

сывороточного уровня мочевой кислоты выше 380 ммоль/л (в среднем ~ 500 ммоль/л), которые недавно начали терапию аллопурином по любой причине, с верифицированным ответом на лечение. Группа сравнения состояла из 40 пациентов с гиперурикемией без клинической манифестации, которые не лечились аллопурином. Все пациенты были распределены по возрасту, полу и по скорости клубочковой фильтрации (СКФ). У пациентов, получавших аллопурином в средней дозе 250 мг в день (SD, 78), было отмечено увеличение уровня СКФ на 11,8 мл/мин. (95% доверительный интервал, доза 4,7-11,8 мг в день, P=0,01), по сравнению с контрольной группой. Установлено, что эффект лечения зависел от исходного уровня СКФ, о чем свидетельствует более значительный терапевтический эффект у пациентов с низким начальным уровнем СКФ (P=0,004). В группе лечения аллопурином был отмечено снижение конечного уровня креатинина на 0,12 мг/дл (95% доверительный интервал, 0,003-0,20 мг/дл, P= 0,04), по сравнению с группой контрольных пациентов, распределенных по начальным уровням креатинина и возрасту. Среди исследуемых пациентов у двух были зарегистрированы побочные явления. Лечение больных гиперурикемией аллопурином средней продолжительностью 15 месяцев привело к значительному улучшению функции почек в когорте мужчин с гиперурикемией. Клиницистам следует учитывать потенциальную пользу аллопуринола при лечении больных гиперурикемией, особенно у тех, кто нуждается в поддержке и контроле функции почек.

Ключевые слова: гиперурикемия, функция почек, аллопурином.

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serum uric acid levels higher than 380 mmol / l (an average of ~ 500 mmol / l) who had recently begun therapy with allopurinol for any reason with a verified response to treatment. The comparison group consisted of 40 patients with hyperuricemia without a clinical manifestation who were not treated with allopurinol. All patients were divided by age, sex and glomerular filtration rate (GFR). Patients receiving allopurinol at an average dose of 250 mg / day (SD, 78) showed an increase in GFR of 11.8 ml / min (95% confidence interval, a dose of 4.7-11.8 mg / day , P = 0.01) than in the control group. It was found that the treatment effect depended on the baseline level of GFR, which is evidenced by a more significant therapeutic effect in patients with lower baseline GFR (P = 0.004). In the allopurinol treatment group, the lower endpoint of creatinine was 0.12 mg / dL (95% confidence interval, 0.003-0.20 mg / dl, P = 0.04) than in the control group of patients at baseline creatinine and age. Among the patients studied, two cases of adverse events were reported. Treatment of patients with hyperuricemia with allopurinol with an average duration of 15 months has led to a significant improvement in renal function in a cohort of men with hyperuricemia. Clinicians should take into account the potential benefits of allopurinol in the treatment of patients with hyperuricemia, especially those who need support and control of kidney function.

Key words: hyperuricemia, renal function, allopurinol.

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OPTION TO PREVENT RADIATION CYSTITIS

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External Beam Radiation Therapy (EBRT) is an efficient method of treatment for many types of tumors. But with different approaches, fields, and combinations of doses, the bladder lesions are inevitable. Therefore, one of the priority unsolved issues in the present day radiology is the issue of prevention and control of radiation reactions and injuries. The purpose of the present study was to develop a method for the prevention and treatment of radiation reactions in the treatment of patients with bladder cancer receiving gamma-ray teletherapy (GRT) and to substantiate the antioxidant and reparative role of the Emoxypin drug in this pathology. The severity of radiation reactions in patients receiving radiation therapy in the usual fractionation mode and with multi-fractionation of dose was under study. The total of 27 patients participated in the observation, those with bladder cancer diagnosed and subjected to the EBRT on the definitive treatment program. Analyzing the results obtained, it can be noted that the use of EBRT in the mode of the daily dose multifraction reliably (p = 0.05) reduces the reaction of the bladder mucosa. Thus, the reactions of the 3rd degree (ulcerative) differ by 4.31 times in favor of group II (experimental) where the mode of multifraction and the Emoxypin drug was used. Reactions of the 2nd degree (erosive-desquamated) differ by 1.24 times and also favor group II, but this indicator is unreliable. Reactions of 1 degree (catarrhal) differ by 3.72 times, which has a sufficient reliability in favor of the treatment performed in the patients of group II. The effect of bladder installations in patients with radiation cystitis, complicated with an infectious process, compared with the traditional methods of therapy, permitted to reduce the term of patients' stay in hospital by 6-7 days.

Key words: bladder cancer, antioxidants, remote gamma therapy, radiation reactions, radiation injury, cystitis

The present study is a fragment of the scientific research project (SRP): "Development of methods for treatment and prevention of medicamentally-induced injuries of visceral organs" (state registration number 0115U001087). Term of the Project performance: from 02.2015 to 02.2020.

External Beam Radiation Therapy (EBRT) is an efficient method of treatment for many types of tumors. In addition, it provides long-term survival without relapses and other manifestations of the disease. The purpose of performing radiation therapy is to bring a dose having a destructive effect to the tumor cell. At the same time, it is necessary to ensure the protection of healthy tissues, to the extent possible, in accordance with the laws of radiobiology and radiation physics [15]. The severe effects of irradiation, distant radiation injuries, are, unfortunately, part of the EBRT. Effective treatment can be

obtained through the skill and the use of modern technologies with the persistent prevention of radiation reactions [7, 13, 15].

Any damage to the tissues of the small pelvis organs (bladder, rectum, endopelvic cellular tissue), whether it could be chemical, mechanical or physical (in this case, radiant) injury, leads to radiation injuries and to formation of scar tissue [3, 11, 13].

Analysis of current literature has shown that the number of papers devoted to this pathology in the domestic and foreign publications is insignificant and, as a rule, they have the descriptive nature. In addition, methods for preventing radiation injuries are studied insufficiently, as well as rehabilitation issues and the life quality of the indoor patients in the postexposure periods [7, 10, 11]. Assessing the existing methods for treating radiation injuries of the pelvic organs that are presented in periodicals it can be stated that the results of diagnosing and treatment of such radiation lesions are unsatisfactory, they are manifested by frequent relapses of cystitis and as a result cause deformation of the bladder; endopelvic radiation fibrosis, and development of the chronic renal failure [1, 2, 3].

One of the priority issues in the treatment of bladder cancer is EBRT, which can be aimed at different purposes, one of which is a definitive treatment performed when surgery is impossible [1, 6].

In Europe, radiotherapy is performed quite frequently for bladder tumors. For example, in the UK at the conventional radiation, the total boost dose (TBD) is brought to 50 – 60 Gy with a single boost dose (SBD) of 1.8 - 2,0 Gy. However, Harvard Medical School researchers believe that in the case of bladder cancer it is necessary to bring TBD to 55-65 Gy. In general, radiotherapy for bladder cancer is carried out in two stages: the first TBD 45-50 Gy with SBD 1.8-2.0 Gy for the entire bladder; the second stage is the direct irradiation of the primary tumor [14].

Radial reactions arise predominantly at the beginning of radiotherapy and bring significant suffering to the patient. Some authors [4, 10] observed bladder lesion in 20% of patients who received 70 Gy or more in 30% of the bladder, or in the irradiation zone in 15% of the bladder - 5% of acute lesions.

Others [7, 8] denote a sharp growth of acute radiation injuries if TBD 65 Gy is delivered to one-third of the bladder. Acute symptoms usually occur 1 month after the irradiation is complete. In addition, it should be borne in mind that persistent hematuria is in most cases well treated with antioxidants and antihypoxants [4, 5, 12].

Taking into account the progress of radiation therapy for bladder cancer, Princess Margaret Hospital staff estimates that TBD 50-60 Gy at a SBD of 1.8-2.0 Gy for the entire bladder is a tolerant dose for most patients, and the TBD 65-70 Gy is only tolerant for a part of the bladder [14]. At the same time, the opinion of the staff at the Department of Oncourology and Radiation Oncology of the Massachusetts General Hospital, Boston, is that, with a conventional fractionation, the dose tolerant for the whole bladder is the TBD 40-45 Gy [8, 15].

There are other treatment regimens having a large number of fractions at low single doses (hyperfractionation) and fewer fractions, but with higher single doses at a lower total boost dose (hypofractionation) [13, 14].

From the above, it can be seen that, with different approaches, the fields and combinations of doses, the bladder injuries are inevitable. Therefore, one of the priority unsolved problems in modern radiology is the issue of prevention and control of radiation reactions and injuries. The issues' topicality is due to the lack of a single algorithm for using drugs that actively and efficiently prevent this process.

The novelty of the work lies in focusing the interest on the direct synthetic antioxidant drug "Emoxypin", which prognostically inhibits the reaction of free radical peroxide oxidation (FRPO) [1, 2, 3, 9].

The purpose of the study was to develop a method for prevention and curing of radiation reactions in the treatment of patients with bladder cancer receiving remote gamma-ray therapy (RGRT) and to substantiate the antioxidant and reparative role of Emoxypin drug in this pathology. The purpose also included prevention of relapses due to the restoration of local hemodynamics.

Materials and methods. The total of 27 patients diagnosed with bladder cancer participated in the observation and received EBRT according the definitive treatment program. To perform the assigned task (to raise the efficacy of treatment for patients with radiation bladder lesions), the patients were blindly divided into the two groups.

The study included patients aged 40 to 75 years old, with an average age of 59.5 years.

For all patients, in the primary and control trials, pelvic organs SCT was performed using a computer tomograph CT / E Dual Hispeed CT produced by GE firm (USA) in the usual mode according to standard techniques.

Distribution of patients by the method of treatment received

	Group I (n = 13) (control) EBRT (classic fractionation) with Dimexidum instillations	Group 2 (n = 14) (experiment) EBRT (dose multifractionation) with Emoxypine instillations
method	EBRT on the definitive program of classic fractionation in 2 stages with a three-week break	EBRT on the definitive program with fractionation of the daily dose
dose	SBD 2.2 Gy to TBD 60 – 65 Gy	SBD 1.1 Gy + 1.1 Gy = 2.2 Gy to TBD 60 - 65 Gy in 2 stages with a three week break
prevention and treatment of radiation reactions	10% Dimexidum solution was infused into the bladder after the radiotherapy session 2 times a day for 12-15 days	infusions of the Emoxypine solution were performed into the bladder after the radiotherapy session: the drug was administered into the bladder by 150 mg 2 times a day for 12-15 days

Ultrasonography of the abdominal cavity, small pelvis and regional lymph nodes was performed using Sonolan G-50 and DP-9900 equipment.

X-ray examination was performed on the basis of the Poltava Clinical Oncology Dispensary, using the RUM-20, RDK BCM equipment.

Cytological studies were performed on the basis of the Poltava Clinical Oncology Dispensary.

Pathohistological investigations were carried out at the Oncomorphology Department of the Poltava Regional Pathoanatomical Bureau.

To analyze the correlation between the quantitative parameters studied, the coefficient of the pair correlation r by Pearson was determined. The correlation coefficient was considered statistically significant in the case of the error probability $p < 0.05$, which was determined by comparison with the critical values by the table of the experimental group size dependence, correlation coefficients, and probability of errors. To determine the interconnections of semi-quantitative and qualitative indicators and their correlation with quantitative indicators, a non-parametric correlation τ criterion by Kendal was calculated. Calculations were performed with a personal computer using Microsoft Excel 2007 and SPSS for Windows Release 13.0 software.

The use of Emoxypin drug is explained by the fact that it is an inhibitor of free radical processes, antihypoxant, antioxidant. It reduces blood viscosity and aggregation of thrombocytes, increases the composition of cyclic nucleotides in tissues and thrombocytes, expresses fibrinolytic activity, reduces vascular permeability and the risk degree of hemorrhages.

The 5% Dimexidum solution was chosen as the control drug, which is classically used for the prevention and treatment of radiation reactions. Dimethyl sulfoxide has a specific feature of penetrating through biological membranes, thus realizing its specific effects, including anti-inflammatory, anti-pyretic, analgetic, antiseptic, moderate fibrinolytic effect. The preparation enhances drugs penetration through the mucous membranes (ability to transport).

Patients were irradiated with the TERAGAM K-01 remote gamma radiation device.

The severity of the radiation reactions in patients receiving radiation therapy in the normal fractionation mode and with the dose multifractionation was studied.

All patients received, in addition to the local treatment, the same type general treatment, which included antibacterial, anticoagulant, vasoactive, immunostimulating and symptomatic therapy.

Results of the study and their discussion. The effect was assessed during the treatment period and the short-range radiation effect (after 3 weeks) was assessed after the EBRT completion. The patients' complains of pain when urinating, blood admixtures were taken into consideration. General urine analysis data: hematuria and leukocytosis, protein admixtures. The control was performed according to cystoscopy and ultrasound investigation data.

In patients of the both groups with catarrhal cystitis after treatment, normal urine values have grown by 36%, bacteriuria completely disappeared in 30% of patients. Concerning hematuria, positive dynamics was observed in all patients. According to ultrasound investigation, in more than 62% of the patients the bladder condition has improved. Significant results were observed in the same group's patients with complicated forms of cystitis: the bladder's capacity has grown, the urinations frequency has reduced, a subjective improvement was observed by all the patients. The positive dynamics was confirmed by the ultrasound investigation and cystoscopy more than in 42% of patients in this group.

In patients with erosion-desquamative and ulcerative cystitis, as a result of the treatment, the therapeutic efficacy analysis has shown its significant effect on the frequency of urinations. In all patients, the inflammatory reaction has reduced, and in 58% of patients with complicated forms of cystitis, leukocyturia reached its normal values; in 87% in 70% of patients, bacteriuria and macrohematuria,

respectively, have disappeared completely. According to the cystoscopy data, till the end of treatment, hyperemia of the bladder mucosa (82.5%) and edema (85%) have reduced.

Ulcerative reactions in group I were detected in 8 (61,54%) patients versus 2 (14,28%) in group II.

Erosion-desquamative reactions did not reliably differ and were observed in 3 (23,07%) patients in group I against 4 (28,57%) patients in group II.

The catarrhal reactions observed in the groups were manifested as follows: in group I they were detected in 2 (15,38%) patients versus 8 (57,14%) in group II.

The results are presented in Tab. 1

Table 2

Frequency of Radiation Reactions in the Bladder Mucosa, Depending on the Type of Treatment

Radiation reactions localization	Group I (n = 13) (control) EBRT (classic fractionation) with Dimexidum instillations			Group 2 (n = 14) (experiment) EBRT (dose multi- fractionation) with Emoxypine instillations		
	Reaction type	Number of cases		Reaction type	Number of cases	
		abs.	(%)		abs.	(%)
Bladder mucosa	Catarrhal	2	15.38%	Catarrhal	8	57.14%
	Erosion-desquamative	3	23.07%	Erosion-desquamative	4	28.57%
	Ulcerative	8	61.54%	Ulcerative	2	14.28%

Note. * - difference is reliable ($p < 0.05$). The response degree of the bladder disorders in the patients of groups I and II was reliably different ($p < 0.05$).

Thus, ulcerative reactions in group I were detected in 8 (61,54%) patients, while in the patients of group II there were 2 (14,28%), respectively, which is 4 times the value of the results in group I and indicates a more pronounced damaging effect when the traditional EBRT and the Dimexidum solution are used.

Erosion-desquamative reactions in group I were found in 3 (23,07%) patients, and in group II in 4 (28,57%), which was not reliably different.

But, as far as catarrhal manifestations are concerned, the picture obviously favors group II of the study. In group I, 2 patients (15,38%) with catarrhal reaction were found, and in group II there were 8 (57,14%).

Analyzing the results obtained, it can be noted that the use of EBRT in the mode of the daily dose multi-fractionation reliably ($p = 0.05$) reduces the radiation reactions of the bladder mucosa.

Thus, the reactions of the 3-d degree (ulcerative) differ by 4.31 times in favor of group II (experimental) where the regimen of multi-fractionation and installations of the Emoxypine drug were used.

Reactions of the 2-nd degree (erosion-desquamative) differ by 1.24 times and also speak in favor of group II, but this indicator is unreliable.

Reactions of 1-st degree (catarrhal) differ by 3,72 times, which has a sufficient reliability in favor of treatment performed in group II of patients.

Summing up the comparison of the proposed treatment regimens of the bladder lesion with existing methods of therapy of this pathology [1,6,13,15] it can be concluded that they correlate with the data of other authors, but to date, no one has been published data on the use of the drug " Emoxipine "which is aimed at regression of cystitis, treatment of the bladder ulcers. There is no practical literature data on the intra-bladder use of this drug. According to the literature sources [13,14], the effect of bladder installations in patients with radiation cystitis encrusted by the infectious process, in comparison with traditional methods of therapy, allowed to shorten the stay of patients in a hospital for 6-7 days [2,7,12].

Thus, the conducted research showed that the used basic dimexid and emoxipine have different direction of action. Thus, with pronounced bladder wall fibrosis and infectious process, the advantage can be given to the use of the solution of dimethoxide, and in patients with hematuria and in violation of the integrity of the bladder wall (erosive or ulcerative-necrotic cystitis), the most effective use of "emoxipine". The choice of treatment method should be based on subjective complaints and objective objective research methods.

Conclusions

The results obtained with the use of the Emoxypine solution in comparison with the traditional treatment with Dimexidum testify to the prospects of the suggested method's further development, which reliably ($p = 0.05$) reduces the radiation responses.

1. The efficacy of treatment in saline encrusted cystitis with severe pain syndrome is provided by the use of 5-10% Dimexidum solution, which efficacy made 56%. The pain syndrome was reversed in all patients.

2. The use of the Emoxyphine drug with its anti-inflammatory, antioxidant, anti-aggregate effects permitted to improve the efficacy of treatment in patients with radiation cystitis: with ulcerative reactions – by 4.31 times, with erosion-desquamative reactions - by 1.24 times, with catarrhal ones – by 3.72 times, that is sufficiently reliable in favor of treatment performed in group II of the patients.

3. The choice of treatment for patients should be based on the nature and severity of the bladder wall radiation injuries. The therapy should be focused, first of all, on the infection fighting, on improving the immune status and on elimination of the bladder radiation fibrosis. The methods of choice are the Dimexidum and Emoxyphine drugs used along with the symptomatic therapy.

Prospects for further research are continuation of the studies and search for the methods to prevent radiation reactions and complications during the radiotherapy, assessment of drugs and their combinations for the above pathologies.

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Реферати

ВАРИАНТ ПРОФИЛАКТИКИ ПРОМЕНЕВОГО ЦИСТИТУ

Жукова Т.О., Васько Л.М., Почерняєва В.Ф., Соколова Н.О., Корнєєв О.В.

Дистанційна променева терапія є ефективним методом лікування для багатьох видів новоутворень. Але при різних підходах, полях і комбінаціях доз променевої ураження сечового міхура неминучі. Тому одним із пріоритетних питань в сучасній радіології є попередження і боротьба з променевими реакціями і пошкодженнями. Метою роботи стала розробка способу профілактики і лікування променевих реакцій при лікуванні хворих на рак сечового міхура, у хворих, які отримують дистанційну променево терапію, а також -

ВАРИАНТ ПРОФИЛАКТИКИ ЛУЧЕВОГО ЦИСТИТА

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Дистанционная лучевая терапия является эффективным методом лечения для многих видов новообразований. Но при различных подходах, полях и комбинациях доз лучевые поражения мочевого пузыря неизбежны. Поэтому одним из приоритетных вопросов в современной радиологии – это предупреждение и борьба с лучевыми реакциями и повреждениями. Целью работы стала разработка способа профилактики и лечения лучевых реакций при лечении больных раком мочевого пузыря, у больных которые получают дистанционную гамма-терапию и

обґрунтування антиоксидантної та репараційної ролі препарату «Емоксипину» при даній патології. Вивчалася вираженість променевих реакцій у хворих, які отримували променеве лікування в режимі звичайного фракціонування і при мультифракціонуванні дози. У спостереженні брало участь 27 хворих з діагнозом рак сечового міхура і яким проводили дистанційну променеву терапію за радикальною програмою. Аналізуючи отримані результати, можна відзначити, що застосування дистанційної променевої терапії в режимі мультифракціонування денної дози достовірно ($p = 0,05$) знижує променеві реакції слизової сечового міхура. Так, реакції 3 ступеня (виразкові) розрізняються в 4,31 рази на користь (дослідної) групи де використовували режим мультифракціонування і заливки препарату «Емоксипину». Реакції 2 ступеня (ерозивно-дескваматозний) відрізняються в 1,24 рази і також говорять на користь II групи, але цей показник не достовірний. Реакції I ступеня (катаральні) відрізняються в 3,72 рази, що має достатню ймовірність на користь лікування проведеного в II-й групі хворих. Дія інсталяцій сечового міхура у хворих з променевими циститами, обтяженими інфекційним процесом, в порівнянні з традиційними методами терапії дозволило скоротити час перебування хворих в стаціонарі на 6-7 днів.

Ключові слова: рак сечового міхура, антиоксиданти, дистанційна гамма-терапія, променеві реакції, променеві uszkodження, цистит.

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обоснование антиоксидантной и репарационной роли препарата «Эмоксипин» при данной патологии. Изучалась выраженность лучевых реакций у больных, получавших лучевое лечение в режиме обычного фракционирования и при мультифракционировании дозы. В наблюдении принимало участие 27 больных с диагнозом рак мочевого пузыря и которым проводили дистанционную лучевую терапию по радикальной программе. Анализируя полученные результаты, можно отметить, что применение дистанционной лучевой терапии в режиме мультифракционирования дневной дозы достоверно ($p=0,05$) снижает лучевые реакции слизистой мочевого пузыря. Так, реакции 3 степени (язвенные) различаются в 4,31 раза в пользу (опытной) группы где использовали режим мультифракционирования и заливки препарата «Эмоксипин». Реакции 2 степени (эрозивно-дескваматозные) отличаются в 1,24 раза и также говорят в пользу II группы, но этот показатель не достоверен. Реакции I степени (катаральные) отличаются в 3,72 раза, что имеет достаточную вероятность в пользу лечения проведенного во II группе больных. Действие инсталляций мочевого пузыря у больных с лучевыми циститами, обтяженными инфекционным процессом, по сравнению с традиционными методами терапии позволило сократить время пребывания больных в стационаре на 6-7 дней.

Ключевые слова: рак мочевого пузыря, антиоксиданты, дистанционная гамма-терапия, лучевые реакции, лучевые повреждения, цистит.

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EFFECT OF PH AND MINERALIZING PROPERTIES OF THE ORAL FLUID ON ENAMEL ACID RESISTANCE IN CHILDREN

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The present study was aimed to investigate the indices of pH, microcrystallization of the oral fluid in 7-9-year-old children with caries and without it, and possibility of occurrence of carious lesions with further use of the obtained results concerning the necessity to initiate preventive measures. The course of caries in 7-9-year-old children occurs against the ground of decrease of pH and saliva microcrystallization indices, and it is caused by reduced dental resistance to caries which is evidenced by the results of examination of the enamel acid resistance according to the enamel resistance test. The analysis of the obtained results demonstrated existence of a reverse correlation in 7-9-year-old children with caries between the index of enamel acid resistance and mineralizing potential ($r = 0.73$ – strong index) and pH ($r = 0.66$ – reverse considerable) of the oral fluid. These children presented direct strong connection between pH index and saliva mineralizing potential ($r = 0.79$). The results obtained promote the necessity to perform primary and secondary prevention directed to the improvement of homeostasis indices in the oral cavity which will enable to decrease prevalence and intensity of caries in children.

Key words: caries, intact teeth, oral cavity pH, saliva microcrystallization, enamel acid resistance.

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Caries is the most spread dental disease found among the world population long ago [2]. Occurrence of the pathology is caused by the action of certain factors producing both external and internal effect on the condition of the hard tissues of temporary and permanent teeth [3,4].

The oral fluid pH changes is one of the risk factors promoting occurrence of dental caries. This index is a regulator of homeostasis in mineral components, and in case it is deviated into acid side a mechanism resulting in dental enamel demineralization is launched. Physiological norm of oral fluid pH is 6.60- 7.08 [5, 6]. Reduced mineralizing properties of the oral fluid lead to decreased acid resistance of the enamel and thus cause occurrence of carious process [7]. Therefore, examination of the indices of the oral fluid microcrystallization and enamel resistance enable to administer preventive measures with the purpose to prevent occurrence of caries in children [8, 9, 10].