with fluoride content of 2800 ppmF^- were used in group 1 (14 people, 138 WSLs), fluoride varnish with 5% NaF was used in group 2 (15 people, 155 WSLs). In groups 3 and 4, microinvasive methods of treatment of WSL were applied: caries infiltrant was used in group 3 (15 people, 99 WSL), amelogenin peptide was used in group 4 (8 people, 59 WSL). The control group was not formed for ethical reasons, since dental disease (WSL) in children should not be left untreated even for a short period of time.

Dynamic observation of the children of the study groups was carried out for 18 months. Examination and registration of the patients' dental status were carried out every three months.

The fifth stage of the study included statistical processing of the obtained data and comparative analysis of the results.

2.2. Methods of cross-sectional study

Cross-sectional dental examination of 528 children aged 7-16 years was carried out. Children were examined using a standard set of dental instruments under artificial light. The presence of carious cavities and fillings, absence of teeth extracted due to caries complications were recorded. The type of bite (physiologic or pathologic) was determined. The state of oral hygiene in children was determined according to the OHI-S index (Oral Hygiene Index-Simplex, simplified oral hygiene index) proposed by J.C. Green and J.K. Vermillion.

The prevalence of caries in permanent and primary teeth was determined according to WHO criteria as the percentage of children with at least one carious, filled or extracted tooth in relation to the total number of children examined. The caries intensity of primary and permanent teeth in each child was assessed using the dmf and DMF indices (DMF+dmf for mixt dentition), which reflect the sum of carious, filled, and extracted teeth in one child. A DMF level of 1-4 was considered low, 5-8 was considered medium, and >8 was considered high.

After cleaning teeth from plaque and drying the surface with an air jet from an air gun, visual detection of local demineralization of permanent teeth (initial caries, caries in the stain stage, codes 1 and 2 according to the ICDAS-II index, enamel caries according to the 10th revision of the International Classification of Diseases was performed.

Based on the results of the examination of children, the prevalence and intensity of caries according to WHO criteria and the prevalence and intensity of WSL according to ICDAS-II criteria were calculated. WSL indicators were evaluated depending on the children's age, level of DMF, oral hygiene status and presence of malocclusion. Clinical characteristics of the distribution of WSL in permanent teeth in children were determined.

2.3. Methods of diagnosis and evaluation of enamel demineralization

In this prospective study, the results of primary visual diagnosis of WSL were confirmed by the method of vital staining and laser fluorescence. The laser fluorescence method was used to evaluate the results of WSL treatment in the dynamics of the study.

Visual method of diagnostics allows to determine the presence of WSL and the severity of the demineralization process. The method consists in cleaning the tooth surface, isolation from saliva, drying, visual assessment of enamel condition. Signs of WSL are lack of shine and matte areas of enamel.

To assess the severity of carious lesions of permanent teeth, the international caries diagnosis and assessment system ICDAS-II was used. Codes and criteria for evaluation of carious lesions: 0 – healthy tooth enamel (light transparent tooth enamel); 1 – first visible changes on tooth enamel (white spots can be detected only after drying); 2 – clear visible changes on tooth enamel (without disturbance of enamel integrity); 3 – localized enamel destruction (carious lesion within the enamel); 4 – carious dentin in the form of darkening translucent through demineralized enamel (enamel surface with or without violation of integrity); 5 – carious cavity in the middle layers of dentin, with visible softened dentin; 6 – carious cavity made by softened dentin with destruction of the tooth crown and involvement of the tooth pulp in the inflammatory process. The prospective randomized clinical study included teeth with ICDAS-II codes 1 and 2, which corresponded to local demineralization of tooth enamel (Fig. 2).

The method of vital staining was used for differential diagnostics of WSL and non-carious lesions of tooth enamel. The method of Aksamit L.A. was used [36]: cleaning of the investigated tooth surface from dental plaque, isolation from saliva, air drying, application of a tampon with dye (2% methylene blue solution), exposure for 3 minutes, removal of the tampon and washing off the dye residue with water.

a

b

Figure 2 – Local enamel demineralization (enamel caries) of upper jaw incisors, ICDAS-II codes: a - code 1, b - code 2

The intensity of staining of the studied enamel area was evaluated on a 10-point scale of blue color. Absence of staining indicated the absence of enamel demineralization process. The staining of the study area confirmed the presence of WSL (Fig. 3).

Figure 3 – WSL staining with methylene blue solution

The laser fluorescence (LF) method was used to diagnose the state of enamel and estimate the depth of the demineralization focus using the DiagnoDent pen device (KaVo, Germany) [24,25]. The device is based on the principle of laser fluorescence. It uses a source with a 655 nm laser diode and a power of 1 mW. The light is transmitted through a downward optical fiber to a probe. The probe is placed close to the surface to be measured, illuminating it with laser light. Healthy and pathologically altered tooth tissue reflects light waves of different wavelengths, which are recorded and the device produces different numerical values. Methodology of LF method application: tooth surface is cleaned from plaque, isolated from saliva using cotton rollers, dried, then a sensor is brought to the investigated area of the tooth and the digital board reflects the study data in the form of a digital indicator (Fig. 4).

a b

Figure 4 – Diagnosis of enamel condition by laser fluorescence method: a – WSL of upper incisors; b – DiagnoDent pen readings

The sensor is shaped like a dental probe, which allows the entire tooth surface topography to be examined. The depth of local demineralization is reflected by digital values of the device. To interpret the LF device values, we used the classification of Almosa N.A. et al., 2013 [75]: LF values 0-13 corresponded to healthy enamel, 14-20 - initial enamel demineralization; 21-29 - deep enamel demineralization, 30 and more – enamel demineralization extended into dentin (Fig. 5).

a b

c d

Figure 5 – Application of LF to assess the state of enamel: a – LF=6, healthy enamel, b - LF=15, initial enamel demineralization, c – LF=24, deep enamel demineralization, d – LF=32, enamel demineralization extended into dentin.

The LF method was used not only as a primary diagnosis of WSL, but also to evaluate the results of treatment. Repeated diagnostics to assess changes in the depth of the demineralization focus was performed after 3, 6, 9, 12, 15 and 18 months.

2.4. Methods of treatment of local enamel demineralization

Non-invasive treatments

✓ **Toothpastes with increased fluoride content** (2800 ppmF^{-}) were used in courses of one month, for a total of 4 courses per year, 2 months apart. In the study we used Colgate Duraphat 2800 ppmF^{-} toothpaste containing sodium fluoride, mass fraction of fluoride - 0.28% (Fig. 6).

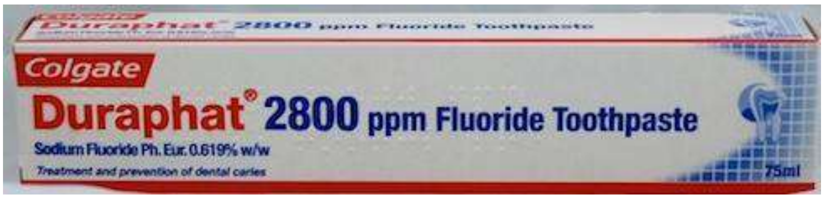

Figure 6 – Toothpaste with increased fluoride content

Patients were advised to use toothbrushing paste twice a day (morning and evening) according to the instructions provided by the manufacturer: apply a 1 cm strip of paste on the bristles of the toothbrush during each brushing; each brushing should be at least 2 minutes; paste residue should be spit out. It was also recommended not to drink or rinse the mouth for 30 minutes after brushing.

✓ **Fluoride varnish** was applied once every three months, the course of treatment included 3 treatments every 1-2 days, for a total of 4 courses per year. Colgate Duraphat natural rosin-based fluoride varnish containing 5% sodium fluoride or 2.26% fluoride ion (22600 ppmF^{-}) was used. The varnish, according to the manufacturer's instructions, was applied to clean and slightly moist tooth surfaces with a brush (Fig. 7). Rosin-based varnish hardens on contact with saliva and forms a thin film on the tooth surface.

a b

Figure 7 – Application of fluoride varnish: a – varnish containing 22600 ppmF$^-$; b – application of varnish to teeth

The yellowish color of the varnish allows visual control of its distribution on the surface. Since the effectiveness of the preparation depends on the duration of fluoride action, patients were advised not to eat solid food and not to brush their teeth for 4 hours after the procedure.

Micro-invasive treatments

✓ **Caries infiltration** was performed using the Icon set (DMG, Germany) in accordance with the manufacturer's instructions (Fig. 8). The treatment procedure consists of removal of the poorly permeable pseudointact enamel layer from the surface of the demineralization focus, its dehydration and infiltration with a high-flow polymer material.

Figure 8 – Caries infiltration set

The caries infiltration procedure was performed according to the following protocol: 1) hygienic cleaning of teeth with brush and paste; 2) isolation of the working field with liquid cofferdam; 3) application of Icon-Etch for 2 minutes; 4) rinsing with water for 30 seconds, air jet drying; 5) drying with ethanol (Icon-Dry) for 20 seconds; if necessary, repeating points 3-5 two more times; 6) application of flowable infiltrant (Icon-Infiltrant) for 3 minutes, removal of excess, curing 40 seconds; 7) reapplication of flowable infiltrant (Icon-Infiltrant) for 1 minute, removal of excess, curing 40 seconds; 8) polishing with finishing discs (Fig. 9).

✓ **Application of amelogenin peptide** (InnoDent Repair, Bachem AG, Switzerland) was performed according to the manufacturer's instructions (Fig. 10).

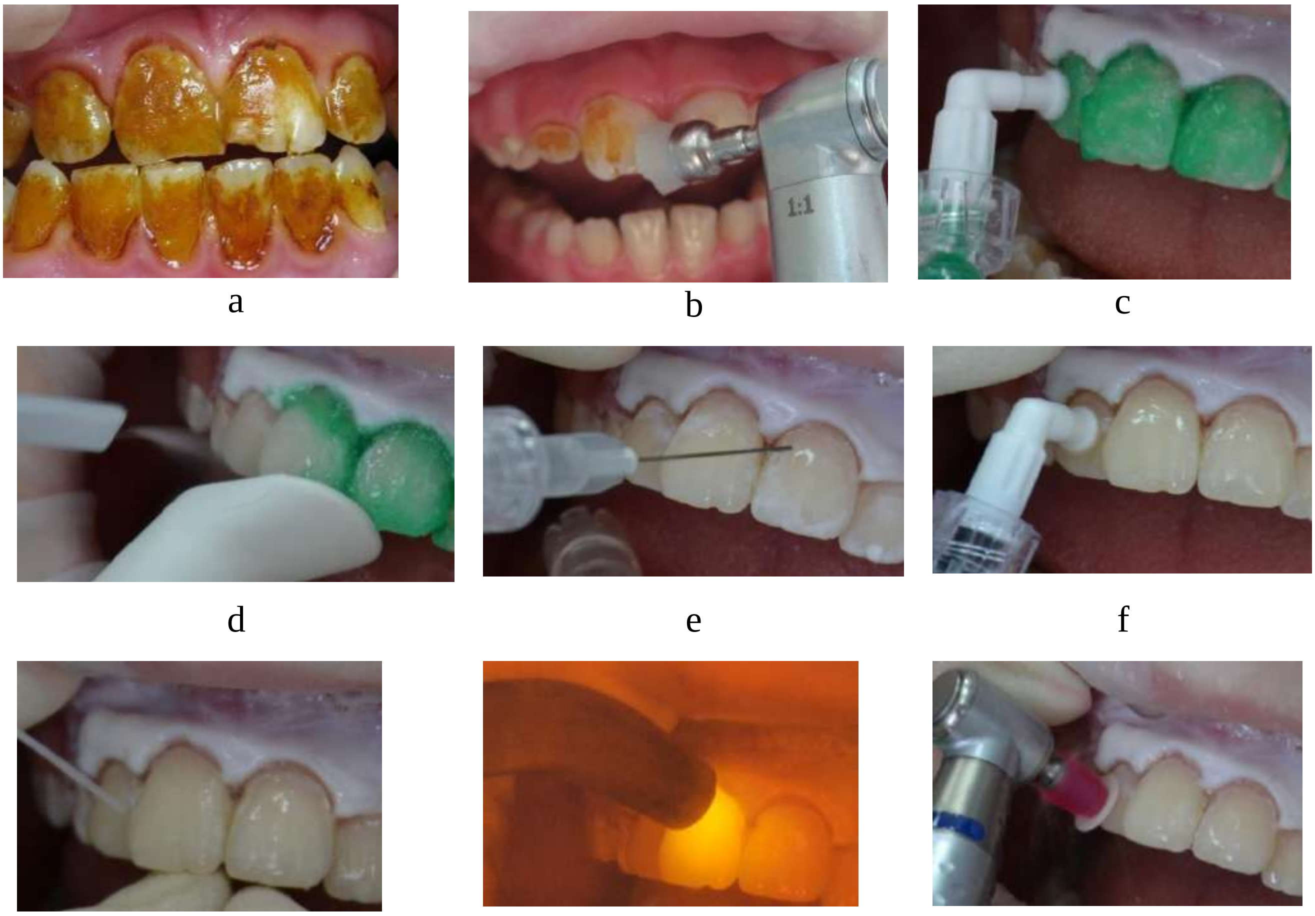

Figure 9 – Stages of caries infiltration: a – plaque detection; b – cleaning of teeth from plaque; c – application of Icon-etch; d – rinsing of the etching gel; e – drying of Icon-dry; f – application of Icon-infiltrant; g – removal of excess infiltrant; h – polymerization; i – polishing.

Figure 10 – InnoDent set

The principle of action of amelogenin peptide is based on the natural processes of enamel maturation. Enamel maturation during histogenesis is accompanied by the formation of organic matrix, which stimulates the crystallization of hydroxyapatite. After the completion of enamel formation, this matrix is reduced, so that further biomineralization is impossible. By introducing the peptide amelogenin as the basis of biomatrix, we artificially start the process of remineralization of enamel, the crystal lattice of which was broken during the pathological process of demineralization.

The procedure of InnoDent application was carried out as follows (Fig. 11):

1) cleaning of the tooth surface with brush and paste;
2) treatment with 0.05% chlorhexidine bigluconate solution;
3) isolation from saliva, drying;
4) treatment with mordant gel of 37% orthophosphoric acid for 10 seconds;
5) rinsing, air jet drying;
6) application of 1 drop of amelogenin peptide (InnoDent™) for 5 minutes;
7) application of 1 drop of nanohydroxyapatite (nanoHAP) for 5 minutes.

Patients were advised to brush their teeth with a soft-bristled brush for three days and to exclude staining foods (beets, etc.) and drinks (black coffee/tea, juices, etc.), hard foods (nuts, seeds, breadcrumbs) and carbonated drinks from their diet.

Toothpastes with fluoride ion concentration of 1400-1500 ppm were recommended for regular tooth brushing for all study participants. Before the study, children were taught the oral hygiene rules and given recommendations to reduce cariogenic foods in diet.

 

a b

 

c d

Figure 11 – Stages of amelogenin peptide application: a – treatment with chlorhexidine solution; b – application of etchant gel; c – application of amelogenin peptide; d – application of nanoGAPs

Assessment of clinical efficacy of the treatment in all groups was carried out every 3 months according to LF data. Clinical efficacy was defined as the percentage of cases of prevention of carious cavity formation in the area of demineralization.

According to LF data, the results of treatment of WSL were defined as:

- regression of demineralization (improvement), when LF values decreased, compared to the initial values; if LF values reached the values of healthy enamel, the recovery of WSL was registered (recovery);
- WSL stabilization, when during the observation period there were no changes in LF values compared to the initial data;
- progression of demineralization (deterioration), when LF values increased compared to the initial values; progression of demineralization can lead to the formation of a carious cavity.

We performed an integral assessment of treatment results with regard to the depth of demineralization according to the criteria of recovery and progression of demineralization (according to LF data).

2.5. Methods of statistical data processing

The results of the study were processed on a computer using standard packages of mathematical statistics programs (Microsoft Excel 2019; MedCalc Software Ltd., Version 22.020).

Observational statistics indicators were determined: frequency of signs (%), the value of the mean (M), the value of the standard error of the mean (±m), 95% confidence intervals (CI). Pearson's correlation coefficient (r) was determined to assess the interdependence of features. Comparative analysis of the obtained data was performed. To determine the degree of significance of differences (p) between groups we used Student's t test, with Bonferroni correction for multiple comparisons, Fisher's criterion (F), chi-square ($\chi 2$), McNemar test. The critical level of significance was considered to be $p<0.05$.

CHAPTER 3. PREVALENCE AND CLINIC OF LOCAL ENAMEL DEMINERALIZATION OF PERMANENT TEETH IN CHILDREN

3.1 Prevalence and intensity of local enamel demineralization

Based on epidemiologic survey data, the prevalence of WSL in children aged 7-16 years was 87.9% (95% CI 85.1-90.7%). In children, there was a tendency for the prevalence and intensity of WSL to increase slightly with increasing age (Table 1). In children aged 7-10 years, the prevalence of WSL was 86.9% (95% CI 82.9-90.9%), 87.2% (95% CI 82.5-91.9%) in 11-14 years, and 89.7% (95% CI 81.8-97.5%) in 15-16 years, but the differences between the rates were not statistically significant ($p>0.05$).

Table 1 – Prevalence and intensity of local enamel demineralization of permanent teeth in children

Age of the children, years	Prevalence of WSL	Intensity of WSL
	% (95% CI)	M±m
7-10	86.9 (82.9-90.9)	7.09±0.51
11-14	87.2 (82.5-91.9)	8.53±0.44*
15-16	89.7 (81.8-97.5)	8.97±0.77*
Total	87.9 (85.1-90.7)	8.20±0.32

* Differences are significant, $p<0.05$, compared to the 7-9 age group

Most (67.1%, 95% CI 56.7-65.9%) children had fewer than 10 teeth with foci of demineralization, about one-third (32.9%, 95% CI 28.9-37.0%) had 10 or more teeth with WSL, including 3.2% (95% CI 1.7-4.7%) of children with 20 to 28 teeth with WSL. The average number of demineralization foci per examined person was 8.20±0.32.

In children aged 7-10 years, the average number of teeth with WSL was significantly ($p<0.05$) lower than in children aged 11-14 and 15-16 years: 7.09±0.51 vs. 8.53±0.44 and 8.97±0.77, respectively. A direct correlation of medium strength ($r=0.59$)

was found between the age of children and the number of teeth with WSL.

It is known that favorable conditions for the development of WSL are created by poor oral hygiene of children. In all age groups, according to the OHI-S index, the majority of children had an unsatisfactory level of oral hygiene (Table 2).

Table 2 – Oral hygiene levels in children aged 7-16 years old

Age of the children, years	Oral hygiene level	Number of children
		% (95% CI)
7-10	Satisfactory Unsatisfactory	27.6 (22.3-32.9) 72.4 (67.1-77.6)
11-14	Satisfactory Unsatisfactory	40.0 (33.1-46.9)* 60.0 (53.1-66.9)*
15-16	Satisfactory Unsatisfactory	43.1 (30.4-55.8) 56.9 (44.1-69.6)
Total	Satisfactory Unsatisfactory	36.9 (32.8-41.0) 63.1 (58.9-67.2)

* Significance of differences, p<0.001, between the values of indicators, compared to the age group of 7-10 years.

Overall, 63.1% (95% CI 58.9-67.2%) of 7-16-year-olds had an unsatisfactory level of oral hygiene, while 36.9% (95% CI 32.8-41.0%) had a satisfactory level, p<0.001. Satisfactory oral hygiene was more frequently detected in children aged 11-14 and 15-16 years than in 7–10-year-olds.

The number of teeth with WSL in children with poor oral hygiene was higher than in children with satisfactory oral hygiene in all age groups (Fig. 12). Teeth with WSL were least in 7-10-year-old children with satisfactory oral hygiene and most in 15-16-year-old children with poor oral hygiene: 6.99±0.38 and 9.94±1.15, respectively, (p<0.05). A direct correlation of medium strength (r=0.52) between the state of oral hygiene of children and the number of foci of enamel demineralization was revealed.

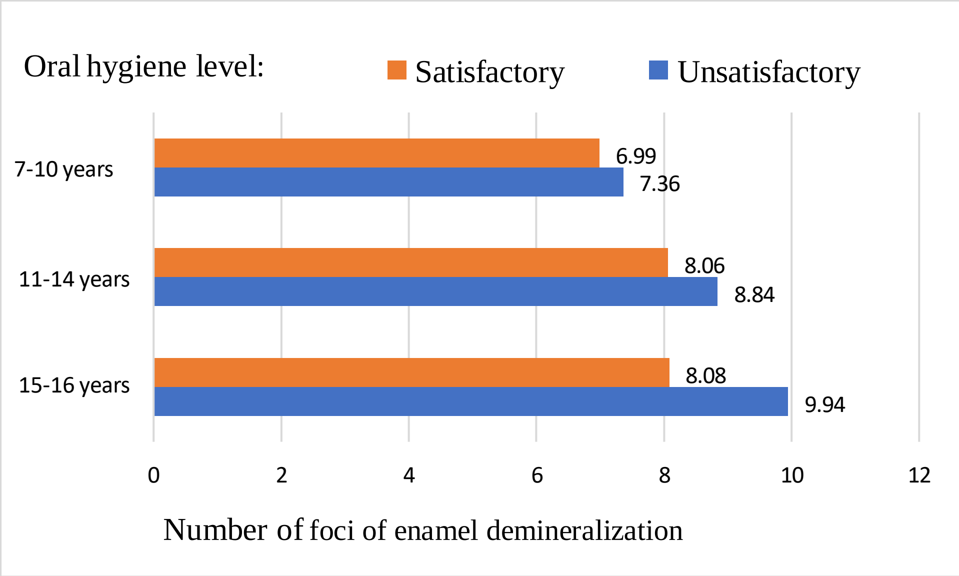

Figure 12 – Number of WSLs in children depending on age and oral hygiene level

Among the children examined, 9.5% (95% CI 7.0-12.0%) had zero DMF (DMF =0), 46.0% (95% CI 41.8-50.3%) had low DMF (DMF =1-4), 29.4% (95% CI 25.5-33.2%) had medium DMF (DMF =5-8) and 15.0% (95% CI 11.9-18.0%) had high DMF (CPUE>8), Figure 13.

Thus, according to the WHO criteria, which record caries with carious cavity formation only, most children had a low level of caries intensity in permanent teeth.

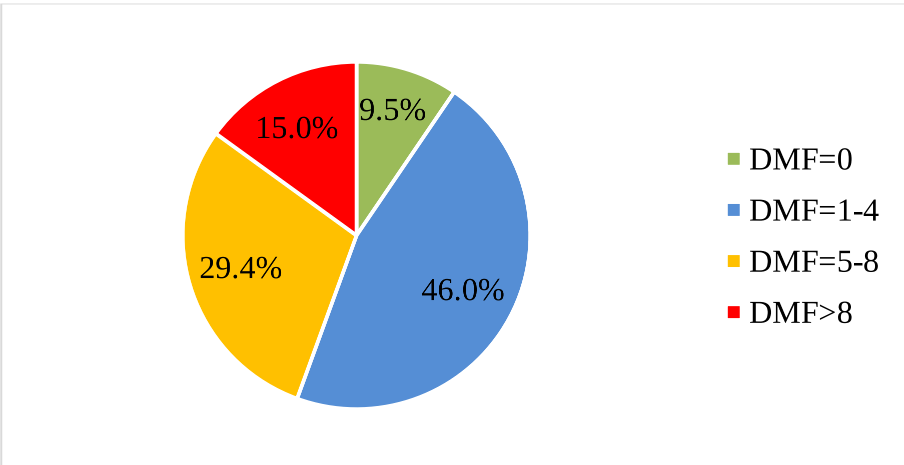

Figure 13 – Distribution of children by level of DMF

There was a trend toward higher prevalence of WSL in children with higher levels of caries intensity in permanent teeth (as measured by DMF), compared with children with zero or low levels. The prevalence of WSL was 82.0% (95% CI 71.3-92.6%) and 80.2% (95% CI 75.2-85.2%) in children with DMF =0 and low DMF, respectively, and 92.3% (95% CI 88.0-96.5%) and 100% (95% CI 96.3-103.7%) in children with medium and high DMF, respectively. However, the differences were not statistically significant (p>0.05), Figure 14.

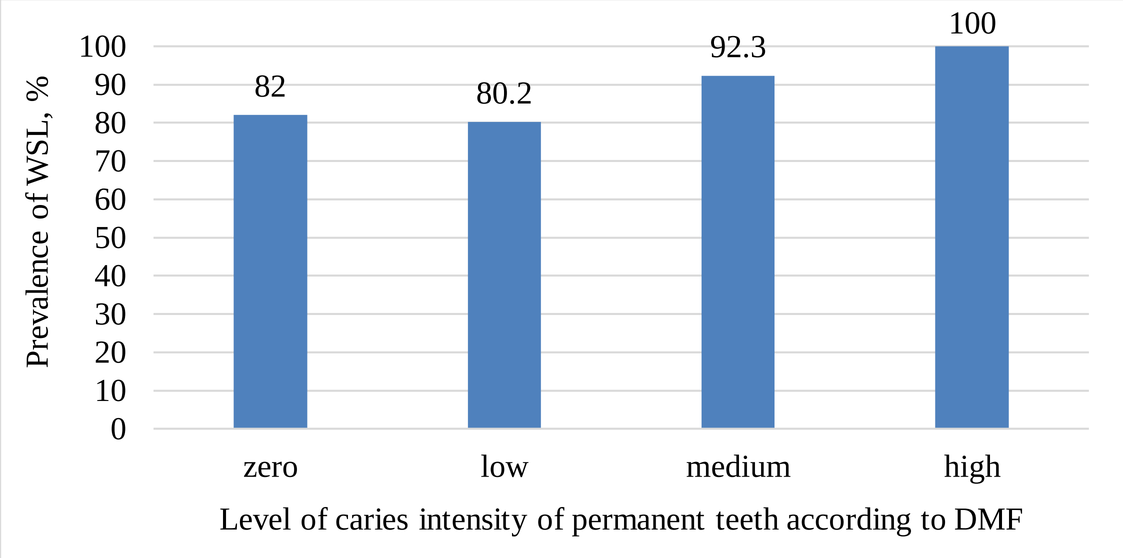

Figure 14 – Prevalence of WSL in children with different levels of caries intensity of permanent teeth according to the DMF

In all age groups, the mean values of the number of WSL s in children with medium and high DMF levels were significantly higher than in children with zero or low DMF levels (p<0.001).

In addition, the number of teeth with WSLs was significantly higher in children with high DMF than in children with medium DMF (p<0.001), Table 3.

Table 3 - Number of teeth with WSL in children of different ages and different levels of caries intensity of permanent teeth according to the DMF

Level of caries intensity (DMF)	Number of WSLs in children aged:		
	7-10	11-14	15-16
	M±m	M±m	M±m
zero	2.44±0.37	6.05±1.52	7.50±1.71
low	3.83±0.25	4.20±0.37	6.00±0.86

medium	10.69±0.57[a,b]	10.72±0.55[a,b]	14.00±1.34[a,b]
high	14.64±2.49[a,b]	15.86±0.99 [a,b,c]	12.75±1.31[a,b]

[a,b] – significance of differences, $p<0.001$, between the values of children with medium/high caries intensity levels compared to children with DMF=0 ([a]) or low DMF ([b]);

[c] – significance of differences, $p<0.001$, between the values of indicators in children with medium and high caries intensity according to DMF.

The mean number of teeth with WSL in children with zero DMF and low caries intensity was approximately the same (4.22±0.67 and 4.23±0.22, $p>0.05$), but significantly ($p<0.001$) 2.6 and 3.5 times less than in children with medium and high DMF levels (11.00±0.38 and 14.88±1.41, respectively, $p<0.01$), Figure 15.

A direct correlation of medium strength ($r=0.53$) was found between the number of WSLs and the level of DMF in children.

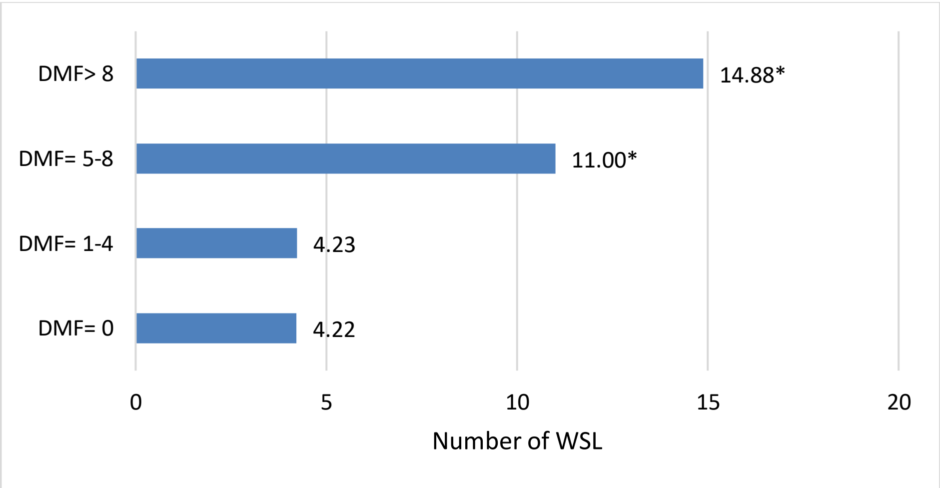

Figure 15 – Number of WSL in children depending on the level of DMF

* Significance of differences, $p<0.001$, compared to the indicators of WSL at other levels of DMF

Most of the children examined had malocclusions, 64.8% (95% CI 60.7- 68.8%). In children aged 7-10 years, malocclusions were slightly more common than in children aged 11-14 and 15-16 years: 67.6% (95% CI 62.1-73.2%), 64.6% (95% CI 57.9-71.3%) and 62.1% (95% CI 49.6-74.6%), respectively, $p>0.05$.

There was a tendency to increase the number of teeth with WSL in children with malocclusions compared to children with physiologic occlusion: 8.52±0.77 and 7.55±0.80, respectively, p>0.05 (Table 4).

The average number of WSLs in children aged 7-10 years with physiological occlusion was 5.67±0.55, with pathological occlusion – 7.78±0.71 (p<0.05), at the age of 11-14 years – 8.30±0.71 and 8.65±0.56, respectively (p>0.05), 15-16 years – 8.68±1.13 and 9.14±1.04, respectively (p>0.05).

Thus, children 7-10 years old with physiologic occlusion had the least number of teeth with WSL, while children 15-16 years old with pathologic occlusion had the most: 7.78±0.71 and 9.14±1.04, respectively (p>0.05).

Table 4 – Prevalence and intensity of WSL in children of different ages with physiologic and pathologic occlusion

Age of the children, years	Number of WSLs in children with occlusion:	
	physiological	pathological
	M±m	M±m
7-10	5.67±0.55	7.78±0.71*
11-14	8.30±0.71	8.65±0.56
15-16	8.68±1.13	9.14±1.04
Total	7.55±0.80	8.52±0.77

* Significance of differences, p<0.05, between the number of WSL s in children with physiologic and pathologic occlusion

Despite the clearly traceable tendency to increase the intensity of WSLs in children with pathologic occlusion compared to children with physiologic occlusion, the correlation between the number of WSLs and the presence of occlusion pathology was weak (r=0.43).

Thus, the conducted studies revealed [26]:

- high prevalence of WSL in children aged 7-16 years and an increase in the number of foci of demineralization with the age of children;
- a greater number of teeth with WSL in children with a high level of caries intensity of permanent teeth according to the DMF, poor oral hygiene and pathological occlusion

than in children with satisfactory oral hygiene, low DMF and physiological occlusion;

- stronger correlation of WSL with the age of children, poor oral hygiene and caries intensity according to the DMF than with occlusion pathology.

3.2. Clinical features of local enamel demineralization

In children aged 10-16 years, local enamel demineralization developed equally often on maxillary and mandibular teeth: 52.3% (95% CI 47.7-56.9%) and 47.7% (95% CI 43.1-52.3%), respectively, p>0.05. WSL was most often localized in premolars and molars: 35.0% (95% CI 30.6-39.4%) and 27.9% (95% CI 23.8-32.1%), respectively. WSL was less frequently detected in incisors and canines: 18.4% (95% CI 14.8-22.0%) and 18.6% (95% CI 15.0-22.2%), respectively. Foci of demineralization were found least in mandibular incisors (5.3%, 95% CI 3.2-7.4%) and most in mandibular premolars (18.2%, 95% CI 14.6-21.7%). Differences in the frequency of WSL localization in different tooth groups were statistically significant overall (p<0.05) and for mandibular teeth (p<0.05), Table 5.

Table 5 – Localization of WSL in permanent teeth in children

Localization of WSL	Number of teeth with WSL, % (95% CI)				
	Incisors	Canines	Premolars	Molars	Total
Upper jaw	13.1 (10.0-16.2)	10.0 (7.2-12.7)	16.8 (13.4-20.3)	12.4 (9.4-15.5)	52.3 (47.7-56.9)
	χ^2 = 1.47, p = 0.69				
Lower jaw	5.3 (3.2-7.4)	8.6 (6.0-11.2)	18.2 (14.6-21.7)	15.5 (12.2-18.7)	47.7 (43.1-52.3)
	χ^2 =9.48, p = 0.02				
Total	18.4 (14.8-22.0)	18.6 (15.0-22.2)	35.0 (30.6-39.4)	27.9 (23.8-32.1)	100
	χ^2 = 8.20, p = 0.04				

According to the LF data, it was found that half of the foci of demineralization were located in the superficial layers of enamel (initial demineralization) – 50.1% (95% CI 45.5-54.7%). Somewhat less frequently (42.8%, 95% CI 38.2-47.4%), demineralization extended to deep enamel layers (deep demineralization). Rarely, 7.1% (95% CI 4.7-9.5%) of cases showed demineralization of superficial dentin layers. Differences between the incidence of WSL of different depths were significant statistically (p <0.001), Table 6. In all groups of upper and lower jaw teeth, the spread of demineralization to dentin (without disturbing the enamel surface) was significantly less frequent (p<0.001) than demineralization limited to superficial or deep enamel layers [24].

Table 6 – Distribution of WSL by depth in permanent teeth in children according to laser fluorescence (in relation to the total number of detected teeth with WSL)

Depth of WSL	Number of teeth with WSL, % (95% CI)				
	Incisors	Canines	Premolars	Molars	Total
	Upper jaw				
Initial enamel demineralization	7.1 (4.7-9.5)	4.0 (2.2-5.8)	8.9 (6.2-11.5)	5.8 (3.6-7.9)	25.7 (21.7-29.7)
Deep enamel demineralization	4.9 (2.9-6.9)	5.5 (3.4-7.7)	7.3 (4.9-9.7)	6.0 (3.8-8.2)	23.7 (19.8-27.6)
Enamel demineralization extended into dentin	1.1 (0.1-2.1)	0.4 (0.0-1,1)	0.7 (0.0-1.4)	0.7 (0.0-1.4)	2.9 (1.3-4.4)
Significance of differences	$\chi^2 = 18.95$ $p < 0.001$	$\chi^2 = 18.53$ $p < 0.001$	$\chi^2 = 30.50$ $p < 0.001$	$\chi^2 = 19.75$ $p < 0.001$	$\chi^2 = 82.74$ $p < 0.001$
	Lower jaw				
Initial enamel demineralization	3.1 (1.5-4.7)	5.5 (3.4-7.7)	9.1 (6.4-11.7)	6.7 (4.3-8.9)	24.4 (20.4-28.3)
Deep enamel demineralization	2.2 (0.9-3.6)	2.2 (0.9-3.6)	7.1 (4.7-9.5)	7.5 (5.1-10.0)	19.1 (15.4-22.7)

Enamel demineralization extended into dentin	0.0 -	0.9 (0.02-1.7)	2.0 (0.7-3.3)	1.3 (0.3-2.4)	4.2 (2.4-6.1)
Significance of differences	χ^2 =13.00 $p < 0.01$	χ^2 =18.00 $p < 0.001$	χ^2 =19.93 $p < 0.001$	χ^2 =19.66 $p < 0.001$	χ^2 = 62,07 $p < 0.001$
	Total				
Initial enamel demineralization	10.2 (7.4-13.0)	9.5 (6.8-12.2)	18.0 (14.4-21.5)	12.4 (9.4-15.5)	50.1 (45.5-54.7)
Deep enamel demineralization	7.1 (4.7-9.5)	7.8 (5.3-10.2)	14.4 (11.2-17.6)	13.5 (10.4-16.7)	42.8 (38.2-47.4)
Enamel demineralization extended into dentin	1.1 (0.1-2.1)	1.3 (0,3-2.4)	2.7 (1.2-4.1)	2.0 (0.7-3.3)	7.1 (4.7-9.5)
Significance of differences	χ^2 =31.40 $p < 0.001$	χ^2 =27.07 $p < 0.001$	χ^2 =49.53 $p < 0.001$	χ^2 =39.19 $p < 0.001$	χ^2 =143.34 $p < 0.001$

In maxillary incisors and premolars, enamel lesions at the initial stage of demineralization predominated, in canines at the stage of deep enamel demineralization, in molars the number of initial and deep foci of enamel demineralization was approximately equal. The proportion of teeth with enamel demineralization extended into dentin in maxillary incisors was higher than in other groups of maxillary teeth (Fig. 16).

In the mandible, initial carious lesions of enamel predominated in incisors, canines, and premolars, while foci of demineralization in the deep layers of enamel predominated in molars. Enamel demineralization extended into dentin in incisors was not detected, and in other groups of teeth the proportions of foci of demineralization spreading to dentin were approximately the same (Fig. 17).

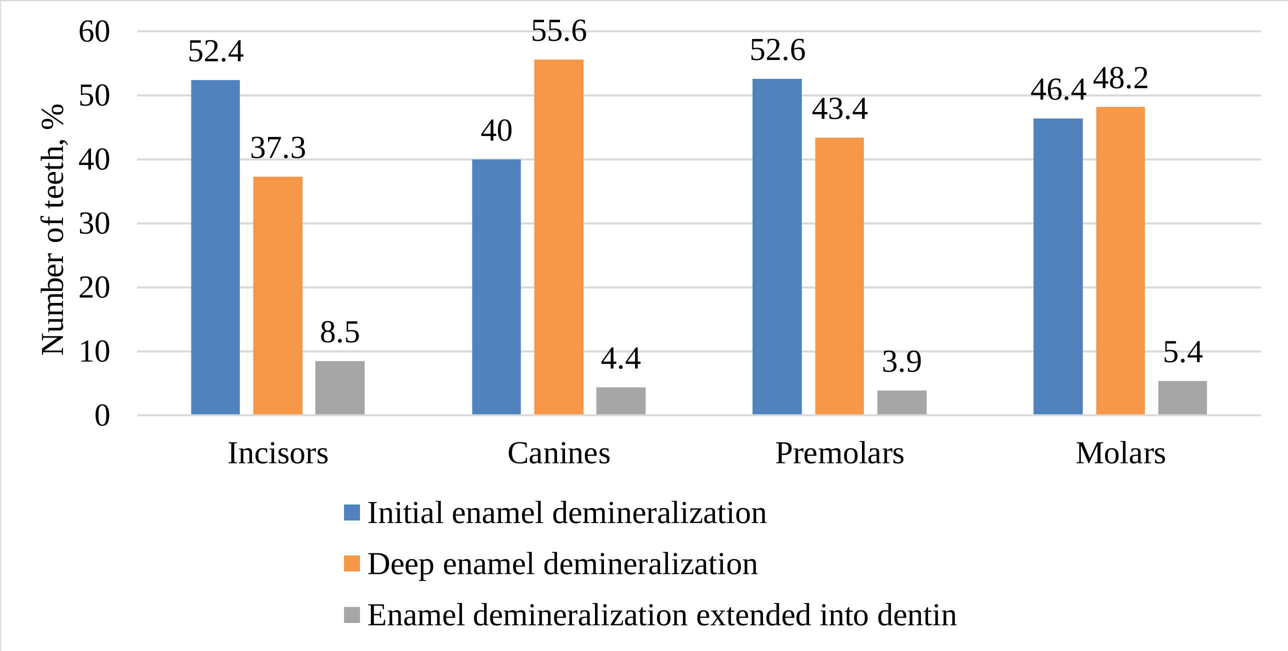

Figure 16 – Depth of WSL in teeth of the upper jaw according to laser fluorescence data

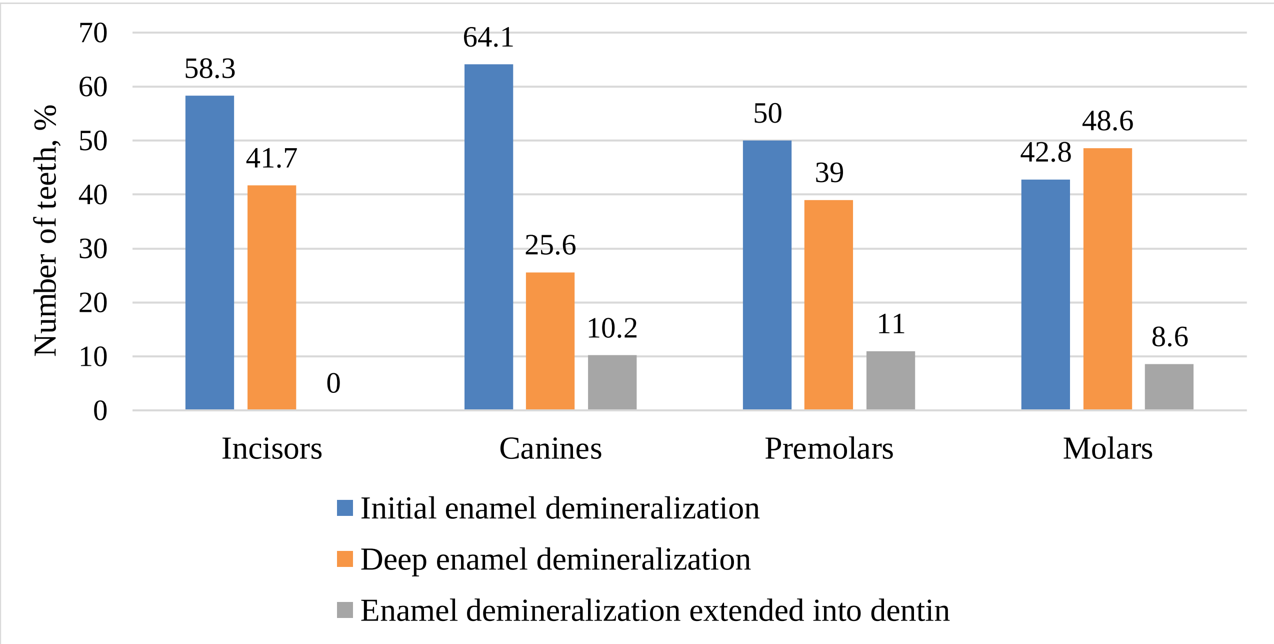

Figure 17 – Depth of WSL in mandibular teeth according to laser fluorescence data

Thus, when examining the hard tissues of permanent teeth in children, it should be taken into account that in some groups of teeth there are clear tendencies to increase the frequency of deep enamel demineralization and the spread of enamel demineralization extended into dentin.

The study of average values of laser fluorescence in different groups of teeth revealed a general tendency to increase the depth of WSL from the center to distant areas: incisors – 20.65±0.59, canines – 20.86±0.56, premolars – 21.31±0.43, molars – 21.77±0.46 ($p>0.05$). This trend was most clearly expressed in the teeth of the lower jaw, the LF values were 19.71±1.03 in incisors, 20.13±0.79 in canines, 21.77±0.60 in premolars, and 22.10±0.66 in molars, but the differences between the values were not statistically significant ($p>0.05$). On the upper jaw, the mean values of LF were approximately the same in all groups of teeth (Table 7).

Table 7 – Mean values of laser fluorescence of WSL in permanent teeth in children

Localization of WSL	Incisors	Canines	Premolars	Molars	Average
	M±m	M±m	M±m	M±m	M±m
Upper jaw	21.03±0.73	21.49±0.78	20.82±0.62	21.36±0.64	21.13±0.34
Lower jaw	19.71±1.03	20.13±0.79	21.77±0.60	22.10±0.66	21.35±0.37
Average	20.65±0.59	20.86±0.56	21.31±0.43	21.77±0.46	21.23±0.25

Apparently, such factors as the degree of saliva washability (most pronounced in incisors and canines of the lower jaw, molars and premolars of the upper jaw) and the quality of hygienic cleaning of teeth (children clean the frontal group of teeth best of all) have a certain influence on the processes of remineralization and demineralization in permanent teeth.

Thus, the main clinical features of WSL in permanent teeth in children consist in the specific localization of lesion and different distribution of demineralization foci by the depth of hard tissue in different groups of teeth of the upper and lower jaw.

CHAPTER 4. RESULTS OF TREATMENT OF LOCAL ENAMEL DEMINERALIZATION OF PERMANENT TEETH IN CHILDREN

4.1. Results of non-invasive treatment

4.1.1. Comparative characteristics of the first and second groups before treatment

Non-invasive treatment of local enamel demineralization was performed by applying a toothpaste with increased fluoride content (group 1) and fluoride varnish (group 2). All study participants received full courses of treatment and were followed up for 18 months after treatment.

The characteristics of groups 1 and 2 before treatment are presented in Table 8. Both groups were identical in terms of children's age (mean age of children in group 1 12.57±0.33 years, in group 2 it was 13.13±0.36 years, $p>0.05$), oral hygiene status (mean OHI-S values was 1.17±0.13 and 1.18±0.13, respectively, $p>0.05$). There were no significant differences ($p>0.05$) between groups 1 and 2 in terms of gender, distribution of WSL by localization and depth of lesions.

In both groups ($p>0.05$), the majority of WSLs were localized in premolars and molars, less frequently in incisors and canines. The ratio of WSLs in the teeth of the upper and lower jaw was approximately the same ($p>0.05$). In both groups, the smallest number of WSLs was localized in the incisors of the mandible, the largest one was in the molars of the mandible ($p>0.05$).

According to LF data, in Group 1, initial enamel demineralization (LF=13-20) was detected in 50.0% of teeth, deep enamel demineralization (LF=21-29) in 43.5%, enamel demineralization extended into dentin (LF=30-39) in 6.5%, in Group 2 its distribution was 57.4%, 36.8% and 5.8%, respectively (p>0.05). The mean values of LF in WSLs in groups 1 and 2 were also comparable: 20.99±0.41 and 20.21±0.43, p>0.05.

Table 8 – Characterization of 1 and 2 observation groups

Characteristics	Group 1	Group 1	Significance of differences, p
Number of children / teeth	14 / 138	15 / 155	
Number of boys, %	50.0	66.7	> 0.05
Number of girls, %	50.0	33.3	> 0.05
Age, M±m	12.57±0.33	13.13±0.36	> 0.05
Hygiene Index OHI-S, M±m	1.17±0.13	1.18±0.13	> 0.05
Localization of WSL: incisors, %	10.1	16.2	> 0.05
canines, %	17.4	17.4	> 0.05
premolars, %	34.1	32.9	> 0.05
molars, %	38.4	33.5	> 0.05
teeth of the upper jaw, %	56.5	49.7	> 0.05
teeth of the lower jaw, %	43.5	50.3	> 0.05
Distribution of WSLs on the upper jaw			
incisors, %	14.1	22.1	> 0.05
canines, %	17.9	16.8	> 0.05
premolars, %	32.1	32.5	> 0.05
molars, %	35.9	28.6	> 0.05
Distribution of WSLs on the lower jaw			
incisors, %	5.0	10.3	> 0.05
canines, %	16.7	17.9	> 0.05
premolars, %	36.6	33.3	> 0.05
molars, %	41.7	38.5	> 0.05
Depth of WSL: LF=13-20, %	50.0	57.4	> 0.05
LF=21-29, %	43.5	36.8	> 0.05

LF=30-39, %	6.5	5.8	> 0.05
Average LF value, M±m	20.99±0.41	20.21±0.43	> 0.05

Thus, 1 and 2 study groups had comparable characteristics in terms of age and sex, oral hygiene status of children, localization and depth of foci of demineralization, average values of LF indicators in foci of demineralization.

4.1.2. Results of using toothpaste with increased fluoride content

The dynamics of LF indices in children of the first group in the course of treatment of WSL using toothpaste with increased fluoride content is presented in Table 9.

Table 9 – LF indicators in the dynamics of treatment of WSL of various depths in children of the first group

Observation period	LF indices			
	Enamel demineralization		Enamel demineralization extended into dentin	Total
	Initial	Deep		
	M±m	M±m	M±m	M±m
Before treatment	16.94±0.22	24.07±0.29	31.44±0.47	20.99±0.41
3 months	16.79±0.24	23.78±0.31	29.56±0.56*	20.67±0.39
6 months	16.57±0.24	23.35±0.30	29.00±0.55*	20.33±0.39
9 months	16.29±0.27	23.20±0.32*	28.38±0.62***	20.14±0.41
12 months	16.16±0.27*	23.02±0.31*	27.88±0.64***	19.96±0.40
15 months	16.07±0.29*	22.98±0.31**	27.25±0.70***	19.85±0.40*
18 months	15.95±0.29**	22.73±0.29*	27.00±0.73***	19.67±0.39*

*Significance of differences, compared to pre-treatment data, p<0.05;

** p<0.01; *** p<0.001

Before treatment, the mean value of LF in group 1 was 20.99±0.41. After application of toothpaste with increased fluoride content, the average value of LF index gradually decreased and after 18 months amounted to 19.67±0.39, the differences with the initial value were statistically significant ($p<0.05$) only after 15 and 18 months after the beginning of treatment.

The same regularities in group 1 were revealed when considering separately the results of treatment depending on the depth of demineralization of hard tissues of teeth. The values of LF indices 18 months after treatment decreased: from 16.94±0.22 to 15.95±0.29 ($p<0.01$) at initial enamel demineralization, from 24.07±0.29 to 22.73±0.29 ($p<0.05$) at deep enamel demineralization, from 31.44±0.47 to 27.00±0.73 ($p<0.001$) at enamel demineralization extended into dentin. Differences with the initial indicators were statistically significant and started after the treatment from month 12 for initial enamel demineralization, from month 9 for deep enamel demineralization, and from month 3 for enamel demineralization extended into dentin.

A decrease in the values of LF indicators was noted in all groups of teeth (Table 10).

Table 10 - LF indicators in the course of treatment depending on the localization of WSL in children of the first group

Observation period	LF indicators in tooth groups			
	Incisors	Canines	Premolars	Molars
	M±m	M±m	M±m	M±m
Before treatment	20.64±1.14	20.79±1.04	20.47±0.65	21.62±0.72
3 months	20.29±1.14	20.29±0.95	20.23±0.64	21.32±0.69
6 months	20.14±1.23	19.75±0.95	19.81±0.59	21.09±0.67
9 months	19.64±1.29	20.00±1.02	19.78±0.66	20.63±0.69
12 months	19.57±1.32	19.95±1.01	19.63±0.66	20.35±0.66
15 months	19.50±1.35	19.43±0.99	19.65±0.65	20.31±0.67
18 months	19.36±1.31	19.33±1.05	19.48±0.64	20.06±0.64

The degree of decrease in the values of LF indices in the process of treatment of WSL, compared to the initial data, was after 3 months 1.5%, 6 months 3.1%, 9 months 4.0%, 12 months 4.9%, 15 months 5.4%, and 18 months 6.5%. In the treatment of initial enamel demineralization, the degree of decrease in LF values increased from 0.9% after 3 months to 5.8% after 18 months, in the treatment of deep enamel demineralization from 1.2% to 5.6%, and in the treatment of enamel demineralization extended into dentin from 6.0% to 14.1%, respectively, but the differences were not statistically significant ($p>0.05$), Fig. 18.

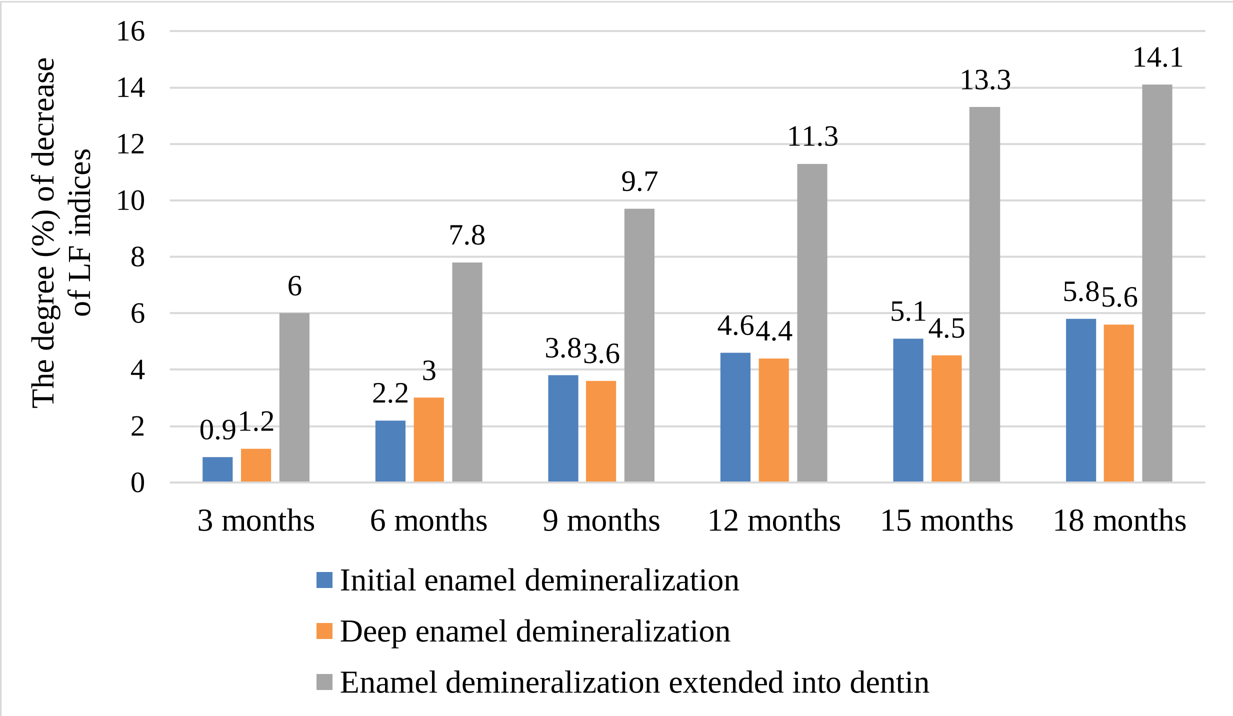

Figure 18 – The degree of decrease in LF values, compared to the initial data, in the dynamics of treatment of WSL of different depths in children of the first group

The degree of decrease in LF values in Group 1 insignificantly depended on the localization of the lesion: in incisors increased from 1.7% after 3 months to 6.2% after 18 months, in canines from 2.4% to 7.0%, in premolars from 1.2% to 4.8%, in molars from 1.4% to 7.2%, respectively, the differences were not statistically significant ($p>0.05$), Fig. 19.

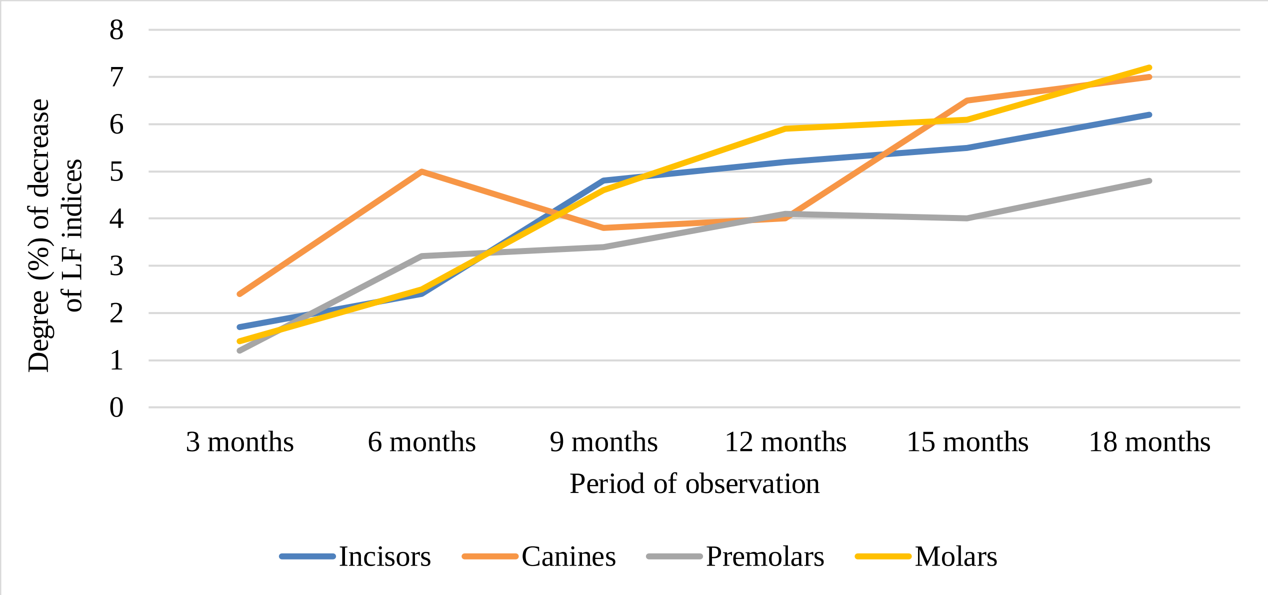

Figure 19 – Degree of decrease in LF indices, compared to the initial data, depending on the localization of WSL in children of the first group

The study of the direction of changes in the demineralization processes in group 1 allowed us to evaluate the outcomes of treatment of WSL of different depth. At treatment of initial enamel demineralization after 3 and 6 months, according to LF data, stabilization of the process was significantly ($p<0.001$) more frequent than regression: 79.7% (95% CI 70.2-89.2%) vs. 15.9% (95% CI 7.3-24.6%) and 63.8% (95% CI 52.4-75.1%) vs. 27.5% (95% CI 17.0-38.1%). Further, WSL regression and stabilization were equally frequent ($p>0.05$). After 9 months of treatment, WSL regression was significantly ($p<0.001$) more common ($p<0.001$) than after 3 months, and after 18 months was determined in 57.5% of cases. However, of these, only 11.6% of cases showed WSL recovery, when LF indices corresponded to healthy enamel. The frequency of WSL stabilization after 18 months significantly ($p<0.001$) decreased to 40.9%, compared to the data after 3 months. Progression of enamel demineralization was the least frequent ($p<0.001$): from 1.6% to 8.7% of cases in different periods of observation, Table 11. Thus, at initial enamel demineralization after 18 months of treatment with the use of toothpaste with increased fluoride content, on the basis of LF data we can consider that the processes of WSL remineralization prevailed in more than half of cases, progression of demineralization was observed only in single cases, and about 40% of demineralization foci were stabilized.

Table 11 – Results of treatment of initial enamel demineralization in children of the first group according to LF data

Observation period (in months)	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3	15,9 (7,3-24,6)[b,c]	79,7 (70,2-89,2)[b,d]	4,4 (0,0-9,2)[c,d]
6	27,5 (17,0-38,1)[b,c]	63,8 (52,4-75,1) [a,b,d]	8,7 (2,0-15,3)[c,d]
9	49,2 (36,6-61,7)[a,c]	42,6 (30,2-55,0)[a,d]	8,2 (1,3-15,1)[c,d]
12	50,8 (38,3-63,4)[a,c]	42,6 (30,2-55,0)[a,d]	6,6 (0,3-12,8)[c,d]
15	55,7 (43,3-68,2) [a,c]	39,3 (27,1-51,6 [a,d]	4,9 (0,0-10,3)[c,d]
18	57,4 (45,0-69,8) [a,c]	41,0 (28,6-53,3)[a,d]	1,6 (0,0-4,8)[c,d]

[a] Significance of differences, compared to the data after 3 months, p<0.05

[b] Significance of differences between "regression" and "stabilization" frequencies, p<0.001

[c] Significance of differences between the frequencies of "regression" and "progress", p<0.001

[d] Significance of differences between frequencies "stabilization" and "progress", p<0.001

In the treatment of deep enamel demineralization, similar trends were observed in Group 1. After 3 months of treatment, stabilization of WSL was more common than regression according to LF: 63.3% (95% CI 51.1-75.5%) vs. 25.0% (95% CI 14.0-36.0%), respectively, p<0.001. Then gradually the frequency of WSL regression increased and the frequency of stabilization decreased, but only after 12 months did the rates start to differ significantly (p<0.05) from the data after 3 months (Table 12). Differences between the frequency of WSL regression and stabilization became statistically significant only 18 months after the start of deep demineralization treatment: 63.6% (95% CI 50.9-76.3% vs. 30.9% (95% CI 18.7-43.1%), respectively, p<0.05. Regression of demineralization did not lead to recovery of WSL in any case after 18 months. Progression of demineralization was noted in all periods of observation in a small number of cases - 3.3-

11.7%, the differences were not statistically significant (p>0.05).

Table 12 – Results of treatment of deep enamel demineralization in children of the first group according to LF data

Observation period (in months)	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3	25.0 (14.0-36.0)[b]	63.3 (51.1-75.5)[b,d]	11.7 (3.5-19.8)[d]
6	40.0 (27.6-52.4)[c]	56.7 (44.1-69.2)[d]	3.3 (0.0-7.9)[c,d]
9	41.8 (28.8-54.8)[c]	54.6 (41,4-67.7)[d]	3.6 (0.0-8.6)[c,d]
12	54.5 (41.4-67.7)[a,c]	38.2 (25.3-51.0)[a,d]	7.3 (0.4-14.1)[c,d]
15	56.4 (43.3-69.5)[a,c]	38.2 (25.3-51.0)[a,d]	5.4 (0.0-11.5)[c,d]
18	63.6 (50.9-76.3)[a,b,c]	30.9 (18.7-43.1)[a,d]	5.4 (0.0-11.5)[c,d]

[a] Significance of differences, compared to the data after 3 months, p<0.05

[b] Significance of differences between the frequencies of "regression" and "stabilization", p<0.001

[c] Significance of differences between the frequencies of "regression" and "progress", p<0.001

[d] Significance of differences between the frequencies of "stabilization" and "progress", p<0.001

Thus, in the treatment of deep enamel demineralization in group 1 after 18 months, according to LF data, remineralization processes prevailed in more than 60% of cases, about 30% of demineralization foci stabilized, and progression of demineralization was observed in less than 6% of cases.

During treatment of enamel demineralization extended into dentin, reduction (regression) of LF parameters was significantly more frequent than stabilization: after 3 months 77.8% (95% CI 50.6-100%) and 22.2% (95% CI 0.0-49.4%), p<0.06; after 6 months 88.9% (95% CI 68.4-100%) and 11.1% (95% CI 0.0-31.6%), p<0.001. After 9-18 months, regression of LF parameters was detected in 100% of cases, but no cases of WSL recovery were reported. There were also no cases of progression of demineralization throughout the follow-up period.

Differences in the results of treatment of WSL of different depths were not statistically significant ($p>0.05$).

The change in WSL status after 18 months in different groups of teeth differed insignificantly ($p>0.05$) (Fig. 20). In incisors, WSL regression was observed in 64.3% (95% CI 39.2-89.4%) of cases, stabilization in 28.6% (95% CI 4.9-52.2%), and progression in 7.1% (95% CI 0.0-20.6%); in canines 71.4% (95% CI 52.1-90.7%), 28,6% (95% CI 9.2-47.9%) and 0.0%; in premolars 62.5% (95% CI 47.5-77.5%), 35.0% (95% CI 20.2-49.8%) and 2.5% (95% CI 0.00-7.3%); and in molars 59.2% (95% CI 45.4-72.9%), 36.7% (95% CI 23.2-50.2%) and 4.1% (95% CI 0.0-9.6%), respectively.

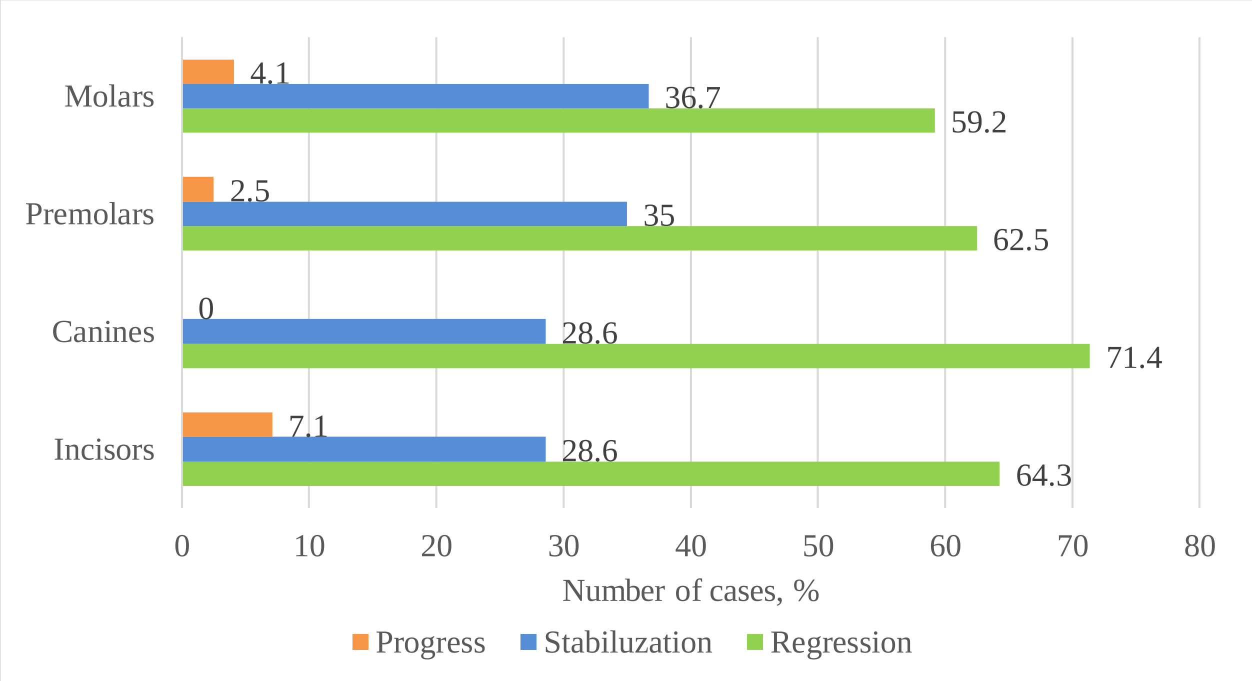

Figure 20 – Treatment results in the first group after 18 months depending on WSL localization

Consideration of the generalized results of WSL treatment in group 1, according to LF data, showed that only after 12 months of the treatment the regression rate of enamel demineralization exceeded 50.0% and after 18 months reached 62.9% (95% CI 54.4-71.4%). However, only 6.5% (95% CI 2.4-10.6%) of cases achieved LF values of healthy enamel. After 18 months, about one-third of the WSL cases remained in a stabilized state, and 3.2% (95% CI 0.0-11.6%) of cases showed progression of demineralization (Fig. 21). The identified overall trends in enamel condition during treatment with fluoride-rich toothpaste were statistically significant (p <0.001).

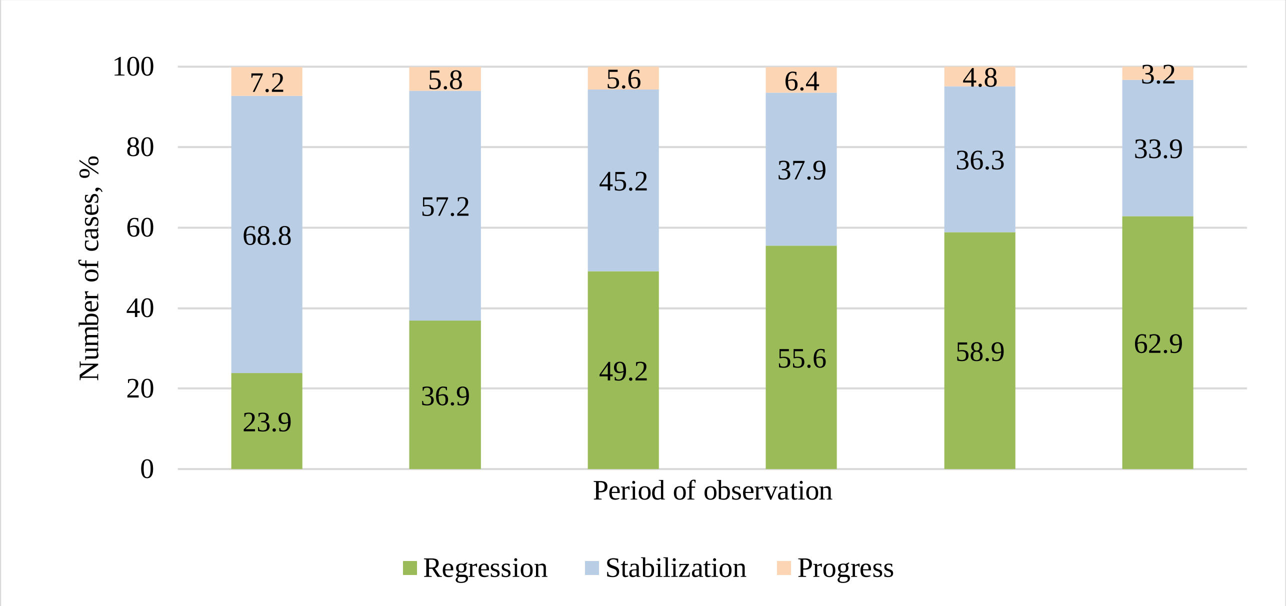

Figure 21 – Directionality of changes in WSL state according to LF indicators during treatment of children of the first group

In the course of dynamic observation, all children had a good level of oral hygiene and during the entire period of the study, according to the ICDAS-II index, there was no increase in caries, which confirms the caries-preventive role of toothpastes containing fluoride.

Thus, the course application of toothpaste with increased fluoride content in children showed 100% clinical efficiency of WSL treatment, which was expressed in the absence of carious cavities formation in the areas of demineralization. Analysis of the results of the treatment of WSL according to laser fluorescence showed [29]:

- gradual regression of WSL from 23.9% after 3 months to 62.9% after 18 months; however, LF values rarely reached the values of healthy enamel (6.5% of cases);
- stabilization of WSL in one third (33.9%) of cases 18 months after treatment;
- single (3.2-7.2%) cases of progression of demineralization in all periods of observation without formation of carious cavities;
- no significant differences in the results of treatment of WSL of different depth and localization.

The obtained data substantiate the necessity to continue treatment of WSL using toothpastes with high concentration of fluoride to maintain the stabilized state and further improve the enamel condition. It is also possible to use more effective methods of treatment in case of progression of enamel demineralization or in order to achieve complete recovery.

4.1.3. Results of fluoride varnish application

Application of fluoride varnish for treatment of WSL in children of group 2 resulted in gradual decrease of the average value of LF index from 20.21±0.43 (before the beginning of treatment) to 18.19±0.42 18 months after the beginning of treatment (Table 13). The differences between the indicators became statistically significant ($p<0.05$) 9 months after the start of treatment.

Positive shifts were observed in the treatment of WSL of different depths. In 18 months after the treatment of initial enamel demineralization, the mean value of LF index decreased from 16.38±0.19 to 14.99±0.26 ($p<0.001$), after treatment of deep enamel demineralization from 24.12±0.32 to 22.00±0.33 ($p<0.001$), after treatment of enamel demineralization extended into dentin from 33.44±1.02 to 28.57±1.36, respectively ($p<0.01$). The differences between the indices became significant ($p<0.05$) from 3 months after the treatment.

Table 13 – LF indicators in the dynamics of treatment of WSL of different depth in children of the second group

Observation period	LF indicators			
	Enamel demineralization		Enamel demineralization extended into dentin	Total
	Initial	Deep		
	M±m	M±m	M±m	M±m
Before treatment	16.38±0.19	24.12±0.32	33.44±1.02	20.21±0.43

3 months	15.81±0.22*	23.07±0.32*	30.44±0.97*	19.31±0.42
6 months	15.71±0.21*	22.59±0.32**	30.00±1.01*	19.14±0.39
9 months	15.45±0.24**	22.46±0.33***	29.29±1.21**	18.75±0.42*
12 months	15.24±0.25***	22.29±0.33***	28.43±1.38**	18.52±0.39**
15 months	14.99±0.26***	22.15±0.31***	28.57±1.38**	18.33±0.39**
18 months	14.89±0.26***	22.00±0.33***	28.57±1.36**	18.19±0.42**

*Significance of differences, compared to pre-treatment data, $p<0.05$;
** $p<0.01$; *** $p<0.001$

The results of WSL treatment depending on the lesion localization are presented in Table 14. In all groups of teeth, a clear tendency of LF indices decrease in the course of the treatment was observed, but significant differences were observed only in the localization of WSL in molars, starting from 9 months after the treatment.

Table 14 – LF indicators during treatment depending on the localization of WSL in children of group 2

Observation period	LF indicators			
	Incisors	Canines	Premolars	Molars
	M±m	M±m	M±m	M±m
Before treatment	17.44±0.89	19.01±0.84	20.81±0.84	21.56±0.71
3 months	16.41±0.91	18.24±0.71	20.23±0.78	20.45±0.62
6 months	16.25±0.90	17.99±0.70	19.92±0.77	20.25±0.58
9 months	16.31±0.94	17.78±0.82	19.55±0.78	19.53±0.61*
12 months	15.89±0.98	17.56±0.80	19.34±0.76	19.34±0.61*
15 months	15.67±0.97	17.23±0.75	19.31±0.72	19.31±0.64*
18 months	15.56±0.96	17.29±0.81	19.11±0.78	19.04±0.64**

*Significance of differences, compared to data before treatment, $p<0.05$; **$p<0.01$

The degree of decrease in the values of LF indicators in Group 2 increased in the dynamics of treatment (Fig. 22): at initial enamel demineralization from 3.5% after 3 months to 9.1% after 18 months, at deep enamel demineralization from 4.4% to 8.8%, at enamel demineralization extended into dentin from 8.9% to 14.6%, respectively. However, the differences between the indicators were not statistically significant.

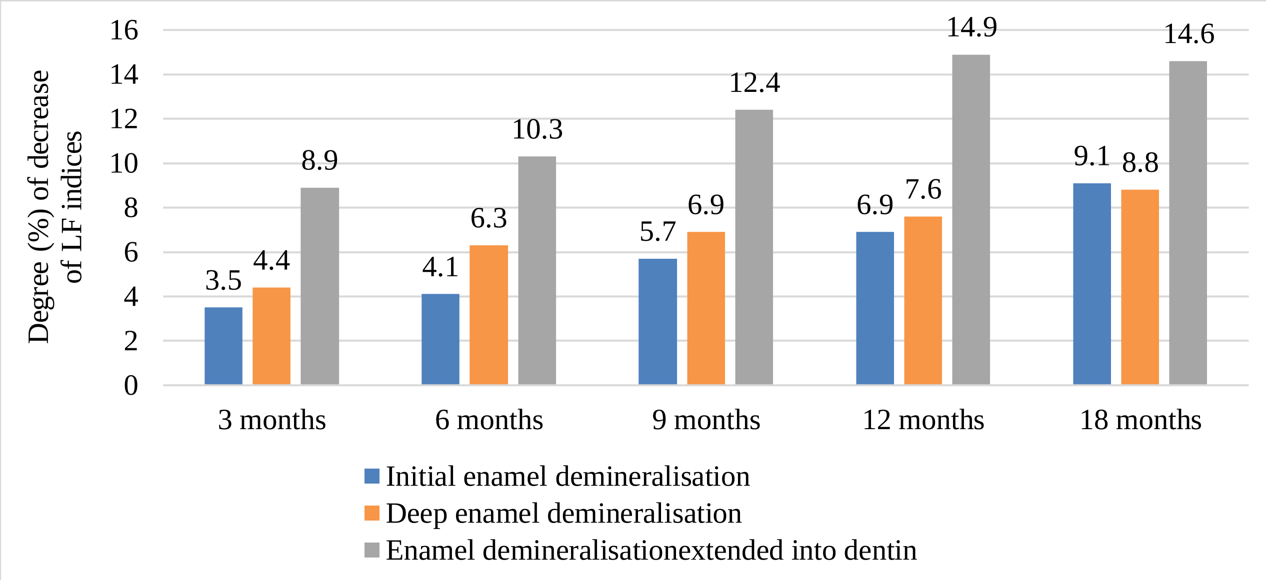

Figure 22 – Degree of decrease in LF indicators, compared to the initial data, in the dynamics of treatment of WSL of different depths in children of the second group

In different groups of teeth, the degree of decrease in LF indices also increased as the treatment period increased (Fig. 23): in incisors from 5.7% after 3 months to 10.5% after 18 months, in canines from 4.1% to 8.6%, in premolars from 2.9% to 8.2%, and in molars from 5.4% to 12.3%, respectively; the differences were not statistically significant ($p>0.05$).

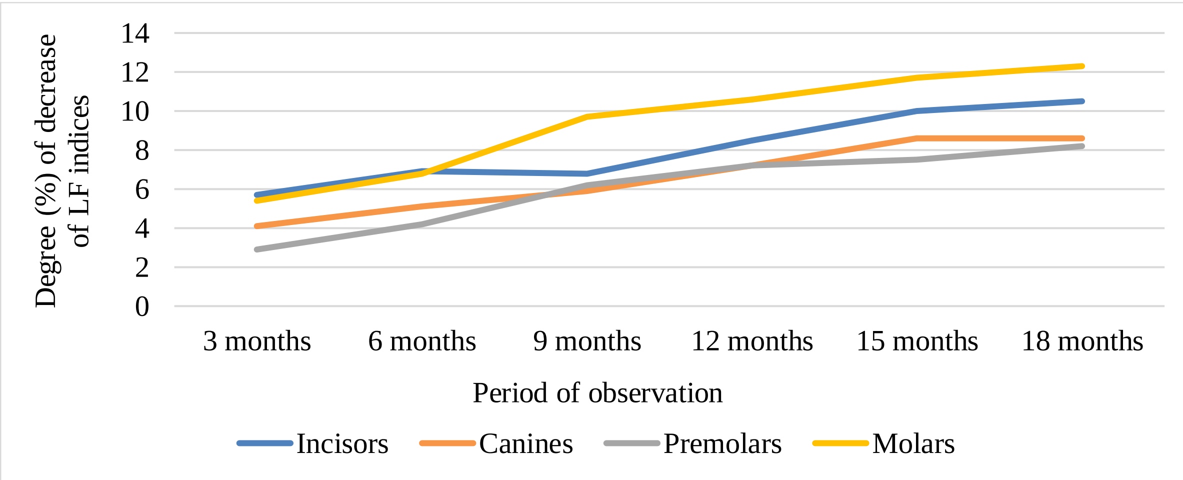

Figure 23 – Degree of reduction of LF indices, compared to the initial data, depending on the localization of WSL in children of the second group

When studying the outcomes of treatment of initial enamel demineralization in group 2, we found that 3 months after the start of treatment, regression of WSL was observed in 38.2% (95% CI 28.8-48.6%) of cases, stabilization – 52.8% (42.5-62.8), $p>0.05$ (Table 15).

Table 15 – Results of treatment of initial enamel demineralization in children of the second group according to LF data

Observation period (in months)	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3	38.2 (28.8-48.6)^{c}	52.8 (42.5-62.8)^{d}	9.0 (4.6-16.7)^{c,d}
6	42.7 (32.9-53.1)^{c}	47.2 (37.1-57.5)^{d}	10.1 (5.4-18.1)^{c,d}
9	56.6 (45.9-66.8)^{a,c}	36.1 (26.6-46.9)^{a,d}	7.2 (3.4-14.9)^{c,d}
12	65.1 (54.3-74.4)^{a,b,c}	26.5 (18.2-36.9)^{a,d}	8.4 (4.1-16.4)^{c,d}
15	65.1 (54.3-74.4)^{a,b,c}	27.7 (19.2-38.2)^{a,d}	7.2 (3.4-14.9)^{c,d}
18	66.3 (55.6-76.0)^{a,b,c}	27.7 (19.2-38.2)^{a,d}	6.0 (2.6-13.3)^{c,d}

^{a}Significance of differences, compared to the data after 3 months, $p<0.05$

^{b}Significance of differences between the frequencies of “regression” and “stabilization” frequencies, $p<0.001$

^{c}Significance of differences between the frequencies of “regression” and “progress”, $p<0.001$

^{d}Significance of differences between the frequencies of “stabilization” and “progress”, $p<0.001$

Further, the frequency of regression of initial demineralization increased and, starting from the 9th month, LF indices significantly differed from the similar data after 3 months. From month 12 the differences between the frequencies of regression and stabilization of WSL became statistically significant and after 18 months reached the values of 66.3% (95% CI 55.6-76.0%) and 27.7% (95% CI 19.2-38.2%) respectively, $p<0.001$. Progression of demineralization was noted at all follow-up periods in 6.0-10.1% of cases ($p>0.05$).

Thus, after application of fluoride varnish for treatment of initial enamel demineralization, according to LF data, regression of WSL (enamel remineralization) was observed in 18 months in two thirds of cases. Of these, 24.7% of cases showed complete recovery (LF values corresponded to those of healthy enamel). Stabilization of the process was noted in 27.7% of cases and only in 6.0% of cases - progression of demineralization.

In the treatment of deep enamel demineralization in Group 2, the differences between the frequency of similar outcomes in different observation periods were not statistically significant ($p>0.05$). At all follow-up periods, regression of WSL, as measured by LF, was more common than stabilization, the rates after 18 months were 71.1% (95% CI 57.7-81.7%) and 26.9% (95% CI 16.8-40.2%), respectively, $p<0.001$. Demineralization progression was significantly ($p<0.05$) less frequent than other outcomes: 1.8-5.8% (Table 16).

Table 16 – Results of treatment of deep enamel demineralization in children of the second group according to LF data

Observation period (in months)	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3	56.1 (43.3-68.2)	43.9 (31.8-56.7)	0.0
6	70.2 (57.3-80.5)^{a,b}	28.1 (18.1-40.8)^{a,c}	1.8 (0.3-8.3)^{b,c}
9	71.1 (57.7-81.7)^{a,b}	25.0 (15.2-38.2)^{a,c}	3.9 (1.1-13.0)^{b,c}
12	71.1 (57.7-81.7)^{a,b}	23.1 (13.7-36.1)^{a,c}	5.8 (2.0-15.6)^{b,c}
15	73.1 (59.7-83.2)^{a,b}	21.1 (12.2-34.0)^{a,c}	5.8 (2.0-15.6)^{b,c}
18	71.1 (57.7-81.7)^{a,b}	26.9 (16.8-40.2)^{a,c}	1.9 (0.3-11.6)^{b,c}

^{a}Significance of differences between the frequencies of “regression” and “stabilization”, $p<0.001$

^{b}Significance of differences between the frequencies of “regression” and “progress”, $p<0.001$

^{c}Significance of differences between the frequencies of “stabilization” and “progress”, $p<0.05$

Thus, when fluoride varnish was used to treat deep enamel demineralization, regression of WSL prevailed starting from the 3rd month of observation and accounted for more than 70% of cases after 18 months. However, in none of the cases there was observed recovery of WSL (compliance of LF values with the indicators of healthy enamel). Stabilization of the process was observed in every fourth case, and progress of demineralization was observed in less than 6% of cases.

At 3 and 6 months after treatment of enamel demineralization extended into dentin in group 2, WSL regression was significantly more frequent than stabilization: 88.9% (95% CI 68.4-100%) and 11.1% (95% CI 0.0-31.6%), $p<0.01$. After 9 months, only regression of WSL was encountered. There were no cases of progression of demineralization during the entire follow-up period. Thus, the treatment of enamel demineralization extended into dentin was dominated by remineralization processes.

Differences between tooth groups in the frequency of various WSL treatment outcomes after 18 months were not statistically significant ($p>0.05$). In all tooth groups, WSL regression occurred most frequently: incisors 65.2% (95% CI 45.7-84.7%), canines 80.0% (95% CI 64.3-95.7%), premolars 62.3% (95% CI 48.1-76.5%), molars 73.5% (95% CI 61.1-85.7%), $p>0.05$, Fig. 24.

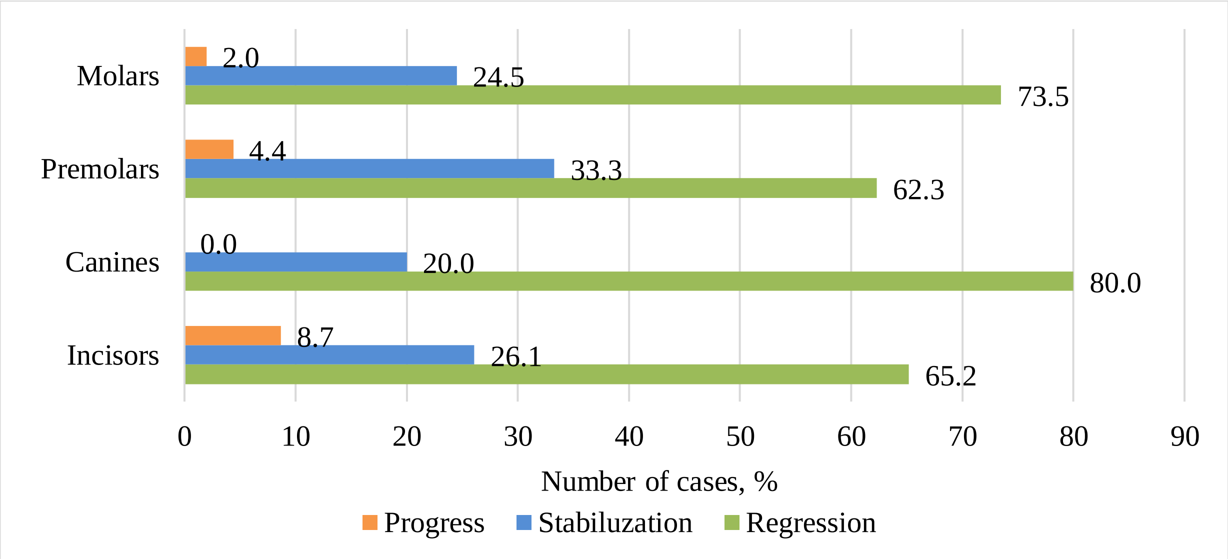

Figure 24 – Treatment results in group 2 after 18 months depending on the localization of WSL

Overall, in Group 2, WSL regression was predominant from 6 months after the start of WSL treatment (Fig. 25).

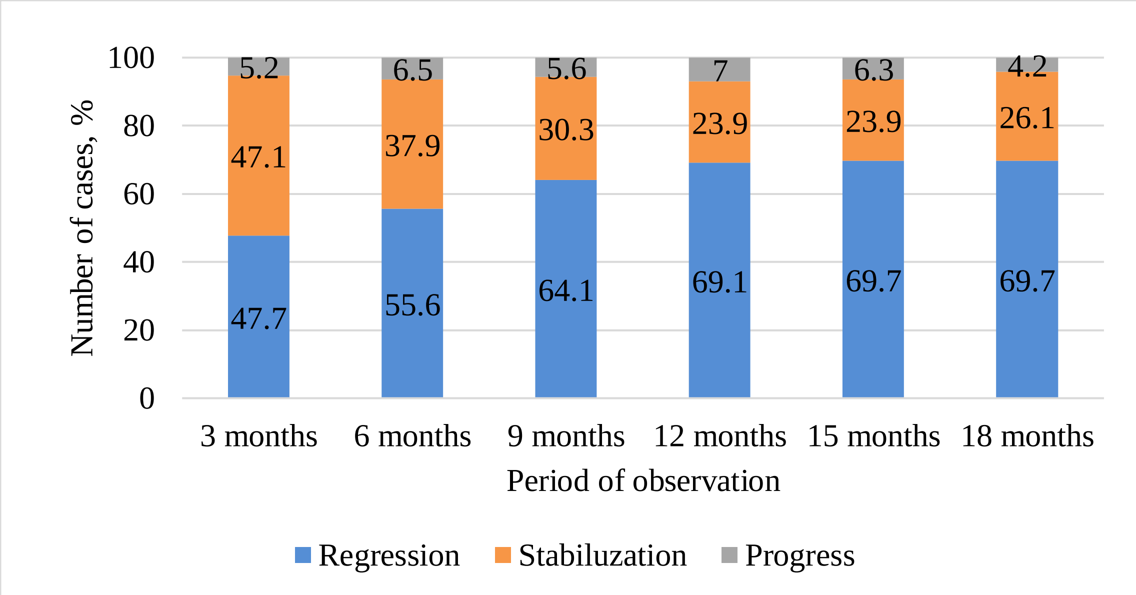

Figure 25 – Directionality of changes in WSL state according to LF indicators during treatment of children of the second group

After 18 months, the WSL regression rate reached 69.7% (95% CI 62.1-77.3%). Of these, in 15.5% (95% CI 9.8-21.2%) of cases there was a recovery of WSL, LF indices corresponded to healthy enamel. Stabilization of the demineralization process in group 2 3 months after the beginning of treatment was as frequent as the regression rate, then it was determined less frequently and was 26.1% (95% CI 18.9-33.3%) after 18 months. Progression of demineralization was rare at all follow-up periods, being recorded in 4.2% (95% CI 0.9-7.5%) of cases after 18 months. Differences between the incidence rates of different WSL treatment outcomes were statistically significant ($p<0.001$) starting 6 months after the start of fluoride varnish application.

Clinical evaluation did not reveal a single case of carious cavity formation as a result of a course of fluoride varnish application for the treatment of WSL (clinical efficacy of treatment - 100%). In addition, all children had a good level of oral hygiene and, according to the ICDAS-II index, there was no caries increment, which confirms the role of fluoride varnish in caries prevention.

Thus, the results of an 18-month course of fluoride varnish for the treatment of WSL were as follows [27]:

- WSL regression rate, according to LF values, increased from 47.7% of cases after

3 months to 69.7% of cases after 18 months, but LF values reached the values of healthy enamel only in few (15.5%) cases;

- after 18 months, every fourth case (26.1%) managed to achieve stabilization of the demineralization process;
- progression of demineralization without carious cavity formation was observed in rare cases (4.2-7.0%) during the entire observation period;
- no significant differences were found in the results of treatment of WSL of different depth and localization.

The obtained data show the expediency of dynamic assessment of the WSL state in the process of treatment with fluoride varnish using hardware diagnostic methods, as well as, if necessary, the use of more effective methods of remineralization of WSL.

4.2. Results of microinvasive treatment

4.2.1. Comparative characterization of the third and fourth groups before treatment

Microinvasive treatment of local enamel demineralization was performed by applying caries infiltration (group 3) and amelogenin peptide (group 4). The treatment was performed once. The study participants were followed up for 18 months after the treatment. The characteristics of groups 3 and 4 before treatment are presented in Table 17.

Table 17 – Characterization of 3 and 4 observation groups

Characteristics	Group 3	Group 4	Significance of differences, p
Number of children / teeth	15 / 99	8 / 59	

Number of boys, %	20.0	25.0	> 0.05
Number of girls, %	80.0	75.0	> 0.05
Age, M±m	13.60±0.21	14.00±0.19	> 0.05
Hygiene index, M±m	0.94±0.11	0.80±0.11	> 0.05
Localization of WSL: incisors, %	26.3	30.5	> 0.05
canines, %	21.2	20.3	> 0.05
premolars, %	40.4	33.9	> 0.05
molars, %	12.1	15.3	> 0.05
teeth of the upper jaw, %	47.5	57.6	> 0.05
teeth of the lower jaw, %	52.5	42.4	> 0.05
Distribution of WSL on the upper jaw			
incisors, %	38.3	38.2	> 0.05
canines, %	23.4	20.6	> 0.05
premolars, %	31.9	32.4	> 0.05
molars, %	6.4	8.8	> 0.05
Distribution of WSL on the lower jaw			
incisors, %	15.4	20.0	> 0.05
canines, %	19.2	20.0	> 0.05
premolars, %	48.1	36.0	> 0.05
molars, %	17.3	24.0	> 0.05
Depth of WSL: LF=13-20, %	34.3	57.6	> 0.05
LF=21-29, %	52.5	40.7	> 0.05
LF=30-39, %	13.2	1.7	> 0.05
LF average, M±m	23.67±0.57	23.79±0.55	> 0.05

Both groups had no significant differences in gender composition, were identical in the age of children: mean age of children in group 3 was 13.60±0.21 years, in group 4 14.00±0.19 years, $p>0.05$. The children had the same level of oral hygiene according to the OHI-S index, the mean values of which were 0.94±0.11 in group 3 and 0.80±0.11 in group 4, $p>0.05$.

Most WSLs in both groups were localized in premolars and incisors, less frequently in canines and molars. Differences between the groups in the distribution of WSLs between the teeth of the upper and lower jaw, between the distributions of individual tooth groups were not statistically significant ($p>0.05$).

According to LF data, the distribution of WSL according to the depth of demineralization in groups 3 and 4 was as follows: initial enamel demineralization (LF=13-20) was diagnosed in 34.3% and 57.5% of teeth ($p>0.05$), deep enamel demineralization (LF=21-29) in 52.5% and 40.7% of teeth ($p>0.05$), enamel demineralization extended into dentin (LF=30-39) in 13.1% and 1.7% of teeth, respectively ($p>0.05$). The mean values of LF indices in demineralization areas in groups 3 and 4 were approximately the same: 23.67±0.57 and 23.79±0.55, $p>0.05$.

Thus, the main characteristics of study groups 3 and 4 were comparable.

4.2.2. Results of caries infiltration method

Since the caries infiltration method was performed once, the LF indices in Group 3 were determined before and immediately after treatment, then in 3, 6, 9, 12, 15 and 18 months after treatment. The average value of LF index before the treatment was 23.74±0.57. Immediately after the treatment (in the same visit), the average value of the index decreased 1.9 times and amounted to 12.72±0.80, which is an indicator of healthy enamel. At follow-up examinations, there was a further slight decrease in the indices, which after 18 months was 11.17±0.75. However, the treatment results varied significantly depending on the initial depth of demineralization (Table 18).

Before treatment of initial enamel demineralization, the average value of LF index was 17.41±0.28. Immediately after caries infiltration procedure, this index decreased 3.4 times and amounted to 5.04±0.83 ($p<0.001$), which corresponded to healthy enamel. Further, the value of LF index values changed insignificantly and after 18 months amounted to 5.45±0.87.

Table 18 – LF indicators in the dynamics of treatment of WSL of different depth in children of the third group

Observation period	LF indicators			
	Enamel demineralization		Enamel demineralization extended into dentin	Total
	Initial	Deep		
	M±m	M±m	M±m	M±m
Before treatment	17.41±0.28	25.40±0.38	33.13±0.66	23.7±0.57
Immediately after treatment	5.04±0.83*	15.34±0.79*	22.49±1.33	12.72±0.80
3 months	5.09±0.86*	14.74±0.77*	21.21±1.25*	12.87±0.80*
6 months	4.91±0.84*	14.14±0.76*	21.22±1.28*	12.32±0.77*
9 months	4.94±0.84*	14.20±0.77*	21.23±1.30*	12.00±0.75*
12 months	5.07±0.88*	13.84±0.78*	20.68±1.31*	12.30±0.77*
15 months	5.24±0.88*	13.78±0.77*	20.77±1.38*	12.12±0.75*
18 months	5.45±0.87*	13.86±0.77*	20.76±1.38*	12.17±0.74*

*Significance of differences, compared to the baseline data, $p<0.001$

In cases of deep enamel demineralization, the average value of LF index before treatment was 25.40±0.38. Immediately after the treatment there was a significant ($p<0.001$) decrease in the value of LF index to 15.34±0.79, which corresponded to the initial enamel demineralization. At further observation there was a gradual decrease in the value of LF index, which after 18 months amounted to 13.86±0.77 (close to the index of healthy enamel).

In enamel demineralization extended into dentin, the average value of LF index before treatment was 33.13±0.66. Immediately after treatment, the value of LF index significantly ($p<0.001$) decreased to 22.49±1.33, which corresponded to deep enamel demineralization. In 3-18 months after treatment, LF values slightly decreased, but remained near the lower limit of values corresponding to deep enamel demineralization (in 18 months 20.76±1.38).

The results of treatment of local demineralization in Group 3 depending on the localization of lesions are presented in Table 19. In all groups of teeth, the average values before treatment corresponded to deep enamel demineralization. Immediately after treatment, there was a significant ($p<0.001$) decrease in LF values. During further observation LF values continued to decrease and after 18 months were 13.42±1.45 for incisors, which corresponded to the lower limit of values for initial enamel demineralization. In other groups of teeth LF values after 18 months corresponded to healthy enamel: canines - 12,42±1,73, premolars - 10,98±1,17, molars - 9,35±1,94. There were no statistically significant differences between LF indices of different groups of teeth ($p>0.05$).

Table 19 – LF indicators in the course of treatment depending on the localization of WSL in children of the third group

Observation period	LF indicators			
	Incisors	Canines	Premolars	Molars
	M±m	M±m	M±m	M±m
Before treatment	24.82±1.09	23.78±1.32	23.03±0.87	22.94±1.81
Immediately after treatment	14.61±1.53*	13.67±1.79*	11.82±1.27*	9.83±2.17*
3 months	14.00±1.43*	13.01±1.80*	11.44±1.23*	9.11±1.89*
6 months	13.54±1.43*	12.54±1.74*	11.25±1.21*	9.24±1.85*
9 months	13.55±1.44*	12.32±1.79*	11.14±1.24*	9.42±1.87*
12 months	13.29±1.46*	12.25±1.72*	10.89±1.20*	9.00±1.74*
15 months	13.11±1.46*	12.31±1.74*	11.00±1.17*	9.33±1.80*
18 months	13.42±1.45*	12.42±1.73*	10.98±1.17*	9.35±1.94*

*Significance of differences, compared to the baseline data, $p<0.001$

There was a high degree of decrease in LF values, compared to the initial data, immediately after treatment - 46.3%. Subsequently, the degree of LF reduction slightly increased and after 18 months amounted to 48.4%. Differences between the degree of LF reduction immediately after treatment and after 3-18 months were not significant ($p>0.05$). The most pronounced in Group 3 was the degree of LF reduction after treatment of initial enamel demineralization (71.1%), which remained at a high level during all periods of observation and was 68.7% after 18 months ($p>0.05$), Fig. 26.

The degree of LF reduction after treatment of deep enamel demineralization in group 3 was 39.6% immediately after treatment and reached 45.4% after 18 months ($p>0.05$). After treatment of enamel demineralization extended into dentin, the degree of LF reduction immediately after treatment was 32.1% and after 18 months 36.7% ($p>0.05$). Differences between the values of the degree of decrease in LF indices after treatment of WSL of various depths were statistically significant ($p<0.001$) in all periods of observation.

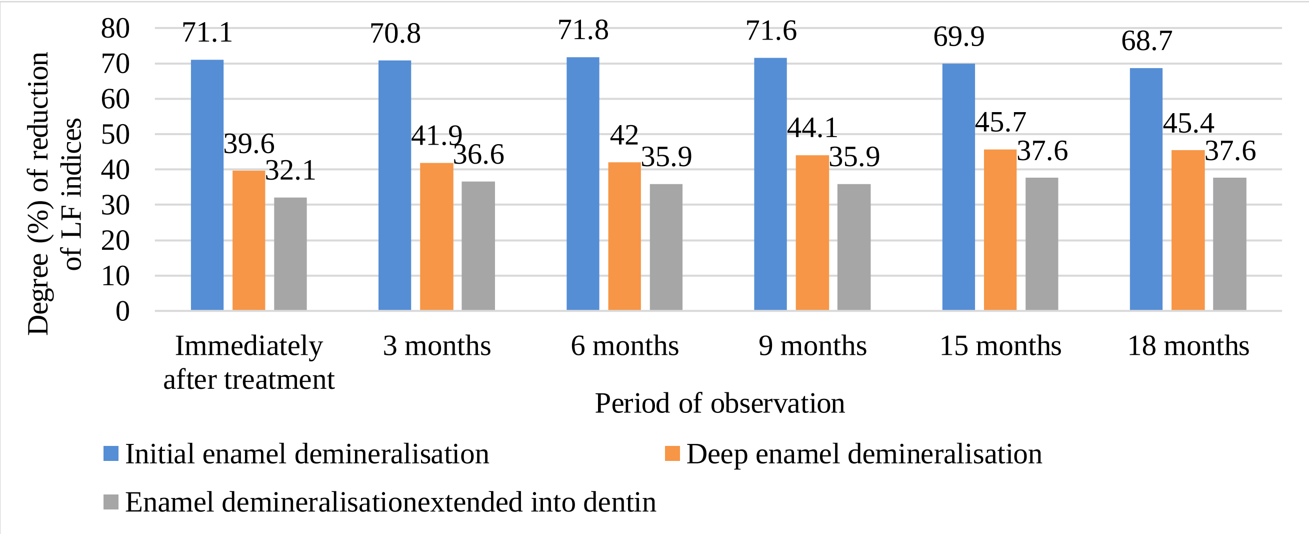

Figure 26 – Degree of decrease in LF indicators, compared to the baseline data, in the dynamics of treatment of WSL of different depths in children of the third group

The localization of WSL did not matter for the degree of LF reduction, which immediately after treatment was 43.6% in incisors, 44.1% in canines, 49.4% in premolars, and 56.3% in molars; after 18 months 41.9%, 47.5%, 50.8%, and 57.2%, respectively ($p>0.05$), Fig. 27.

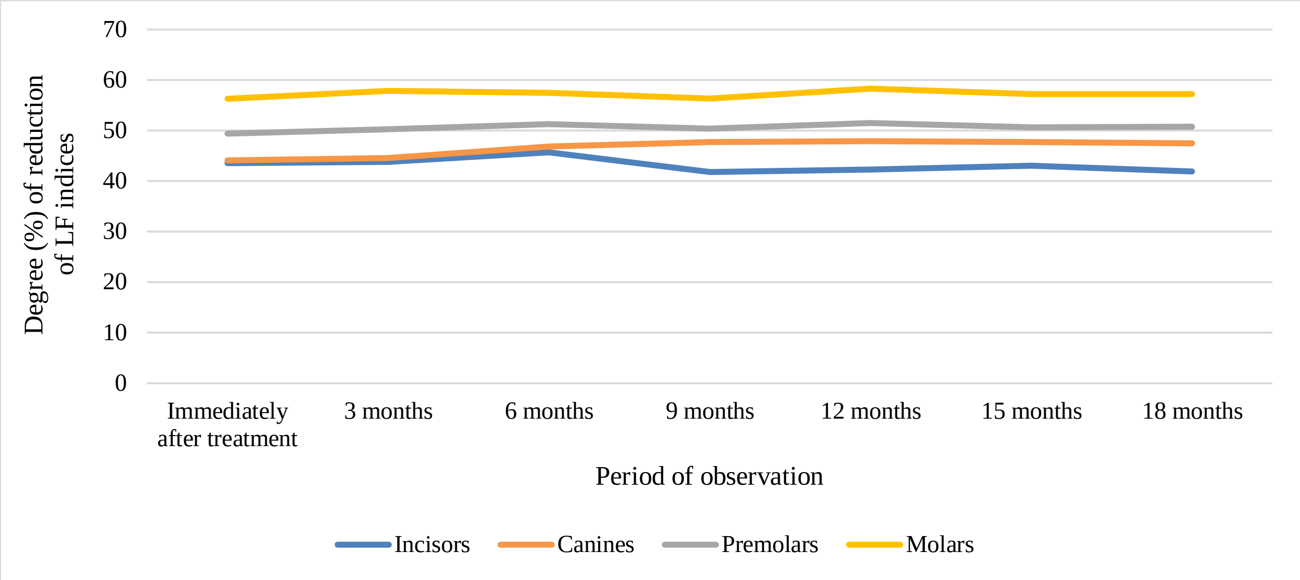

Figure 27 – Degree of decrease in LF values, compared to the initial data, depending on the localization of WSL in children of the third group

Thus, the degree of decrease in LF indices after treatment in group 3 depended not on the localization of WSL, but on the depth of demineralization. The direction of changes in the state of enamel, according to LF data, also depended on the depth of demineralization of the lesion, and the treatment outcomes were different for initial enamel demineralization, deep enamel demineralization, and enamel demineralization extended into dentin.

The outcomes of WSL treatment in Group 3 were recorded immediately after treatment and were maintained throughout the entire observation period. After treatment of initial demineralization, almost all children showed recovery of WSL: a decrease in LF values immediately after treatment and their compliance with healthy enamel in 94.1% of cases. In 5.9% of cases, regression of WSL was noted, stabilization or progression was not registered.

In deep enamel demineralization, regression of WSL immediately after treatment was observed in 94.1% of cases, in 18 months - 98.1% ($p>0.05$), in half of cases (50.0%) LF values corresponded to the indicators of healthy enamel, the rest - to the indicators of initial demineralization. Stabilization of the demineralization process was observed in 5.9% of cases immediately after treatment and in 1.9% of cases after 18 months ($p>0.05$). There were no cases of WSL progression. Thus, WSL regression was observed significantly more often ($p<0.001$) than stabilization in all periods of observation (Table 20).

Table 20 – Results of treatment of deep enamel demineralization in children of the third group according to LF data

Observation period	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Significance of differences, p
	% (95% CI)	% (95% CI)	% (95% CI)
Immediately after treatment	92.3 (85.1-99.5)	7.7 (0.4-14.9)	<0.001
3 months	94.2 (87.9-100)	5.8 (0.0-12.1)	<0.001
6 months	96.1 (90.9-100)	3.8 (0.0-9.1)	<0.001
9 months	96.1 (90.9-100)	3.8 (0.0-9.1)	<0.001
12 months	98.1 (93.3-100)	1.9 (0.0-5.7)	<0.001
15 months	98.1 (93.3-100)	1.9 (0.0-5.7)	<0.001
18 months	98.1 (93.3-100)	1.9 (0.0-5.7)	<0.001

In the treatment of enamel demineralization extended into dentin, regression of WSL was observed immediately after treatment in all cases (Table 21).

Table 21 – Results of treatment of enamel demineralization extended into dentin in children of the third group according to LF data

Observation period	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
Immediately after treatment	100	0.0	0.0
3 months	100	0.0	0.0
6 months	7.7 (0.0-22.2)	92.3 (77.8-100)	0.0
9 months	30.8 (5.7-55.9)	38.5 (12.0-64.9)	30,8 (5.7-55.9)

12 months	38.5 (12.0-64.9)	61.5 (35.1-88.0)	0.0
15 months	23.1 (0.2-46.0)	53.8 (26.7-80.9)	23,1 (0.2-46.0)
18 months	15.4 (0.0-35.0)	76.9 (54.0-99.8)	7,7 (0.0-22.2)

Dynamic observation of children revealed that the values of LF indices gradually increased and after 18 months regression of WSL was registered in only 15.4% of cases (to the level of initial or deep demineralization indices - 7.7%, recovery - 7.7%), stabilization - 76.9%, progress - 7.7% ($p>0.05$). The obtained data substantiate the necessity of dynamic monitoring of patients after application of caries infiltration method for treatment of enamel demineralization extended into dentin in order to timely detect deterioration of LF indicators and application of other treatment methods.

The direction of changes in LF indices did not depend on the localization of WSL; after 18 months, the results of treatment in incisors, canines, premolars, and molars were approximately the same (Fig. 28).

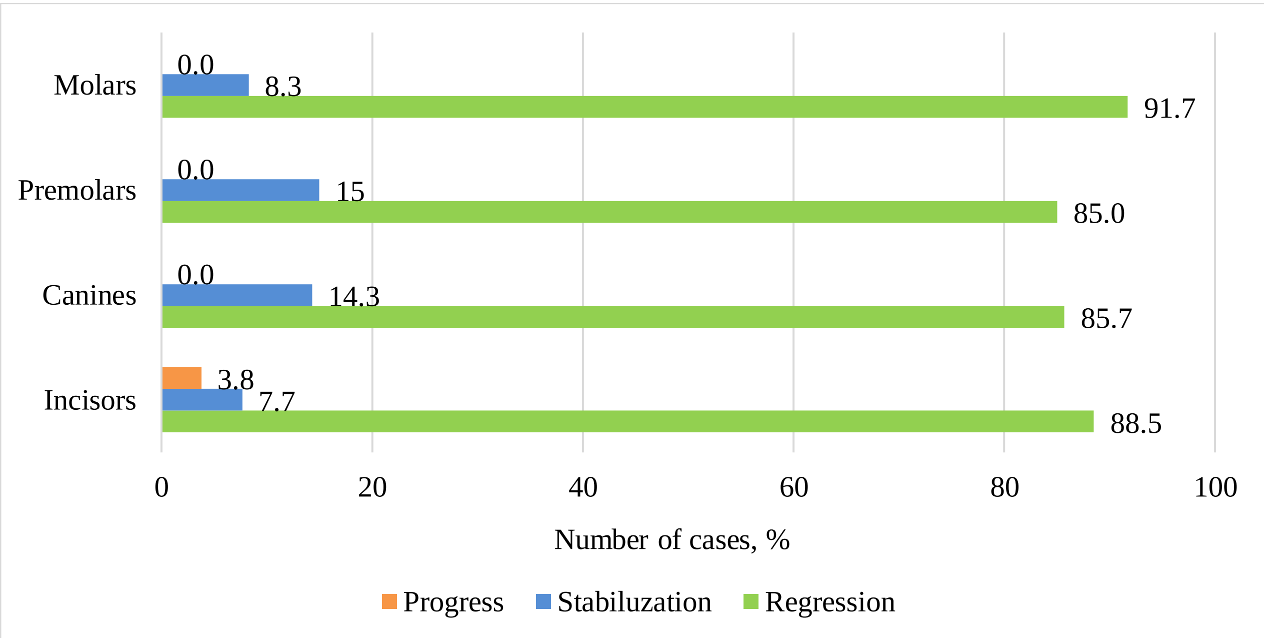

Figure 28 – Treatment results in the third group after 18 months depending on WSL localization

Thus, treatment outcomes in incisors, canines, premolars, and molars depended only on the depth of demineralization. In initial enamel demineralization, all outcomes were positive. In deep enamel demineralization, treatment outcomes were mostly positive, and in rare cases stabilization of the process was noted. In enamel demineralization extended into dentin, WSL regression was registered within 3 months after treatment, but after 18 months, stabilization of the process prevailed, regression was less common, and in some cases, progression of demineralization was noted.

Overall, regression of WSL was predominant in Group 3 at all follow-up periods: 97.0% (95% CI 93.6-100%) of cases immediately after treatment and 87.9% (95% CI 81.6-94.4%) after 18 months. Of these, 59.6% (95% CI 49.9-69.3%) of cases showed recovery of WSL, with LF values corresponding to those of healthy enamel. Stabilization of the process or progression of demineralization was observed significantly ($p<0.001$) less often, 3.0-14.0% and 0.0-4.0% of cases respectively (Fig. 29).

After application of the caries infiltration method for treatment of WSL in children, no carious cavity formation was detected (clinical efficiency of WSL treatment - 100%). All children had good oral hygiene and no increase in caries according to the ICDAS-II index. Since all children used fluoride toothpaste (1400-1500 ppmF) for regular oral hygiene, the data obtained once again confirm the caries-preventive role of fluorides.

Figure 29 – Directionality of changes in the state of WSL according to laser fluorescence indices during treatment of children of the third group

Thus, after the application of the caries infiltration method for the treatment of WSL in children, according to laser fluorescence data, were observed [23]:

- regression of WSL cases immediately after treatment in the majority of cases (97.0%);
- preservation of the achieved regression of WSL within 18 months in 87.9% of cases, of which compliance of LF indicators with healthy enamel in more than a half (59.6%) of cases;
- dependence of treatment results on the depth of enamel demineralization: at initial demineralization after 18 months the compliance of LF indicators with healthy enamel was 94.1% of cases, at deep demineralization – 50.0%, at enamel demineralization extended into dentin – 7.7%;
- similar treatment results in case of localization of WSL in different groups of teeth;
- absence of carious cavities formation during the whole period of observation.

The obtained data show the high efficiency of caries infiltration method for the treatment of WSL in permanent teeth in children, especially in the case of initial and deep enamel demineralization. After the treatment of enamel demineralization extended into dentin, dynamic monitoring using laser fluorescence is necessary in order to apply other methods of treatment in a timely manner in case of deterioration of WSL indicators.

4.2.3. Results of amelogenin peptide application

In Group 4, immediately after the application of amelogenin peptide, there were no changes in the LF indices of demineralization sites. Then there was a gradual decrease in the average values of LF indices, but only after 15 and 18 months the differences with the initial data became statistically significant: before treatment – 20.16±0.50, after 15 months – 18.56±0.57 ($p<0.05$), after 18 months – 17.82±0.58 ($p<0.01$), Table 22. Due to a small number (1.7%) of cases of enamel demineralization extended into dentin in this group, further, only the results of treatment of initial and deep enamel demineralization were analyzed separately.

At initial enamel demineralization in group 4, the differences between the mean values of LF indices before and after treatment became statistically significant only after 18 months: 17.59±0.32 and 15.85±0.56 respectively, p<0.01. In the treatment of deep enamel demineralization, the differences between LF indices, compared to the initial data, were statistically significant after 12 and 15 months (p<0.05), as well as after 18 months (p<0.01) after treatment: before treatment, the mean LF value was 23.79±0.56, after 12, 15 and 18 months 21.71±0.88, 21.33±0.87, and 20.54±0.89, respectively.

Table 22 – LF indices in the dynamics of treatment of WSL of different depth in children of the fourth group

Observation period	LF indices		
	Initial enamel demineralization	Deep enamel demineralization	Total
	M±m	M±m	M±m
Before treatment	17.59±0.32	23.79±0.56	20.16±0.50
Immediately after treatment	17.59±0.32	23.79±0.56	20.16±0.50
3 months	16.88±0.45	22.50±0.76	19.21±0.55
6 months	16.50± 0.49	22.25±0.79	18.88±0.57
9 months	16.71±0.57	22.04±0.84	18.91±0.59
12 months	16.65±0.61	21.71±0.88*	18.74±0.60
15 months	16.55±0.52	21.33±0.87*	18.56±0.57*
18 months	15.85±0.56**	20.54±0.89**	17.82±0.58**

*Significance of differences, compared to the original data, p<0.05; **p<0.01

In all groups of teeth in Group 4, a decrease in the values of LF indices was registered starting from 3 months after treatment (Table 23). However, statistically significant (p<0.05) differences between LF values before and after treatment were registered only in incisors and premolars after 18 months. In canines and molars, the differences between LF indices before and after treatment were not statistically significant (p>0.05) at all periods of observation.

Table 23 – LF indices during treatment depending on the localization of WSL in children of the fourth group

Observation period	LF indices			
	Incisors	Canines	Premolars	Molars
	M±m	M±m	M±m	M±m
Before treatment	19.06±0.78	20.08±0.89	21.10±1.23	22.00±1.27
Immediately after treatment	19.06±0.78	20.08±0.89	21.10±1.23	22.00±1.27
3 months	18.33±0.81	19.08±0.83	19.75±1.41	21.67±1.22
6 months	17.78±0.62	19.08±0.79	19.25±1.40	21.56±1.29
9 months	17.50±0.85	19.92±1.00	19.10±1.38	21.44±1.41
12 months	17.28±0.91	20.08±1.17	18.75±1.30	21.22±1.49
15 months	17.56±0.78	19.36±1.13	18.70±1.32	20.89±1.56
18 months	16.72±0.70*	18.45±1.24	17.42±1.23*	20.11±1.53

*Significance of differences, compared to the original data, $p<0.05$

The degree of decrease in LF indices after treatment in Group 4 gradually increased, from 4.7% after 3 months to 11.6% after 18 months. A similar picture was observed in the treatment of initial enamel demineralization (increase from 4.0% after 3 months to 9.9% after 18 months). In the treatment of deep enamel demineralization, the degree of decrease in LF indicators was slightly higher, increasing from 5.4% after 3 months to 13.7% after 18 months (Fig. 30). However, the differences between the indicators were not statistically significant.

The degree of decrease in the values of LF indices in separate groups of teeth tended to increase starting from 3 months after application of amelogenin peptide (Fig. 31).

The trend of decreasing LF values after amelogenin peptide application was most pronounced in premolars (6.4% after 3 months and 17.4% after 18 months) and incisors (3.8% and 12.3%, respectively), less pronounced in canines (4.9% and 8.1%, respectively) and molars (1.5% and 8.6% respectively). However, the differences between tooth groups were not statistically significant ($p>0.05$).

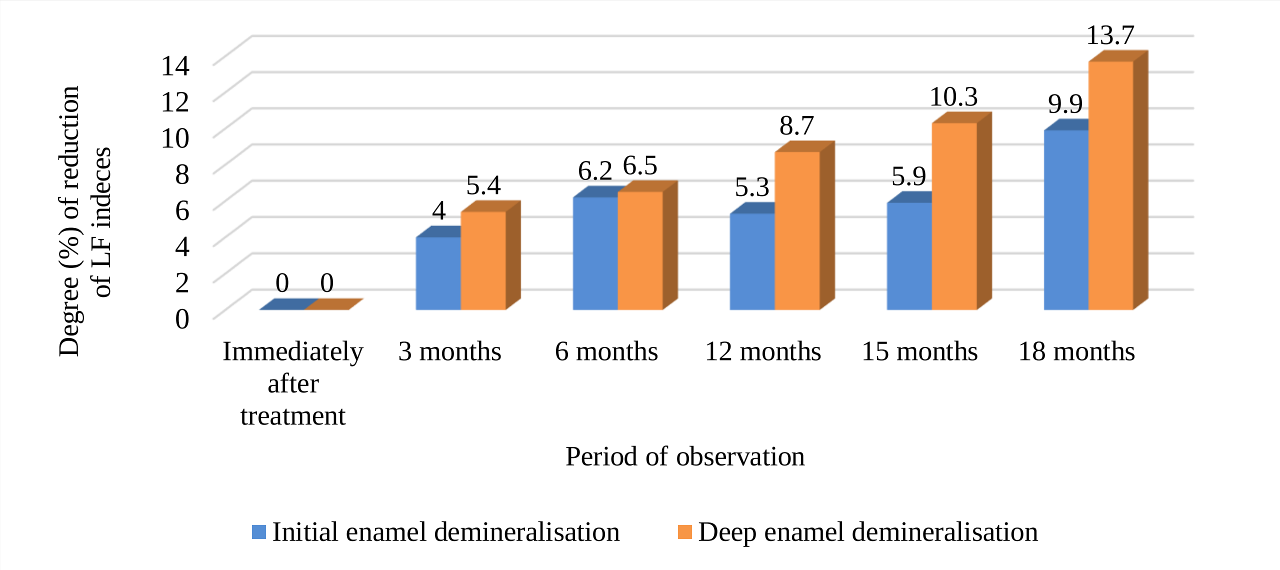

Figure 30 – Degree of reduction of LF indicators, compared to the initial data, in the dynamics of treatment of initial and deep enamel demineralization in children of the fourth group

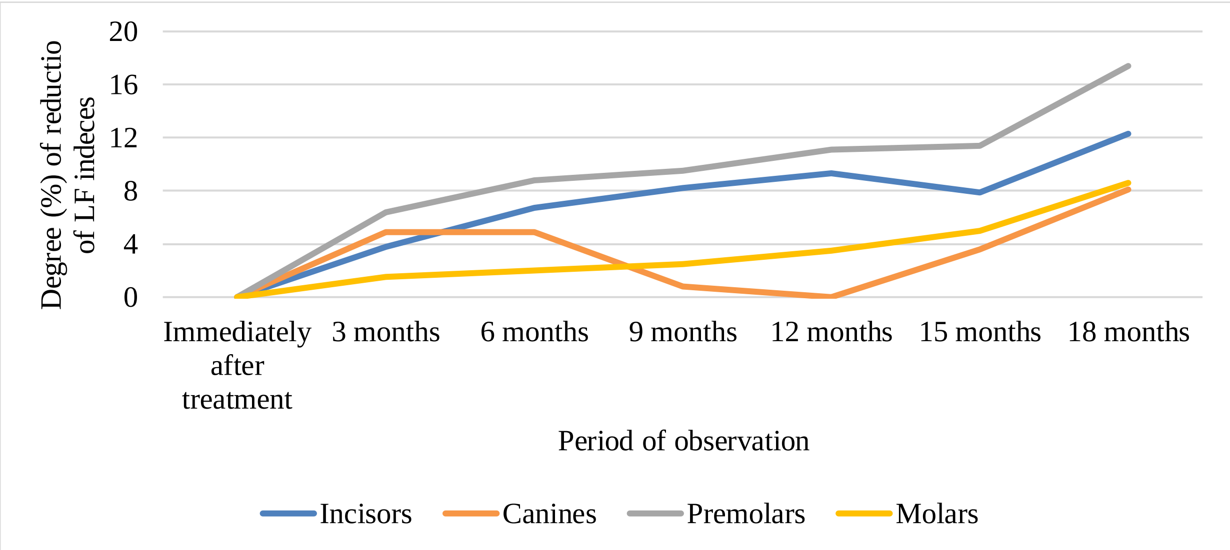

Figure 31 – Degree of decrease of laser fluorescence indices, compared to the initial data, depending on the localization of WSL in children of the fourth group

Treatment outcomes of initial enamel demineralization in group 4 were determined, according to LF data, starting from the third month after treatment: regression of WSL – 35.3% (95% CI 19.2-51.4%), stabilization – 50.0% (95% CI 33.2-66.8%), progression – 14.7% (95% CI 2.8-26.6%), Table 24.

Table 24 – Treatment results of initial enamel demineralization in group 4 children according to LF data

Observation period	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3 months	35.3 (19.2-51.4)	50.0 (33.2-66.8)[c]	14.7 (2.8-26.6)[c]
6 months	47.1 (3.3-63.9)[b]	38.2 (21.9-54.5)[c]	14.7 (2.8-26.6)[b,c]
9 months	52.9 (36.1-69.7)[a,b]	26.5 (11.7-41.3)[a]	20.6 (7.0-34.2)[b]
12 months	55.9 (39.2-72.6)[a,b]	26.5 (11.7-41.3)[a]	17.6 (4.8-30.4)[b]
15 months	58.8 (42.3-75.3)[a,b]	23.6 (9.3-37.9)[a]	17.6 (4.8-30.4)[b]
18 months	64.7 (48.6-80.8)[a,b]	26.5 (11.7-41.3)[a]	8.8 (0.0-18.3)[b]

[a]Significance of differences between the frequencies of “regression” and “stabilization”, $p<0.05$

[b]Significance of differences between the frequencies of “regression” and “progress”, $p<0.01$

[c]Significance of differences between the frequencies of “stabilization” and “progress”, $p<0.05$

Further, the incidence of positive treatment outcomes (regression) of initial enamel demineralization in Group 4 gradually increased to 64.7% (95% CI 48.6-80.8%) after 18 months. Of these, recovery of WSL was noted in 11.8% of cases. Starting from 9 months after treatment, stabilization of WSL was significantly ($p<0.05$) less frequent than regression. After 18 months, stabilization of WSL was found in 26.5% (95% CI 11.7-41.3%) of cases. Progression of demineralization was less frequent than other treatment outcomes, the frequency of progression of initial enamel demineralization at different follow-up periods ranged from 8.8% to 20.6% ($p>0.05$).

When deep enamel demineralization was treated in group 4, WSL regression was more common than stabilization or progression at all follow-up periods (Table 25): after 18 months, 75.0% (95% CI 57.7-92.3%) versus 20.8% (95% CI 4.6-37.1%) and 4.2 (95%

CI 0.0-12.2%), respectively (p<0.01). v recovery was not recorded in any case.

Table 25 – Directionality of changes in enamel condition according to laser fluorescence indices during treatment of deep enamel demineralization in children of the fourth group

Observation period	WSL status after treatment (number of cases, %)		
	Regression	Stabilization	Progress
	% (95% CI)	% (95% CI)	% (95% CI)
3 months	50.0 (30.0-70.0)[b]	45.8 (25.9-65.8)[c]	4.2 (0.0-12.2)[b,c]
6 months	58.3 (38.6-78.1)[b]	37.5 (18.1-56.9)[c]	4.2 (0.0-12.2)[b,c]
9 months	62.5 (43.1-81.9)[a,b]	25.0 (7.7-42.3)[a]	12.5 (0.0-25.7)[b]
12 months	66.7 (47.8-85.5)[a,b]	16.7 (1.8-31.6)[a]	16.7 (1.8-31.6)[b]
15 months	70.8 (52.6-89.0)[a,b]	16.7 (1.8-31.6)[a]	12.5 (0.0-25.7)[b]
18 months	75.0 (57.7-92.3)[a,b]	20.8 (4.6-37.1)[a]	4.2 (0.0-12.2)[b]

[a]Significance of differences between the frequencies of “regression” and “stabilization”, p<0.01

[b]Significance of differences between the frequencies of “regression” and “progress”, p<0.001

[c]Significance of differences between the frequencies of “stabilization” and “progress”, p<0.05

The results of WSL treatment in different tooth groups had some differences: regression of WSL was more frequent in premolars (85.0%; 95% CI 69.3-100%), stabilization in incisors and molars (33.3% each), and progression in canines (25.0%; 95% CI 0.5-49.5%), Fig. 32. However, the differences between the treatment outcomes in the different tooth groups were not statistically significant (p>0.05).

Overall, the incidence of positive treatment outcomes in group 4 increased from 41.4% (95% CI 28.7-54b1%) after 3 months to 68.9% (95% CI 57.0-80.8%) after 18 months, p<0.01. Of these, only 6.8% (95% CI 0.4-13.2%) of cases showed recovery of WSL (matching LF values to those of healthy enamel). The frequency of WSL stabilization decreased from 48.3% (95% CI 35.4-61.2%) after 3 months to 24.2% (95% CI 13.2-35.2%) after 18 months, $p<0.01$ (Fig. 33).

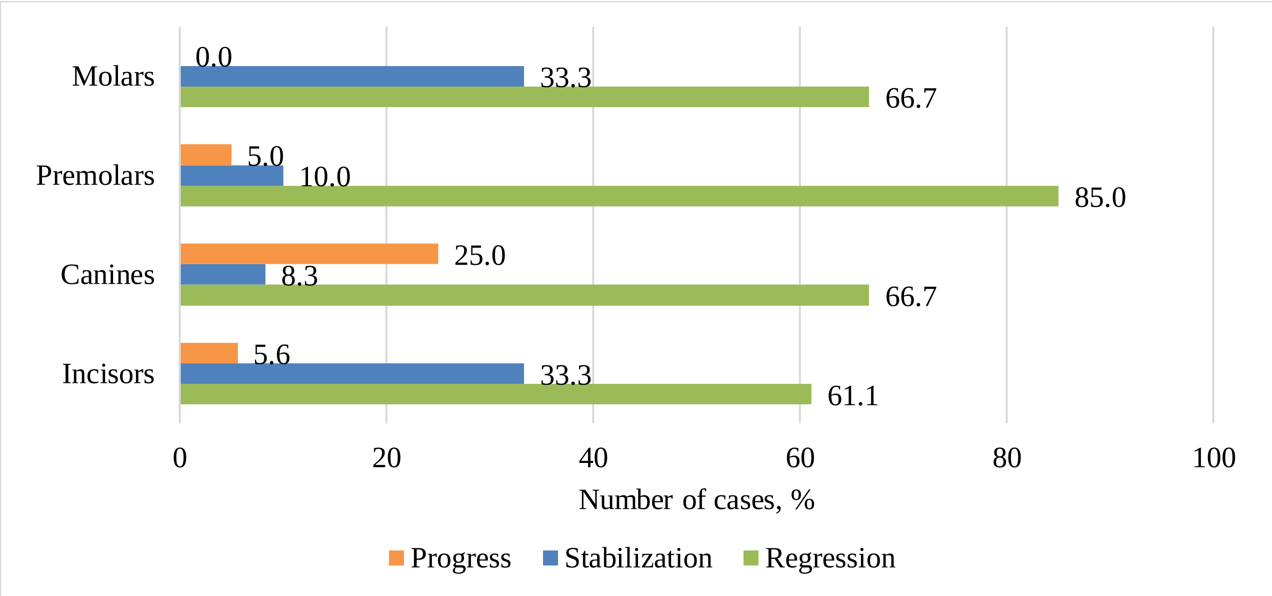

Figure 32 – Treatment outcomes in fourth group after 18 months depending on WSL localization

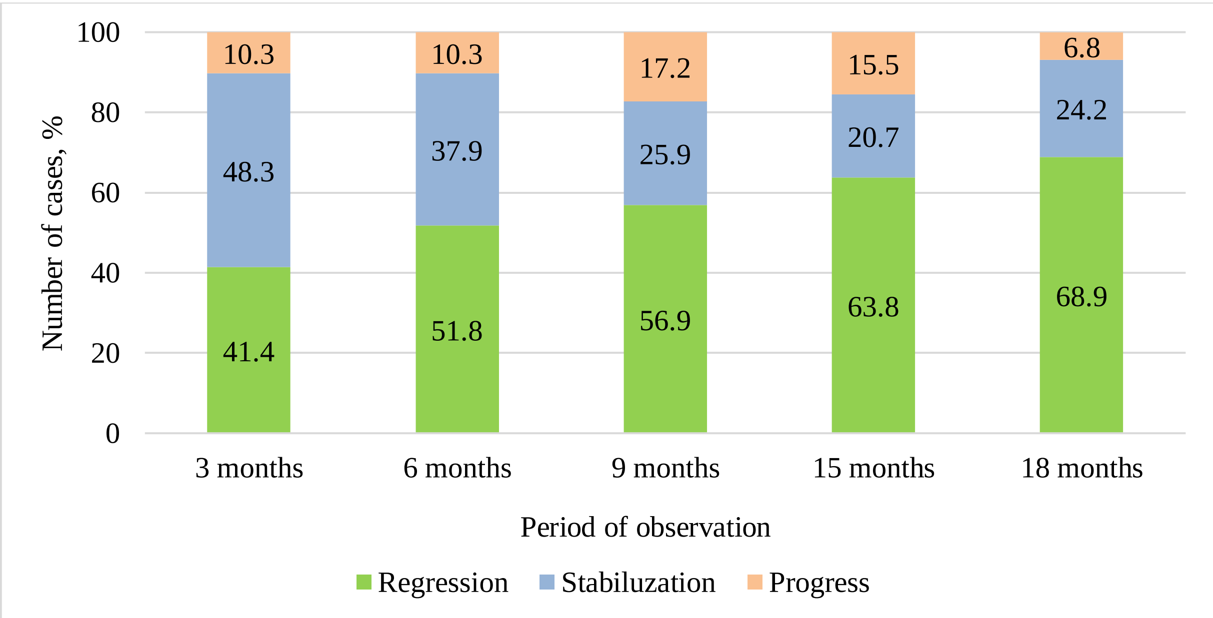

Figure 33 – Directionality of changes in WSL state according to LF indicators during treatment of children of the fourth group

Progress of demineralization in group 4 was less frequent ($p<0.001$) than regression at all periods of observation, and less frequent ($p<0.05$) than stabilization after 3, 6 and

18 months of observation. After 9, 12 and 15 months, the differences between the frequencies of stabilization and progression of WSL were not statistically significant (p>0.05). Only one case of treated v in group 4 had a carious cavity diagnosed after 18 months, which was 1.7% of cases (95% CI 0.0-5.0%). The clinical efficacy of treatment was 98.3%.

All children had a good level of oral hygiene during the follow-up period, no new carious lesions were registered according to the ICDAS-II index, only the level of one carious lesion changed from code 2 to code 5. Overall, a good result in caries prevention was achieved by regular use of regular fluoride toothpaste.

Thus, when using amelogenin peptide for the treatment of WSL, according to laser fluorescence data, there were [22,28]:

- increase in the regression rate of WSL from 41.4% after 3 months to 68.9% after 18 months;
- no significant differences in the results of treatment of WSL in different groups of teeth;
- progression of WSL in 6.9-17.2% of cases in different periods of observation, which led to carious cavity formation in 1.7% of cases in 18 months after treatment;
- low frequency (6.8%) of WSL recovery 18 months after treatment.

Thus, the use of amelogenin peptide caused regression of WSL in most cases, but rarely led to enamel restoration. Given the large fluctuations in the frequency of progression of demineralization during 18 months of follow-up, it is advisable to dynamically monitor WSL using laser fluorescence for timely connection of more effective remineralization agents.

CHAPTER 5. COMPARATIVE EVALUATION OF THE EFFICIENCY OF TREATMENT OF LOCAL ENAMEL DEMINERALIZATION OF PERMANENT TEETH IN CHILDREN AND DISCUSSION OF RESEARCH RESULTS

High clinical efficiency of treatment of WSL of permanent teeth in children was observed in all observation groups, which was expressed in the prevention of carious cavity formation within 18 months: 100% in groups 1-3 and 98.3% in group 4. However, objective methods of enamel condition assessment revealed clear differences between the groups.

5.1. Efficiency of treatment of initial enamel demineralization

After treatment of initial enamel demineralization after 18 months, the mean LF values decreased significantly ($p<0.001$) in group 3 and reached the values of healthy enamel: 5.45±0.87 (Fig. 34).

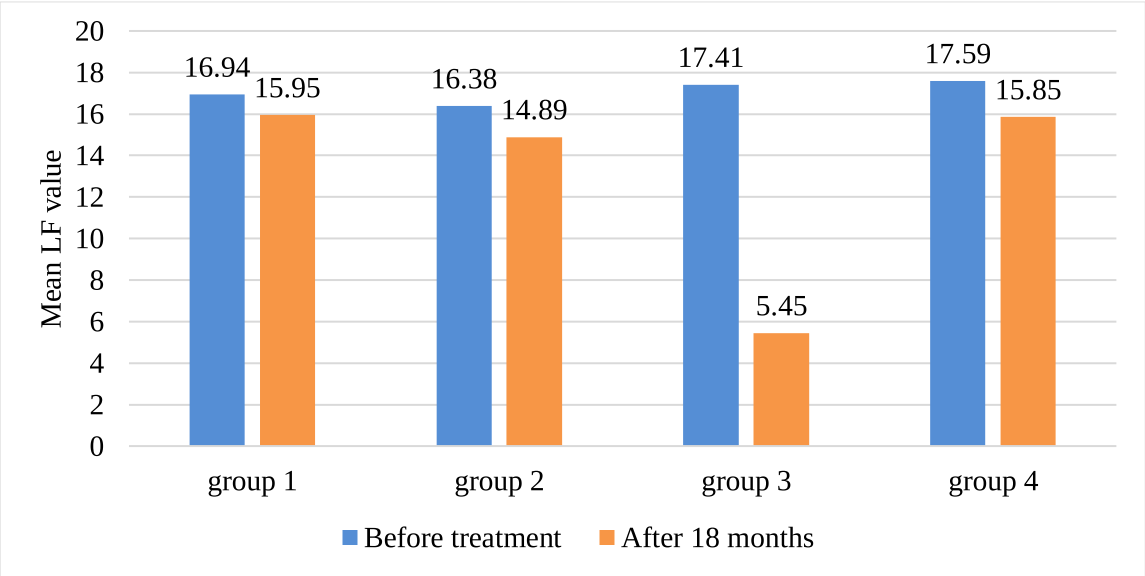

Figure 34 – LF values in the observation groups 18 months after the beginning of treatment of initial enamel demineralization

Compared to group 3, the corresponding LF values in groups 1, 2 and 4 were 2.7-2.9 times higher and were still within the limits of initial enamel demineralization: 15.95±0.29, 14.89±0.26 and 15.85±0.56, respectively. The differences of LF indices between groups 1 and 2 were statistically significant (p<0.01), between groups 1 and 4, 2 and 4 were not significant (p>0.05). Thus, LF indices reflected remineralization of WSL, which after 18 months was most pronounced in group 3.

The study of the outcomes of treatment of initial demineralization showed that, according to LF data, in group 3 in almost all cases (94.1%) there was a recovery of WSL (LF indices corresponded to healthy enamel). In the other groups the frequency of WSL recovery was significantly (p<0.001) lower: group 1 – 11.6%, group 2 – 24.7%, group 4 – 11.8% (Fig. 35).

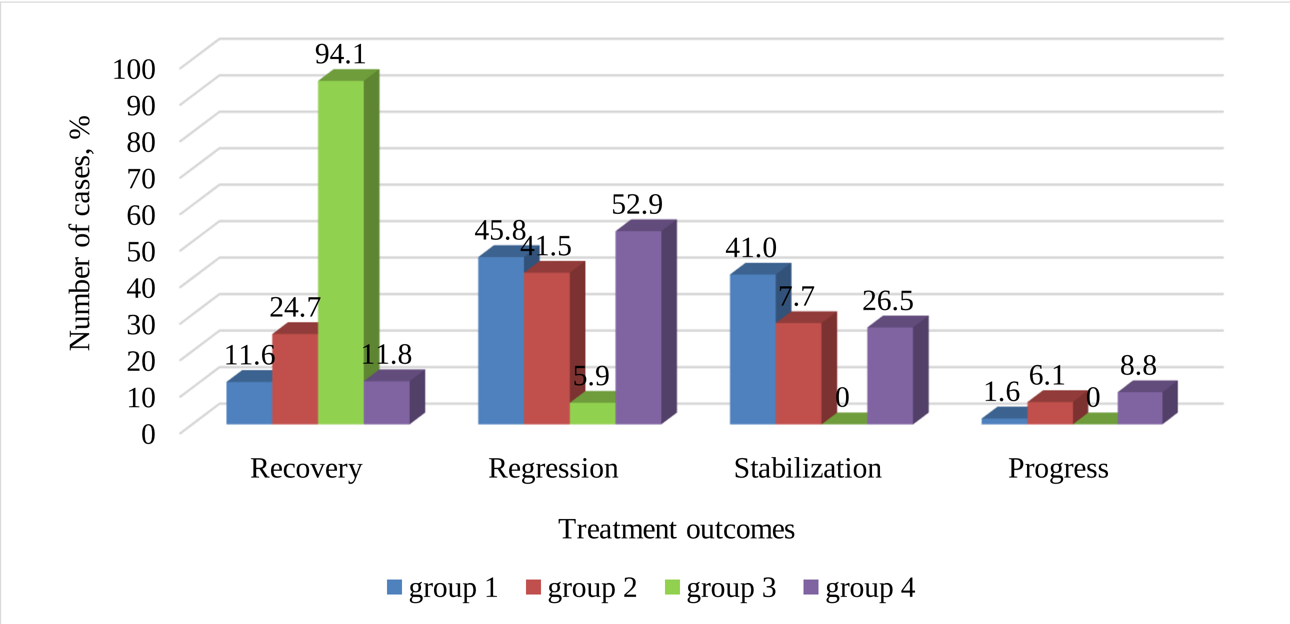

Figure 35 – Treatment outcomes of initial enamel demineralization after 18 months in the observation groups

Between the frequency of WSL regrowth in groups 1 and 2 the differences were statistically significant (p<0.05), between groups 1 and 4, 2 and 4 it was insignificant (p>0.05). The regression rate of demineralization in groups 1, 2 and 4 was 45.8%, 41.5% and 52.9%, respectively, p>0.05. No progression of initial demineralization was found in group 3, while in groups 1, 2 and 4 it occurred in single cases (1.6%, 6.1% and 8.8% respectively, p>0.05). Only in group 4 the progression of initial demineralization in one case led to the formation of a carious cavity.

Thus, in the case of initial enamel demineralization, non-invasive treatment methods of WSL led to the restoration (remineralization) of WSL only in a small number of cases, but 2.1 times more often after periodic application of fluoride varnish (group 2) than after the course application of toothpastes with increased fluoride content (group 1). At the same time, the number of cases of WSL regression was approximately the same in groups 1 and 2, and the progression of demineralization, though occurring in isolated cases, was more frequent in group 2 than in group 1. The obtained data emphasize the importance and necessity of repeated courses of non-invasive therapy with fluoride preparations to maintain the achieved results, prevent progression of initial enamel demineralization and formation of carious cavities.

Among microinvasive treatment methods, caries infiltration (group 3) had significantly better results than amelogenin peptide (group 4). The caries infiltration method provided restoration of initial demineralization in most cases (8 times more often in group 3 than in group 4), whereas after application of amelogenin peptide in many (35.3%) cases only suspension (stabilization) or even progression of enamel demineralization process was observed. Apparently, the laser fluorescence method gives a more accurate assessment of the WSL state, revealing unfavorable trends after treatment, whereas visual assessment of the color and size of the demineralization focus in the form of a white spot, applied in the study by Brunton P.A. et al., showed only positive results of peptide application [92]. In addition, our data correlate with the results of the study by Solovieva J.V. et al., 2019, which in adult patients did not reveal the elimination of enamel demineralization processes after the application of amelogenin peptide [60].

Thus, the results of microinvasive treatment of initial enamel demineralization of permanent teeth in children by caries infiltration were significantly better than noninvasive treatment. At the same time, non-invasive treatment using fluoride gave better results than the use of amelogenin peptide [47].

5.2. Efficiency of treatment of deep enamel demineralization

In children with deep WSL of permanent teeth in all observation groups there was a high clinical efficiency of treatment, expressed in the prevention of carious cavities formation during 18 months of observation in 100% of cases.

After treatment of deep enamel demineralization after 18 months, LF values decreased significantly ($p<0.001$) in group 3 and approached the upper limit of healthy enamel values: 13.86±0.77 (Fig. 36).

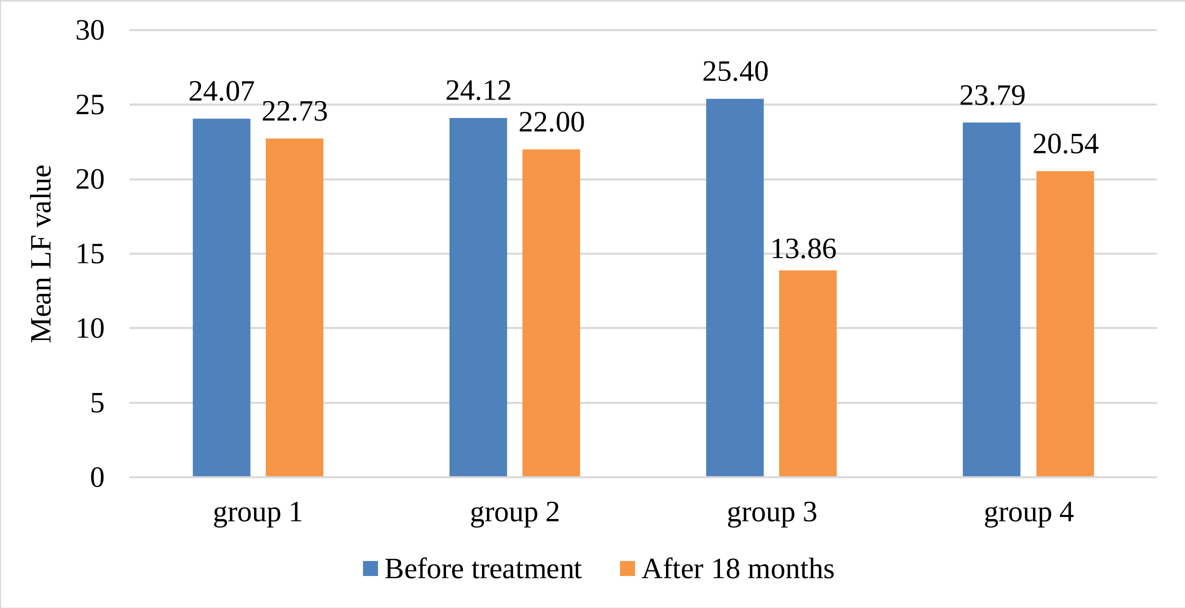

Figure 36 – LF values in the observation groups 18 months after the start of treatment for deep enamel demineralization

The corresponding LF values in groups 1, 2 and 4 decreased, but remained within the values of deep demineralization at approximately the same level (22.73±0.29, 22.00±0.33 and 20.54±0.89, respectively, $p>0.05$), and were 1.5-1.6 times higher than in group 3.

The study of the outcomes of treatment of deep demineralization showed that, according to LF data, in group 3 in half (50.0%) of the cases there was a recovery of WSL. There were no such cases in the other groups (Fig. 37).

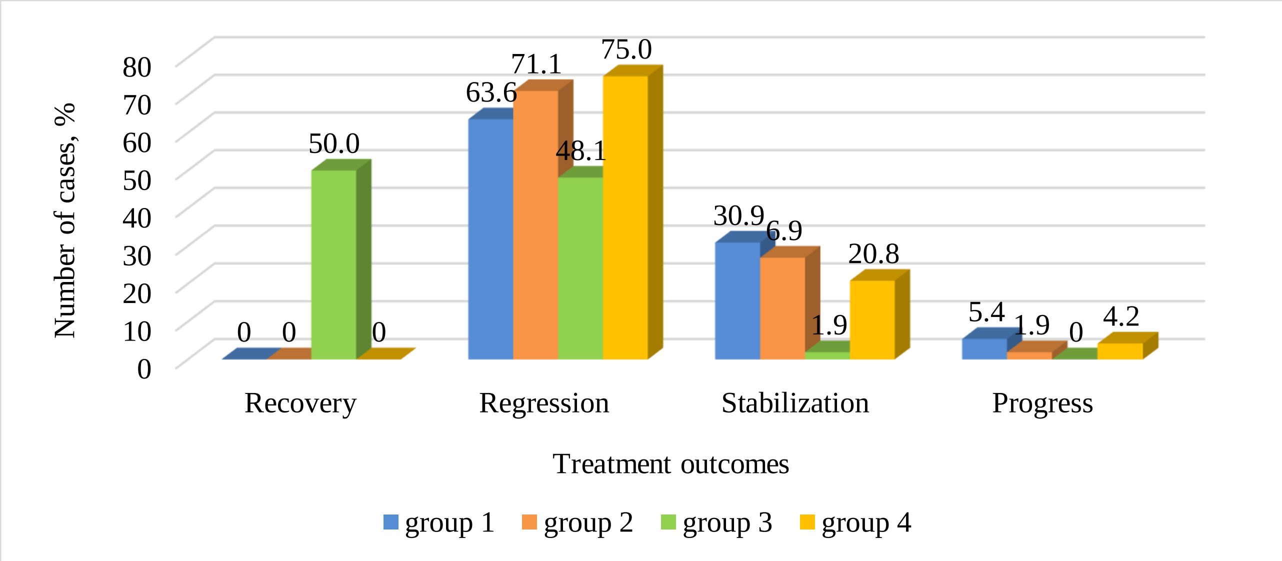

Figure 37 – Treatment outcomes of deep enamel demineralization after 18 months in the observation groups

In groups 1, 2 and 4, regression of WSL was more frequent (63.6%, 71.1% and 75.0%, p>0.05) and stabilization was less frequent (30.9%, 26.9% and 20.8%, respectively, p>0.05). In group 3, in half of the cases, the outcome of treatment of deep demineralization was assessed as recovery, so regression and stabilization of WSL were less frequent (48.1% and 1.9%, respectively) than in the other groups. Further progression of deep enamel demineralization was found only in groups 1, 2 and 4 in single cases (5.4%, 1.9% and 4.2%, respectively, p>0.05). The obtained data on the results of the caries infiltration method correlate with the results of the study by Paris S. et al., 2020, which showed the high efficiency of the method in reducing the progression of WSL, compared to non-invasive therapy [166].

Thus, during the treatment of deep enamel demineralization with non-invasive methods, LF indices decreased more pronouncedly with fluoride varnish (group 2) than with the use of toothpaste with increased fluoride content (group 1), but in no case in both groups reached the values of healthy enamel. Progression of demineralization was more frequent in group 1 than in group 2. However, there were no statistically significant differences (p>0.05) between all parameters of groups 1 and 2.

Microinvasive methods of treatment of deep enamel demineralization gave different results: the use of infiltration method (group 3) was significantly more effective than the use of amelogenin peptide (group 4).

The infiltration method also gave statistically significantly better results of treatment of deep enamel demineralization than non-invasive methods of treatment with fluoride. Only after caries infiltration LF indices in half of cases corresponded to the indices of healthy enamel. At the same time, regression of WSL was slightly more frequent with amelogenin peptide than with fluoride toothpaste and fluoride varnish, although the differences were not statistically significant.

5.3. Efficiency of treatment of enamel demineralization extended into dentin

Comparative assessment of the results of treatment of enamel demineralization extended into dentin according to LF data revealed certain differences between the groups (Fig. 38). In 18 months after the beginning of treatment, the greatest decrease in LF indices was revealed in group 3, the average LF value approached the upper limit of the index corresponding to the initial enamel demineralization – 20.76±1.38. In groups 1 and 2 LF indices also decreased, but the average LF values were closer to the upper limit of the index of deep enamel demineralization: 27.00±0.73 and 28.57±1.36 respectively, $p>0.05$.

Thus, the mean value of LF in group 3 18 months after treatment was statistically significantly ($p<0.001$) lower than the same values in groups 1 and 2.

When studying treatment outcomes, it was found that only in Group 3, 7.7% of cases showed recovery of WSL and LF values corresponded to healthy enamel. In other groups, there were no such results (Fig. 39). At the same time, WSL regression was detected in all (100%) cases of treatment in groups 1 and 2, whereas in group 3 - only in 7.7% of cases. WSL stabilization was observed in 76.9% of cases in group 3, and progression of demineralization was observed in 7.7% of cases. In groups 1 and 2, neither stabilization nor progression of WSL, according to laser fluorescence data, was observed.

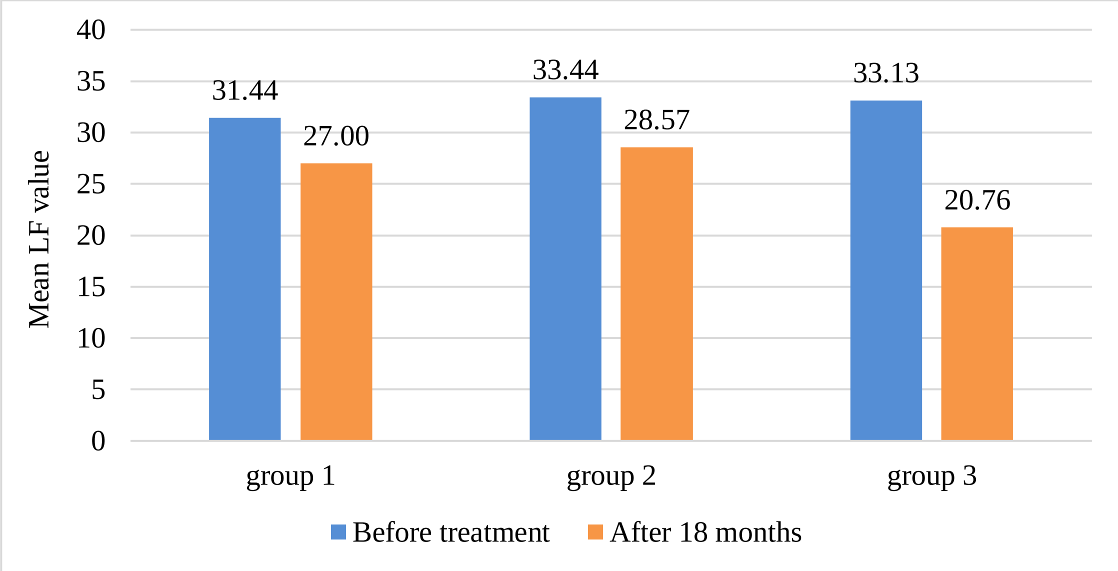

Figure 38 – LF values in the observation groups 18 months after the start of enamel demineralization extended into dentin

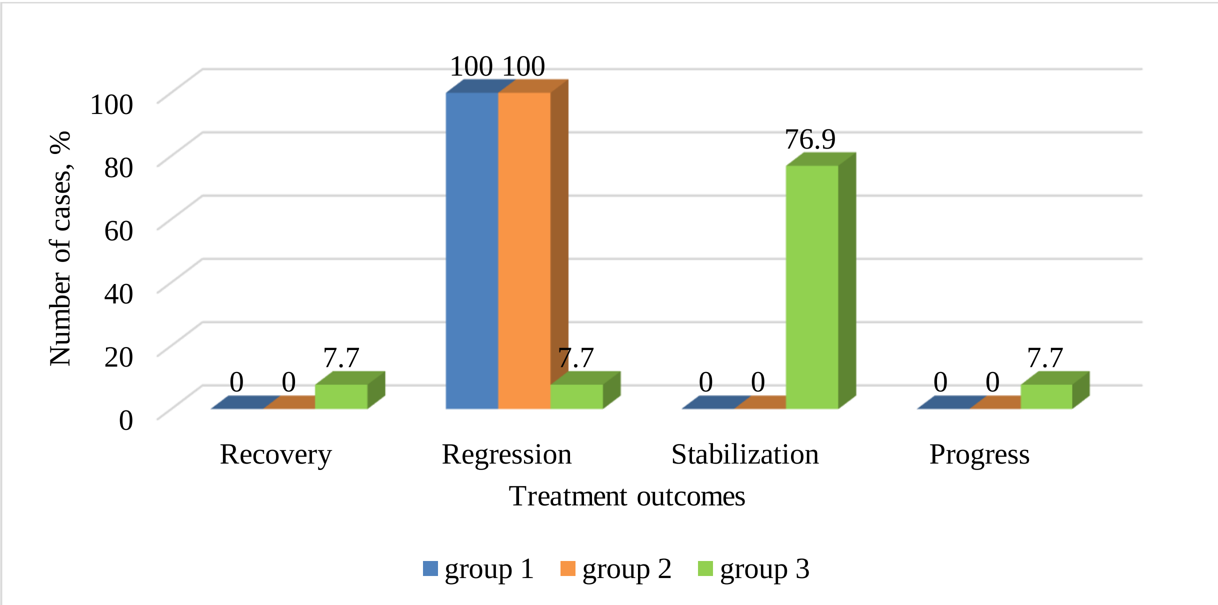

Figure 39 – Outcomes of enamel demineralization extended into dentin treatment after 18 months in the observation group

Thus, it should be recognized that none of the observation groups achieved the desired results of enamel demineralization extended into dentin treatment. When non-invasive methods of treatment were applied, very slow regression of demineralization was observed, LF indices decreased to the values of deep enamel demineralization. In none of the cases was it possible to achieve recovery - complete remineralization of WSL.

The results of using toothpaste with increased fluoride content and fluoride varnish were approximately the same. Apparently, only regular course application of these non-invasive methods of treatment can provide stability of results of enamel demineralization extended into dentin treatment and prevention of carious cavities formation.

When using the microinvasive infiltration method, only in a small number of cases, recovery or regression of WSL was observed. In most cases, stabilization of LF parameters was registered, and in 7.7% progress of demineralization was observed. Therefore, in the treatment of enamel demineralization extended into dentin by infiltration method, it is necessary to dynamically monitor patients with control of WSL state using laser fluorescence for timely decision-making on the need for more invasive methods of treatment.

The obtained data correlate with the conclusions of Makarova N.E. and Vinnichenko Y.A., 2017, who consider the issue of indications for the use of methods and means of treatment depending on the depth of demineralization of dental hard tissues unresolved [40]. Perhaps, the improvement of treatment results of enamel demineralization extended into dentin can be achieved by combining methods of non-invasive remineralization and caries infiltration, the successful application of which is reported in the study of Doğu Kaya B. et al., 2024, in-vitro [112].

5.4. Comparative integral assessment of results local enamel demineralization treatment

Figure 40 shows the outcomes of treatment of WSL in the observation groups. It was found that the greatest amount of WSL recovery (according to LF data), regardless of the depth of demineralization, was observed in group 3, the least - in groups 1 and 4. WSL progression was observed most often in group 4.

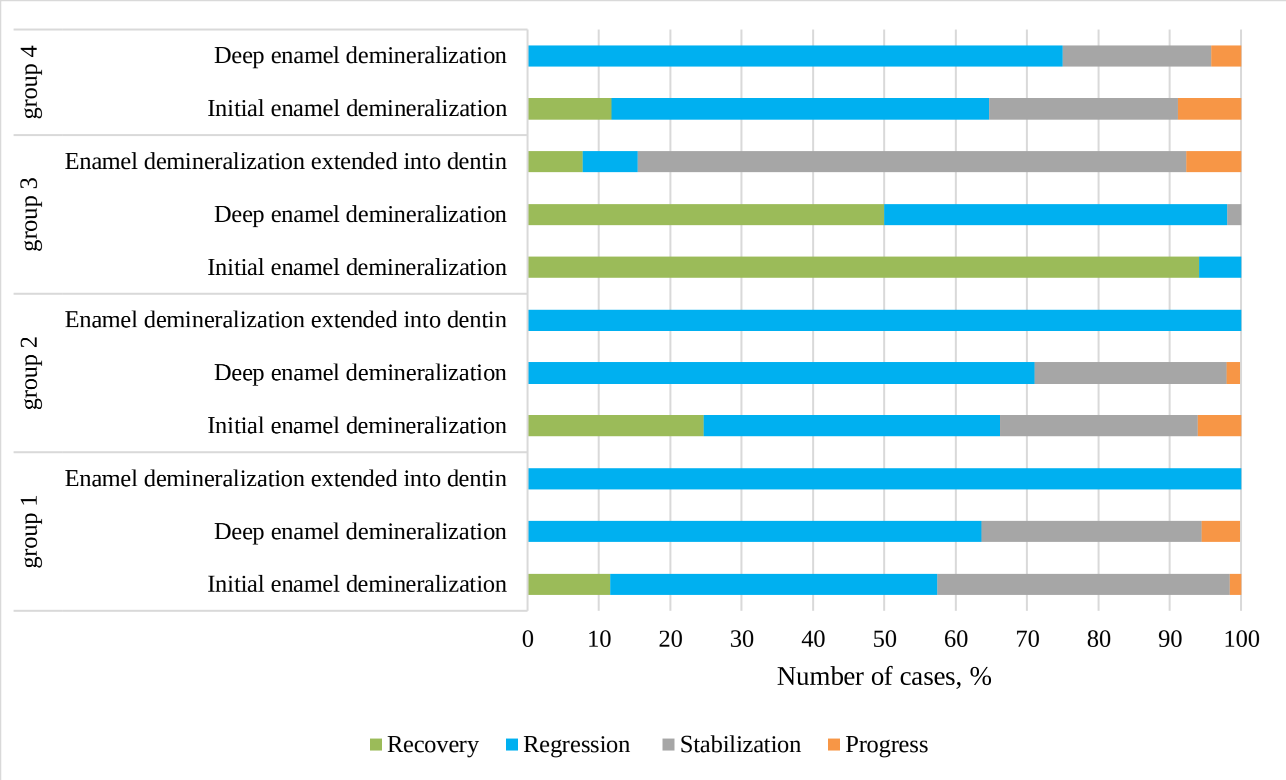

Figure 40 - Outcomes of treatment of WSL of various depths after 18 months in the observation groups

Comparative integral evaluation of the results of enamel demineralization treatment after 18 months was carried out in 4 groups according to the following criteria of WSL recovery and WSL progression. The results of the integral evaluation are presented in Table 26.

Table 26 – Rank evaluation of the results of enamel demineralization treatment after 18 months in the observation groups

Group	Ranking of WSL treatment outcomes			Final rank
	Initial	Deep	Sum of ranks	
1	5.5	7.0	12.5	3
2	5.0	5.0	10.0	2
3	2.0	2.0	4.0	1
4	7.5	6.0	13.5	4

According to the results of integral evaluation it was found that the best results of enamel demineralization treatment were obtained in group 3 – the first rank place. The second rank was in group 2, the third rank was in group 1 and the fourth rank was in group 4.

Comparative integral assessment of the results of enamel demineralization extended into dentin treatment performed in groups 1-3 according to similar criteria did not reveal advantages of any of the groups. In terms of WSL recovery, Group 3 ranked first, in terms of WSL progression this group ranked third, and the ranks of Groups 1 and 2 were the same.

Aesthetic result was observed only in study group 3 in the treatment of initial, deep demineralization and enamel demineralization extended into dentin (Fig. 41-43).

Figure 41 – Result of treatment of initial enamel demineralization by infiltration method

Figure 42 – Result of treatment of deep enamel demineralization by infiltration method

Figure 43 – Result of treatment of enamel demineralization extended into dentin by infiltration method

Thus, in the treatment of initial and deep enamel demineralization, the best results were obtained after the application of the caries infiltration method, followed by fluoride varnish, toothpaste with increased fluoride content and amelogenin peptide. In the treatment of enamel demineralization extended into dentin, the use of fluoride varnish and toothpaste with increased fluoride content promoted regression but not recovery of WSL, whereas in caries infiltration there was mainly stabilization of WSL, and in a small number of cases there was recovery, regression and progression of demineralization [47].

CONCLUSIONS

1. A high (87.9%; 95% CI 85.1-90.7%) prevalence of local enamel demineralization was found in children aged 7-16 years. About one-third of the children had 10 or more teeth with WSL. The number of teeth with WSL increased with increasing age of the children. There was a direct correlation between the number of foci of enamel demineralization and the state of oral hygiene ($r=0.52$), the level of DMF ($r=0.53$), and occlusal pathology ($r=0.43$).

2. In children, local enamel demineralization developed equally often on the teeth of the upper and lower jaws. WSL localization in premolars and molars was more frequent than in incisors and canines. The smallest number of WSLs was localized in the incisors of the mandible. According to laser fluorescence data, half (50.1%, 95% CI 45.5- 54.7%) of the lesions were related to initial enamel demineralization, slightly less frequently (42.8%, 95% CI 38.2-47.4%) demineralization spread to the enamel depth and significantly less frequently to the superficial dentin layers (7.1%, 95% CI 4.7-9.5%). Differences in the depth of demineralization in different groups of teeth were not statistically significant.

3. The use of non-invasive methods of treatment of WSL showed high clinical efficiency (100% prevention of carious cavity formation) during 18 months of observation. In the treatment of initial enamel demineralization, the restoration of WSL occurred more often when using fluoride varnish than toothpaste with increased concentration of fluoride: 24.7% and 11.6% respectively, $p<0.05$. In the treatment of deep enamel demineralization and enamel demineralization extended into dentin there was no recovery of WSL, only regression of demineralization was observed. Progression of WSL was observed in single cases (1.6-6.1%).

4. High clinical efficiency of microinvasive methods of treatment of WSL was revealed: prevention of carious cavities formation in 100% cases when using caries infiltration, and 98.3% one when using amelogenin peptide. When using the infiltration method, restoration of WSL at initial demineralization occurred in 94.1% cases, at deep

enamel demineralization in 50.0% cases, at enamel demineralization extended into dentin in 7.7% cases. When amelogenin peptide was used, recovery of WSL occurred only in the treatment of initial enamel demineralization in 11.8% cases.

5. According to laser fluorescence data, microinvasive caries infiltration method gave significantly better results of treatment of initial and deep enamel demineralization (ranked first), compared to non-invasive treatment methods. Non-invasive treatment of WSL using fluoride varnish and fluoride-rich toothpaste gave better results compared to the use of amelogenin peptide (rank 2, 3 and 4, respectively). When demineralization spread to dentin, non-invasive treatment methods contributed to the regression of demineralization, while the infiltration method resulted mainly in stabilization and, in some cases (7.7%), in the progression of demineralization.

PRACTICAL RECOMMENDATIONS

1. The choice of the method of treatment of WSL in permanent teeth in children should be carried out taking into account the depth of demineralization. In case of initial and deep enamel demineralization, the most effective method is caries infiltration, which gives the greatest number of immediately restored WSL cases after treatment and during 18 months of follow-up.

2. The use of fluoride varnish and toothpaste with increased fluoride content for the treatment of enamel demineralization, especially extended into dentin, should be carried out for a long time, since the improvement of demineralized enamel occurs gradually. In the process of treatment, objective monitoring of the state of WSL is necessary, which allows to detect the progression of demineralization timely.

3. Single application of amelogenin peptide is not recommended for the treatment of WSL in children, as it gives the highest number of cases of progression of demineralization, compared to other treatment methods.

4. The method of laser fluorescence is expedient to use in the process of treatment of demineralization of enamel of permanent teeth in children to control the state of WSL. The method allows comparing the current LF values with the initial data and determining the outcome of treatment:

- recovery of WSL (LF indices correspond to healthy enamel);
- regression of the demineralization process (LF indices decrease);
- stabilization of WSL state (LF values do not change);
- progress of demineralization (LF indices increase).

LIST OF ABBREVIATIONS

VolgSMU	- Volgograd State Medical University
CHI	- compulsory health insurance
CI	- confidence interval
CPP- ACP	- casein-phosphopeptide-amorphous calcium phosphate
DIFOTI	- Digital Imaging Fiber-Optic Transillumination
dmf	- index of the intensity of caries of primary teeth, characterized by the number of "d" – decay (carious), “m” – missing (extracted) and "f" - filled teeth
DMF	- index of the intensity of caries of permanent teeth, characterized by the number of "d" – decay (carious), “m” – missing (extracted) and "f" - filled teeth
ECM	- Electronic Caries Monitor
F	- Fluoride
FSBEI HE	- Federal State Budgetary Educational Institution of Higher Education
FOTI	- Fiber-Optic Trans-Illumination
ICDAS	- International Caries Diagnosis and Assessment System
ICD-10	- The 10^{th} revision of the International Classification of Diseases
LF	- laser fluorescence
M	- mean value
m	- error of mean value
MEI SS	- Municipal Educational Institution Secondary Schools
Nano-GAP	- nano-hydroxyapatite
NIDIT	- Near infrared digital imaging transillumination
OHI-S	- Oral Hygiene Index-Simplex
p	- significance of differences

ppm - parts per million

QLF - Quantitative Light-induced Fluorescence

r - Pearson correlation coefficient

WHO - World Health Organization

WSL - White spot lesion

χ^2 - chi-squared

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