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PECULIARITIES OF NASAL IRRIGATION IN ACUTE VIRAL RHINOSINUSITIS

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The article describes the problems of choosing a solution for the nasal cavity irrigation in acute viral rhinosinusitis. The purpose of the study was to establish the effectiveness of restoring the physiological function of nasal structures by adding to the traditional (3% NaCl solution) saline solution, 6% N-acetylcysteine solution in combination with classical treatment regimen of acute rhinosinusitis. It was found that this combination can effectively restore the mucociliary transport of the nasal mucosa and thus reduce the risk of complications or the migration of the disease into a bacterial form. As a result of the study, we concluded that the combination of N-acetylcysteine with saline solution in the treatment of acute viral rhinosinusitis and improving both the objective and subjective condition of patients.

Key words: acute viral rhinosinusitis, irrigation, N-acetylcysteine, saline solutions.

The work is a fragment of the research project "Development of new medical technologies in the diagnosis and treatment of the upper respiratory tract pathologies", state registration No. 0115U006761.

Acute rhinosinusitis is one of the most common diseases in the world. According to statistics, every seventh person in Europe is diagnosed with rhinosinusitis every year, and the number of detected cases is constantly increasing. Given the data of the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS 2020) [6], the incidence of acute rhinosinusitis has increased over the past 20 years almost 2 times and ranges from 6% to 15% of the population.

The mucociliary clearance is the first and most important line of airway protection in the respiratory system against destructive pathogens and harmful environmental factors, which requires a coordinated cilia beating and the appropriate composition and amount of mucus on the epithelium surface, which provides the mucus transport into the oropharynx. Changes in this process make a person susceptible to nasal diseases [11].

Nasal mucus is a heterogeneous adhesive viscoelastic material that is released as a product of goblet epithelial cells and mucous cells of the submucosal glands. It is divided into two layers: gel and sol, which has a low viscosity, close to the water or plasma viscosity. The viscosity of the gel is about 1,000 times higher than the viscosity of the sol [2]. It is believed that the nasal gel transport with viruses, bacteria, allergens that have settled on it, becomes possible only after the rupture of transverse disulfide bonds between glycoproteins [1].

The main factors in the respiratory diseases pathogenesis, including rhinosinusitis, include a violation of the mucociliary transport mechanisms [1], as well as with a decrease in the number of intact active ciliated cells and an increase in goblet cells [2].

The main generally accepted principle of treatment is the fastest recovery of physiological action of nasal structures. Irrigation of the nasal cavity with saline solutions is one of the most popular methods of treatment [9], which helps to improve both the subjective well-being of the patient and potentiate the recovery rate.

Acetylcysteine, due to the presence of sulfhydryl groups, protects mucous cells from free radicals both by direct reaction with them and by supplying cysteine for glutathione synthesis [3]. Nasal mucus becomes more dense and viscous. The mucolytic action of N-acetylcysteine allows NaCl to overcome the viscosity of the gel, i.e. serves as a mean of delivering salt to the mucous epithelium.

Many species of bacteria live in colonies and form protective biofilms, which are a factor in the microorganisms resistance. N-acetylcysteine has been shown to inhibit the formation of biofilms [4, 12].

There is controversy about the actual effectiveness of mucolytic agents prescription in the treatment of rhinosinusitis. They are usually prescribed in clinical practice to reduce the viscosity and improve the mucus clearance, which helps to restore the physiological mechanisms of the paranasal sinuses and nasal epithelial barrier [5, 8].

The purpose of the study was to substantiate the effectiveness of N-acetylcysteine administration in combination with hypertonic saline in the treatment of patients with acute viral rhinosinusitis.

Materials and methods. On the basis of ENT Department of Poltava Regional Clinical Hospital in 2019-2020, employees of the Department of Otorhinolaryngology and Ophthalmology of the Ukrainian Medical Stomatology Academy performed a study of the effectiveness of the drug Flu-Acyl Rino in patients with a clinical diagnosis of acute viral rhinosinusitis. A total of 56 patients were observed in the study, which were divided into two groups: experimental (29 patients) and control (27 patients).

Inclusion criteria: 1) Age – 18 years and older; 2) The clinical diagnosis of acute viral rhinosinusitis.

Exclusion criteria: 1) Allergy to N-acetylcysteine; 2) Any surgery in the nasal cavity in the last 3 months; 3) The diagnosis of systemic nasal disease (e.g. cystic fibrosis, Kartagener's syndrome); 4) Inability to give informed consent form due to consciousness impairment; 5) Inability to adhere to the prescribed treatment or the specified visits.

All study participants were included only after signing an informed consent form. We used a classic scheme for the treatment of patients in the control group, including: nasal lavage with hypertonic (3%) saline [10] 2 doses in each nostril 3 times a day, topical corticosteroids (Mometasone furoate) 2 doses in each nostril 2 times a day. Patients in the experimental group received classical therapy, in which the standard hypertonic saline solution was replaced by the drug Flu-Acyl Rino (3% hypertonic NaCl solution + 6% N-acetylcysteine) – administration in the form of 2 doses of spray in each nostril 3 times a day.

Assessment of treatment methods on the basis of subjective signs of general well-being was performed using the Sino-Nasal Outcome Test (SNOT-22) [7]. The patient's health status questionnaire was performed on the day of the first visit, as well as on days 3 and 7. Symptoms will be presented by the sum of all criteria on a 5-point scale for each in SNOT-22.

Objective data were collected using the Karl Storz, Storz telecam II, Hopkins II endoscope with 0° angle of view, during the endoscopic examination at scheduled visits.

The study of the mucociliary transport function in the nasal mucosa was performed using a saccharin test with sodium saccharin. A piece of saccharin up to 1 mm³ was applied to the inferior nasal concha 1 cm away from its anterior end. The time from the moment of indicator application on the mucous membrane of the nasal cavity to the sweet taste sensation in the mouth was recorded. This method allows to obtain an integrated assessment of the state of mucociliary transport, as the result of the study depends on the rheological properties of mucus and motor activity of the ciliated epithelium. To determine the “conditional” rate of mucociliary clearance of the nasal mucosa by saccharin test, control studies of this indicator were performed in 32 practically healthy volunteers without significant anomalies of intranasal structures, who underwent a single study.

Determination of the state of nasal respiration in the studied patients was carried out by measuring the nasal airway resistance (NAR) by the method of active posterior rhinomanometry. The study was performed according to the developed regulations twice for the entire period of observation: 1 – during hospitalization; 2 – on the 7th day.

Clinical trial data were statistically processed by the method of variation statistics using Student's test, determination of arithmetic mean values of indices, confidence intervals and probability values (p) was performed using the computer programs Microsoft Excel 2016 and Statistica 13. The data in the tables and figures are presented as mean values and their standard deviations ($M \pm \sigma$) and standard errors ($M \pm m$).

Results of the study and their discussion. At the time of the initial examination, all patients in the study groups had subjective and objective signs that are characteristic of the diagnosis: Acute viral rhinosinusitis. Symptoms that could indicate the transition of this stage of the disease to the form of bacterial rhinosinusitis with signs of mucositis were not observed in any case. If viscous mucus with signs of stagnation was detected in the area of the osteomeatal complex during endomicroscopy, the patients underwent computed tomography examination of the paranasal sinuses. No subjective and objective signs of purulent rhinosinusitis were detected in any of the studied patients. In patients who had undergone polynosotomy for inflammatory diseases of the paranasal sinuses at various times in the past, endoscopy included examination of the sinuses through existing artificial openings. However, in any of the cases no excessive exudation in the sinuses was observed.

The condition of the nasal mucosa, which was assessed by endoscopic examination, suggested that the degree of its edema and abnormal discharge did not completely obstruct the patency of the nasal sinuses. This, in our opinion, was the basis for the assertion of the correctness of the study of the mucociliary transport.

According to the data obtained during the saccharin test (fig. 1), the speed of the mucociliary transport on the first day was 24.75 ± 5.83 minutes, for the experimental group and 22.85 ± 5.58 minutes – for the control group; on the third day – 16.68 ± 3.76 minutes in the experimental group and 19.6 ± 3.71 min

in the control group; on the seventh day – 11.15 ± 1.66 min in the experimental group and 14.53 ± 2.82 min in the control group.

Thus, already on the 7th day of treatment was determined a statistically significant difference in the functioning of the mucociliary transport on the indicators of the saccharin test between patients of the experimental and control groups ($p = 0.000001$), and indicators of recovery of mucociliary clearance activity in the experimental group are more dynamic, which is a statistically significant difference. If we compare the indicators with the conditional norm – 13.17 ± 4.72 minutes (fig. 2), we can conclude about the normalization of motor activity of the cilia of the ciliated epithelium immediately after the end of the pathological factors manifested against the background of acute rhinosinusitis, and this allows us to consider it as one of the main criteria for clinical recovery. In almost healthy volunteers there was a tendency to increase the time of mucociliary clearance (MCC) on the background of active smoking.

Analysis of the dynamics of changes in MCC showed that the greatest impact on its level had the manifestations of acute inflammatory process in the nasal cavity and paranasal sinuses. Thus, in patients in whom acute viral rhinosinusitis had signs of polysinusitis or pansinusitis, i.e. the frontal and posterior groups of paranasal sinuses were involved in the viral process at once, mucociliary clearance index was the highest in the preliminary study. Its level was also the highest in the study carried out on the 7th day and significantly exceeded the level of mucociliary clearance of patients with limited acute rhinosinusitis. The level of mucociliary clearance was also affected by the presence in the patient of intranasal structure disorders, such as nasal septum deviation, hypertrophy of the posterior ends of the inferior nasal concha, and so on.

In patients of the 1st study group, the dynamics of MCC significantly differed in patients with acute polysinusitis. Thus, against the background of administration of 3% hypertonic NaCl solution with 6% N-acetylcysteine, already on the 7th day of the study, the MCC in the experimental group was significantly different from patients in the control group, receiving traditional therapy, and the rate of MCC recovery to normal values was significantly faster ($p \leq 0.05$).

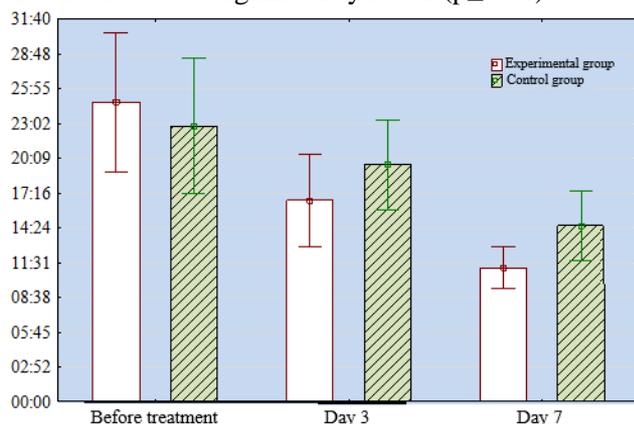


Fig. 1. Results of MCC study using saccharin test in patients of the studied groups; $M \pm \sigma$, min: sec.

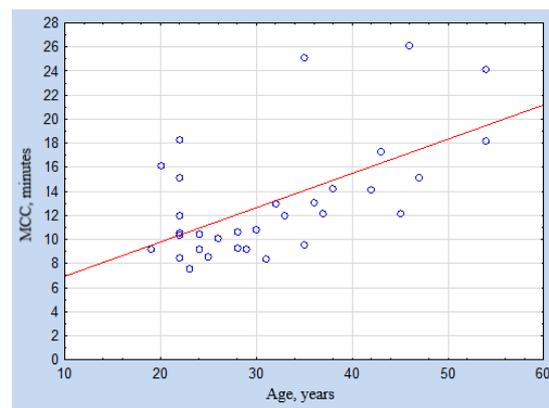


Fig. 2. Results of MCC study using saccharin test in almost healthy individuals.

For adequate interpretation of the obtained objective data, it is also necessary to correlate the results with the subjective condition of patients. The SNOT-22 scale allows to do it most effectively, as it covers all aspects of the patient's subjective well-being. This allows us to more accurately evaluate the objective data obtained during the visits, such as the saccharin test or posterior active rhinomanometry. It also allows for a more adequate assessment of the results obtained during endoscopic examination of the patient, and better assess the dynamics of the disease at all stages of treatment. This is crucial for achieving quality recovery of the patient because it allows timely response to changes and make decisions as quickly as possible on the treatment plan correction.

When performing the survey on SNOT-22 (fig. 3), on the first day there were worse results in the experimental group – 37.79 ± 8.22 points at 34.44 ± 7.45 points in the control one. On the third day, the obtained data were 33.55 ± 7.94 points in the experimental group and 29.89 ± 7.99 points in the control group. On the seventh day, the results for the experimental group were 11.66 ± 2.45 points and 12.67 ± 3.43 points in the control group. The data obtained in the first days of the disease do not reflect a significant improvement, which is the expected result for the start of treatment, as the disease process is in the acute phase and is not subject to significant, clinically significant correction.

From the fourth day onwards, patients' subjective well-being improved rapidly in both groups. On the 7th day of treatment, there was no statistically significant difference in SNOT-22 between patients in

the experimental and control groups ($p = 0.211626$). These data indicate a rapid reduction in the inflammatory process, as similar improvements in the disease are observed in patients during the convalescence period, the results of the survey on day 7 of the disease are expected changes in subjective well-being. This may indicate that it is the inflammatory process of the mucous membrane of the nasal cavity and paranasal sinuses that has a decisive influence on all the subjective signs observed by patients during the disease. The intoxication syndrome specifically attributed to the bacterial form of rhinosinusitis is not characteristic of the viral or post-viral form of the disease. Therefore, during treatment it is necessary to pay considerable attention to accelerating the inflammatory process convalescence, which in turn will not only improve the patient's well-being but also significantly accelerate recovery.

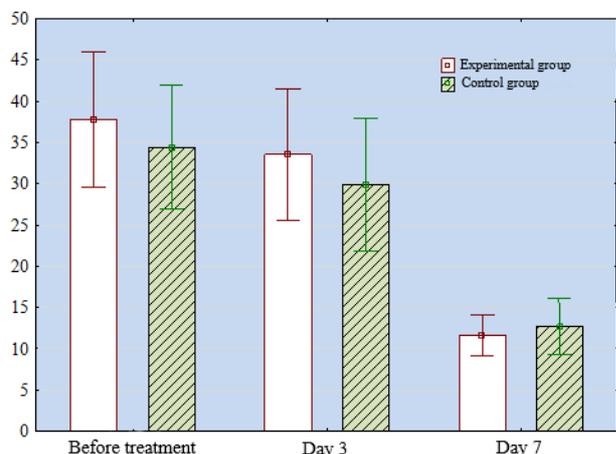


Fig. 3. The results of the patients' examination in the study groups; $M \pm \sigma$, SNOT 22 points.

decongestants was completely over, and had no effect on the results. Comparing the values of this indicator with the level of the conditional norm of nasal air resistance in healthy people, which corresponds to the value from 0.3 to 1.5 kPa/l *s, it can be concluded that on the 7th day of treatment in patients of both groups there is a normalization of nasal breathing index. Such a large range of indicators of the NAR level indicates a fairly high adaptive reserve of nasal breathing in different people, which depends not only on the architecture of the nasal cavity, but also on the physiological characteristics of the organism as a whole. The NAR magnitude was characterized by a significant amplitude, which indicates a fairly large adaptive reserve of the level of nasal breathing in different people, which significantly depends on the architecture of the nasal cavity. The difference in the A^1/A^2 coefficients between the control and experimental groups set out in table 1 has an improvement in the experimental and control groups, and does not have a statistically significant difference on day 7 of the study ($p = 0.294571$).

Rhinomanometry made it possible to study the dynamics of changes in the NAR in patients of the experimental and control groups, as shown in the table.

The results of the study of the NAR status by performing active posterior rhinomanometry revealed the magnitude of violations of this indicator in patients of different study groups. The greatest influence on the state of nasal breathing, in addition to the acute inflammatory process, had functional disorders of intranasal structures.

Due to technical aspects, not all patients of the studied groups underwent rhinomanometry before treatment and on the 7th day. At the time of the survey, the effect of previously used

Table 1

The level of NAR according to the results of active posterior rhinomanometry in patients of the studied groups (kPa/l*s)

Group	Before treatment		Day 7		Coefficient A^1/A^2
	n	$A^1 \pm m$	n	$A^2 \pm m$	
Experimental group	18	2.28 ± 0.13	14	1.27 ± 0.11	1.79
Control group	16	2.08 ± 0.09	11	1.41 ± 0.07	1.47

When reviewing the materials, it was noted that the indicators of rhinomanometry correlated with the changes obtained during endoscopic examinations of the nasal cavity, so we can talk about improving the objective state of its physiological functions. To determine the effectiveness of the topical action of the drugs used on the mucous membrane of the nasal cavity and to control the possibility of side effects, all patients underwent endoscopic examination at different times. In none of the cases any local manifestations of allergy or irritant effects of the studied drugs were observed.

During this study, we reported one case of a mild allergic reaction to the drug Flu-Acyl Rino in the form of a rash on the skin of single pink blisters, accompanied by itching. This patient was immediately excluded from this study and treated according to a standard protocol that takes into account allergic reactions to drugs. The effects of the allergic reaction completely disappeared after discontinuation of the drug the next day and then no longer bothered the patient.

The results of the study of mucociliary transport confirm the thesis that during the active inflammatory process of the mucous membrane, the significant gel viscosity violates the rate of mucus drainage containing pathological agents, and in turn prolongs inflammation of the mucous membrane as

described in Kunelska N.L. [2]. The results of the saccharin test confirm that the property of N-acetylcysteine to break the disulfide cross-links between glycoproteins, which in turn reduces the mucus viscosity and facilitates drainage of the nasal cavity, is of paramount importance to reduce the inflammatory process as reflected in the work Aldini G., Altomare A. et.al [3].

The results of the assessment of the patients' condition correlate with the results of clinical studies using the mucolytic agent N-acetylcysteine, which are described in the work of Bahtouee M., Monavarsadegh G. et.al. [4] and in our previous study on the treatment of acute rhinosinusitis [1]. Also, given the correlation between the results of well-being in patients in our study and the work of Macchi A, Terranova P, Castelnovo P. [5], the presented method of treatment will help optimize approaches to the choice of therapy, as it will allow less frequent use of systemic non-steroidal anti-inflammatory drugs, instead of choosing topical forms of drugs that have a better safety profile to improve the subjective symptoms in patients with acute rhinosinusitis.

Conclusions

After the study, it can be concluded that when using a hypertonic solution in combination with N-acetylcysteine (Flu-Acyl Rino) in the experimental group there was an objective indicators improvement (statistically significant difference on the 7th day of treatment according to the saccharin test, $p = 0.000001$), both the patient's subjective well-being and objective treatment outcomes improved, which in turn contributed to a more effective recovery of the patient compared to classical therapy, which uses saline solutions without additional components. Based on the study, we can recommend Flu-Acyl Rino as a front-line therapy for the treatment of acute viral rhinosinusitis in combination with standard therapy, to obtain a more pronounced effect of restoring the physiological function of the nasal structures.

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Реферати

ОСОБЛИВОСТІ ІРИГАЦІЇ НОВОЇ ПОРОЖНИНИ ПРИ ГОСТРИХ ВІРУСНИХ РИНОСИНУСИТАХ

Безшапочний С.Б., Лобурець В.В., Лобурець А.В., Джиров О.Р., Подовжний О.Г.

У статті описані проблеми вибору розчину для зрошення порожнини носа при гострих вірусних риносинуситах. Метою дослідження була перевірка ефективності відновлення фізіологічної роботи носових структур при додаванні до традиційного (3% розчин NaCl) сольового розчину, 6% розчину N-ацетилцистеїну в поєднанні з класичною схемою терапії гострих риносинуситів. Було встановлено, що дана комбінація дозволяє ефективно відновити роботу мукоциліарного транспорту слизової оболонки носа і таким чином зменшити ризики виникнення ускладнень процесу або переходу захворювання в бактеріальну форму. В

ОСОБЕННОСТИ ИРРИГАЦИИ НОВОЙ ПОЛОСТИ ПРИ ОСТРЫХ ВИРУСНЫХ РИНОСИНУСИТАХ

Безшапочный С.Б., Лобурец В.В., Лобурец А.В., Джиров А.Р., Подовжний А.Г.

В статье описаны проблемы выбора раствора для орошения полости носа при острых вирусных риносинуситах. Целью исследования была проверка эффективности восстановления физиологической работы носовых структур при добавлении к традиционному (3% раствор NaCl) солевому раствору, 6% раствора N-ацетилцистеина в сочетании с классической схемой терапии риносинуситов. Было установлено, что данная комбинация позволяет эффективно восстановить работу мукоцилиарного транспорта слизистой оболочки носа и таким образом уменьшить риски возникновения осложнений процесса или перехода заболевания в

результаті дослідження ми зробили висновок про ефективність комбінації N-ацетилцистеїну з сольовим розчином в лікуванні гострого риносинуситу та покращенні як об'єктивного, так і суб'єктивного стану пацієнтів.

Ключові слова: гострий вірусний риносинусит, іригація, N-ацетилцистеїн, сольові розчини.

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бактериальную форму. В результате исследования мы пришли к выводу об эффективности комбинации N-ацетилцистеина с соевым раствором в лечении острого риносинусита и улучшении как объективного, так и субъективного состояния пациентов.

Ключевые слова: Острый вирусный риносинусит, ирригация, N-ацетилцистеин, солевые растворы.

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FREQUENCY, STRUCTURE, AND DYNAMICS OF ADENTIA DEVELOPMENT AND RELATED SECONDARY DENTAL DEFORMATIONS AMONG YOUNG PEOPLE

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As part of the epidemiological survey study on dental health in young people, the data of clinical dental examination of 137 boys and 142 girls, the students of dental faculty of Vinnytsya National Pirogov Memorial Medical University, were analyzed. For comparative analysis of the structure of adentia the data of epidemiological study held in 2010 on the the Department of Orthopedic Dentistry were used. Statistical processing of the results was carried out in the Statistica 6.0 licensed package. The comparison of structure and frequency of adentia of young population in 2010 and 2019 revealed a decrease of frequency of this pathology. Change of the structure of adentia toward the relief of orthopedic pathology due to the significant decrease of adentia in the form of edentulous areas located posterior to the remaining natural teeth according to the topography should also be emphasized. A significant frequency of secondary deformations in the examined group with the prevalence of horizontal form was identified. In the structure of adentia there is a ninefold prevalence of adentia in the posterior area above the anterior one, a significant prevalence of adentia of the lower jaw.

Key words: missing teeth, epidemiology, secondary deformations.

The work is a fragment of the research project "Optimization of diagnostics, orthopedic treatment and prevention of jaw and facial system pathology", state registration No. 0119U103951.

In all age groups adentia occupies one of the dominant places in the structure of dental diseases [4]. Pulling teeth out in itself reduces the effectiveness of the masticatory function and, much more importantly, affects the morphology, development, and function of the entire dentition system [1]. At least one tooth pulled out triggers a whole cascade of changes and adjustments aimed at offsetting the loss of dentition integrity. These changes affect both the local adaptive mechanisms and the general ones and also cause psycho-emotional disorders [6].

Identifying indicators of the quality of life in dentistry as general indicators of a comprehensive assessment of the patient's condition [8] is often used to evaluate the effectiveness of treatment of the dentition system pathology, including adentia [12]. A great number of patients pay attention to function declining, disturbance of emotional and social well-being [10]. Concerns about appearance and behavior change aimed at masking defects of dentition are noted [13]. Aesthetics are the dominant motivating factor that encourages a patient to receive orthopedic or orthodontic dental care.

In adentia cases, there is a local functional sub- or decompensation of periodontal tissue of teeth around the defects of dental arches or opposite teeth. Along with inflammatory-destructive diseases of periodontal tissue that destroy its structure, missing tooth inevitably lead to the emergence of secondary deformations of dental arches [2].

The purpose of the study was to determine the frequency, structure, and dynamics of the development of adentia and related secondary deformations of dental arches among young people.

Material and methods. As a part of the epidemiological survey of dental health of young people, the data from clinical dental examination of 137 boys aged 17 to 21 years and 142 girls aged 16 to 20 years, the students of dental faculty of Vinnytsya National Pirogov Memorial Medical University, were analyzed.

The results of clinical examination were entered into a specially designed "patient's examination dental record", which displayed the whole spectrum of dental status.

The types of secondary deformations were determined according to the classification of Havrylov E. I. (1966) and Lebedenko N. Yu. (2007) [2]; dentition defects were determined according to Kennedy classification [1].

Determination of the minimum sufficient number of surveyed was carried out according to the recommendations of WHO [15].