

СПКЯ було запропоновано комбінований препарат на основі міо-інозитулу в комбінації з екстрактом *Lagerstroemia speciosa*, вітаміном D3, метилфолатом і хромом. Лікування тривало упродовж 3 місяців. Клінічним підтвердженням ефективності лікування є самостійні овуляції (25%) та позитивні спроби індукції овуляції у резистентних пацієток (40%), ймовірно, за рахунок покращання якості яйцеклітин, гормонального балансу та зменшення частоти інсулінорезистентності. У результаті лікування у 64% (43/67) пацієток з СПКЯ відбулось врегулювання менструального циклу. 33% (22/67) жінок повідомили про зменшення проявів гіперандрогенної дерматити. Побічних ефектів у ході лікування не спостерігали.

Ключові слова: синдром полікістозних яєчників, міо-інозитол, лікування.

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пациентки с СПКЯ был предложен комбинированный препарат, содержащий мио-инозитол, экстракт *Lagerstroemia speciosa*, витамин D3, метилфолат и хромю. Лечение продолжалось в течении трёх месяцев. Клиническим подтверждением эффективности лечения были самостоятельные овуляции (25%), положительные результаты индукции овуляции у резистентных в прошлом пациенток (40%), вероятно, за счет улучшения качества яйцеклеток, гормонального баланса и уменьшения частоты инсулинорезистентности. В результате лечения у 64% (43/67) пациенток с СПКЯ произошло урегулирование менструального цикла. 33% (22/67) женщин сообщили об уменьшении проявлений гиперандрогенной дерматити. Побочных эффектов в ходе лечения не наблюдалось.

Ключевые слова: синдром поликистозных яичников, мио-инозитол, лечение.

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STATE OF THE PALATE TISSUES REPARATIVE REGENERATION IN CHILDREN AFTER RADICAL URANOSTAPHYLOPLASTY

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The purpose of the work was to study the state of the soft palate tissues reparative regeneration after radical uranostaphyloplasty by assessing the clinical situation and morphological structure of the palatine mucosal periosteal flaps. A sophisticated complex of interrelated homeostasis disorders, which occurs after uranostaphyloplasty, significantly affects the process of scar formation and the nature of wound healing. The study of reparative regeneration processes in soft palate tissues on the 13-14th and 29-30th days after radical uranostaphyloplasty permits to predict the probability of forming a dense scar at early stages and to influence this process using the individual plan of treatment and prevention and rehabilitation measures for this category of patients.

Key words: palate, soft tissues, children, uranostaphyloplasty, reparative regeneration.

The work is a fragment of the research project «Integrative-differentiated substantiation for the selection of optimal methods for surgical interventions and volume of medical measures in surgical pathology of maxillofacial area», state registration No. 0116U003821.

Labial cleft and fissured palate remain widespread forms of congenital defects, and surgery is an integral part of their treatment comprehensive support. Surgical treatment of congenital clefts is accompanied by significant blood loss and intense nociceptive stimulation, which is largely due to traumatic surgery, profuse vascularization and a high concentration of nerve endings in this area. A complex set of interrelated homeostasis disorders that occurs after uranostaphyloplasty significantly affects the process of scar formation and the nature of wound healing [1, 2, 4].

Data reported in the literature indicate that the formation and reorganization of the scar lasts for a long time after scarring and epithelialization of the wound tissue surface, and therefore, in the short term after the wound epithelialization, the scar cannot be considered a complete physiological formation [7].

It is proved that the mechanism of sequential scar remodeling is based on a stable balance between the processes of the formed collagen destruction under the action of collagenase and the new collagen synthesis. When the intensity of collagenosynthesis prevails over collagenolysis, the normal process of scar formation is disturbed and it acquires hypertrophic properties, enlarges in volume and protrudes over the surface of the tissues surrounding it. Such scars cause various secondary deformations and functional disorders [5, 9].

Some scientists believe that one of the reasons for such scars formation after surgery is the presence of disturbances in the histological structures architectonics of the mucous membrane tissues in the area of the operating field. The leading role in the pathogenesis of pathological scarring is played by the disruption of close corporate links between tissue basophils, monocytes, and fibroblasts against the background of general and local autosensitization. Information about the recovery of the epithelium in the area of the postoperative wound healing is questionable, the period of 10 to 25 days is reported [8].

Recent studies have shown that the regeneration of tissues injured after uranostaphyloplasty, and then the function of the palatine-pharyngeal complex, is directly influenced by the state of the muscle

components of the soft palate, namely by the level of myogenin and myostatin mRNA expression. It has been found that with age the level of myogenic potential in a patient decreases, which was a medical-genetic justification of recommendations for early surgery and for determination of the preoperative medication correction algorithm to obtain higher functional results of surgical treatment [2].

However, at present there is no explicit methodological concept regarding the application of preventive components in this case aimed at preventing gross scarring. Indications and contraindications to the purposeful pharmacological correction of the scar formation process itself have not been determined, which has prompted us to carry out scientific work in this direction with the purpose of developing further pathogenetically justified preventive measures [11].

The purpose of the work was to study the reparative regeneration of the palate soft tissues after radical uranostaphyloplasty by assessing the clinical situation and morphological structure of the palatine mucosal- periosteal flaps.

Materials and methods. The results of the clinical work are based on the analytical generalization of a comprehensive examination in 27 children with congenital unilateral cleft palate at the age of 2 to 5 years (11 girls, 16 boys). Among these, in 15- (55.5%) the cleft defect was left-sided and in 12 ones - (44.5%) right-sided. The clinical examination included a visual examination and assessment of the wound condition on the 13th-14th and the 29th-30th days after surgery.

Substrate for morphological study were bioplates from scar tissue of the palate obtained in the area of the vascular-nerve bundle's exit, which were collected on the 13th-14th and the 29th-30th days from the time of uranostaphyloplasty by means of the needle to collect material proposed by the authors (fig. 1).

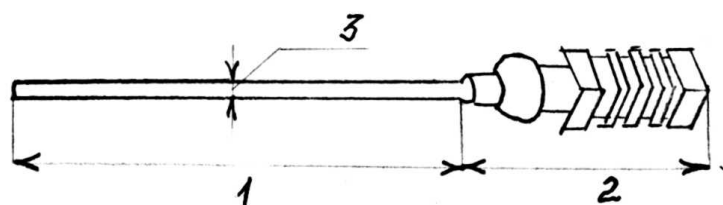


Fig. 1. Needle for taking soft tissue biopsies of the palate.

For its manufacture, a special needle was used for blood transfusion with a diameter of 3 mm, changing the angle of its bevel to 90° and making a fine sharpening at the end of the working part, which permitted to receive enough material for further morphological study.

For further study of the structural elements, it was subjected to pre-fixation in 4% solution of glutaric aldehyde in phosphate buffer at pH 7.4 for 60 min at the temperatures of 4°C. From the scar palatine tissues contained in EPOX-812, semi-thin sections were obtained with MPS-2 rotary microtome and stained with a fresh 0.1% solution of methylene blue [3].

For the purity of the study, radical uranostaphyloplasty was performed by a single surgeon - Professor Tkachenko P.I. according to the method proposed by Professor Kharkov L.V. using one type of suture material. Medical support was carried out in compliance with the recommendations presented in the protocols of providing medical care for this category of patients [6].

Results of the study and their discussion. The studies presented in this paper are a continuation of our previous scientific work, where we studied the clinical situation in children with congenital malformations and the morphological structure of the mucosa-periosteal flaps of the palate before surgery and in the early postoperative period (on the 6th-7th days) after performing radical uranostaphyloplasty [4].

It is known that the structure of the oral mucosa changes strictly depending on the age. Each age period is characterized by its own inherent features, which must be taken into account when performing uranostaphyloplasty, when we are dealing with tissues compromised by the phenomena of dysontogenic disorders.

We also established it when these children revealed the presence of vacuolar dystrophy in the stratum spinosum of the biopsy epithelium sampled immediately before surgery, which, in our opinion, is a consequence of the combined effect of the microcirculatory bed disorders and increased antigenic load on the underdeveloped palatine tissue structures. Reduction of keratinization phenomena and manifestations of dystrophic processes in the epithelium in the form of acanthosis, testified to their modified response to physical load against the background of impaired chewing function and impaired blood circulation. Of course, these features of the mucous membrane structure in children with congenital malformations are a prerequisite for defective scar formation and epithelial regeneration in this area.

When comparing the results of morphological studies on biopsy specimens taken with unilateral, bilateral perforating and isolated medial palate clefts, we did not establish significant differences in their structure. As both methods of surgery were used in both observation groups, the healing in the postoperative period was followed by primary intension along the median line of the palate and by secondary intention in other areas.

It should be reminded that on the 6-7th day the wound along the medial line in the area of hard and soft palate is covered by a layer of fibrin, its edges had a crown of hyperemia up to 2 mm wide and were immersed compared to the surrounding tissues. In some areas, the bone tissue remained partially denuded.

Microscopically during this period of observation, pronounced leukocyte infiltration prevailed, which indicated the presence of an inflammatory component in the wound. It is necessary to point to the unity of the inflammatory and actually reparative components in a holistic reaction, since the proliferative phase of inflammation is also reparative. The inflammation and regeneration are separated conditionally, all phases of the process are overlapped. Conditionally separated are also regeneration and fibrosis, especially in the case of substitutional regeneration (fig. 2).

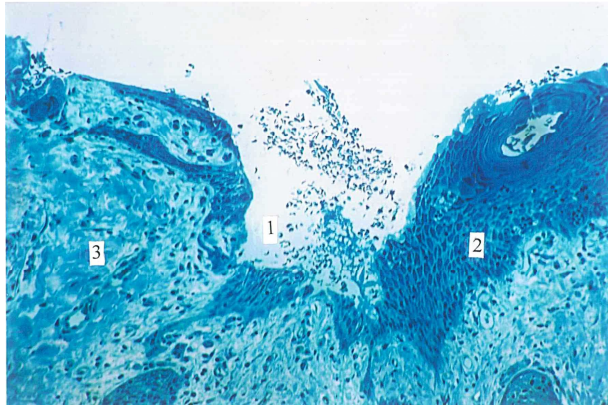


Fig. 2. Micrograph of a wound biopsy surface fragment in the area of surgical intervention in a child with congenital right cleft of palate on the 6th day. Patient B., medical history No. 2224. Semifine section. $3b \times 900$. Stain - methylene blue. The wound canal (1), epithelium infiltration (2), edema and swelling of collagen fibers in connective tissue (3) are determined.

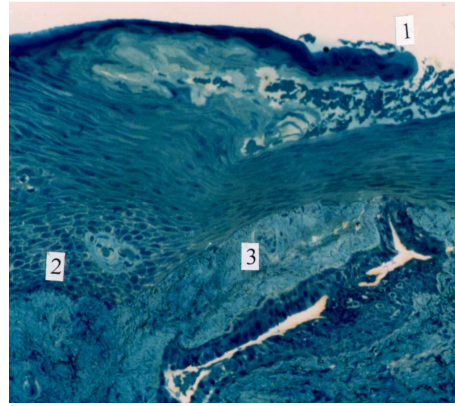


Fig. 3. Micrograph of a wound biopsy surface fragment in the area of surgical intervention in a child with congenital right cleft of palate on the 13th day. Patient B., medical history No. 2224. Semifine section. $3b \times 900$. Stain - methylene blue. The wound canal (1), epithelial growth on top of the fibrin-erythrocyte clot (2), basal layers of the epithelium (3), connective tissue (4) are determined.

In the clinical aspect, on the 13th-14th day of the postoperative period, in most patients the crown of hyperemia around the scar was slightly pronounced, and the wound canal was completely filled with granulations, the volume of which increased, they were compacted over the entire surface and slightly overtopped the surrounding tissues level.

At that time, in two patients (7.4%) with unilateral perforating cleft, complete suture line disruption was observed in the area of the uvula, and in one case (3.7%), postoperative complication was observed in the form of partial divergence of sutures in the superficial layer of the mucous membrane of the oral cavity. Another patient (3.7%) was also found to have a partial suture line disruption in the same area with the formation of a residual defect.

In the morphological aspect, on the 13th-14th day, 87% of microslides showed initial signs of hemodynamic normalization in the operation area. At this time of the observation, the fibrous structures began to prevail over cellular elements. Thus, at this time in the wound there was a transformation of granulation tissue into connective tissue (fig. 3).

In parallel with the development of connective tissue and subsequent vascularization of the wound, the process of epithelialization is completed. It should be noted that in 34% of microslides the epithelium was infiltrated into the leukocyte-necrotic layer, i. e., in these cases there was no strong epithelialization, which indicated the inability of the granulation tissue to accept the epithelial structures on itself and the imperfection of its cellular composition at the time of observation.

In 66% of the microslides young granulation tissue was found, which filled both the primary and secondary defects that arose after the rejection of the microbotic zone and the wound surface cleansing. At this time of observation, the processes of concentric contraction of the wound edges to the center due to migration of the mucous membrane surrounding the defect to the granulation tissue and due to the off-wound intercalation, that means hyperplasia and hypertrophy of the mucous membrane, were taking place.

On the 29th-30th days, 15 children (55.6%) showed slight manifestations of swelling and hyperemia in separate isolated sites of scar tissue, which mostly had a pink color and was at the level of the surrounding unchanged soft tissue of the palate. The medial line scar became flatter and more flexible within the soft palate and the uvula.

On the 29-30th day of the postoperative period in all microslides there were signs inherent in the third phase of the wound healing process according to Shekhter A.B., namely the formation and rearrangement (remodeling or resimulation) of the scar [7].

During this period, the number of fibroblasts compared to collagen fibers reduced significantly. In 89% of microslides there were signs of the final stage in granulation tissue maturation, which was characterized by the development of collagen fibers, a gradual decrease in the number of blood vessels and cellular elements, the dehydration of tissues with the prerequisites for the restructuring of young connective tissue into the mature fibrous tissue. The edges of the wound were connected by a scar, which was

characterized by the presence of fibrous collagen tissue, without a characteristic orientation of connective tissue fibers in the scar. In this case, bundles of collagen fibers were presented in different directions (fig. 4).

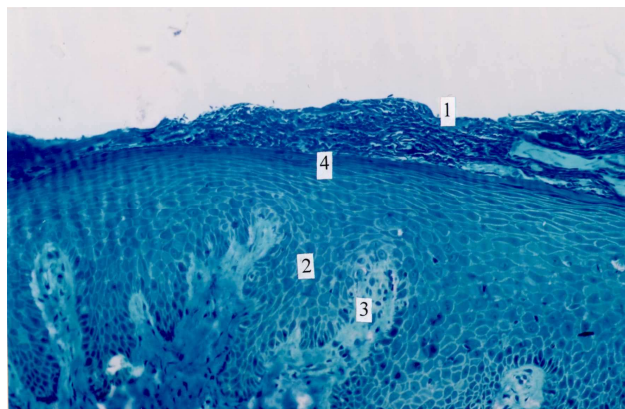


Fig. 4. Micrograph of a wound biopsy surface fragment in the area of surgical intervention in a child with congenital right cleft of the palate on the 30th day. Patient B., medical history No. 2224. Semifine section. 3b × 900. Stain - methylene blue. The epithelium surface is covered with fibrin (1), epithelial papilla (2), connective tissue papilla with the blood vessel (3), surface layers of the epithelium (4).

imperfection of its cellular composition and the inability of its scar tissue to accept it. In all other cases, the processes of concentric contraction of the wound edges to the center were observed due to migration of the mucous membrane surrounding the defect onto the granulation tissue and due to the off-wound intercalation.

On the 29th-30th day of observation, the scar tissues in their bulk had a pink color and were at the level of surrounding unchanged soft tissues of the palate. The medial line scar became flatter and more flexible within the soft palate and the uvula.

Morphologically, at this time, there was a slowing in the marginal epithelialization of the wound, which could contribute to the precocious maturation of granulation tissue and to the preconditions for the formation of denser scars.

In general, our results are consistent with those of other researchers [1, 4, 6, 10]. With regard to inflammation and adaptive responses, our findings correlate with the results of the analysis of intercellular interactions performed by Russian colleagues [7]. In Ukraine, the problems of the palatine soft tissues regeneration after uranostaphyloplasty were studied by Kharkov L.V. and Egorov R.I. [5, 6]. These researchers have studied in detail the energy processes and the level of myogenic potential in the tissues of the palate in children with its cleft. The results obtained by these authors were supplemented by the data on the healing process features in the postoperative wound at different stages of the palatine tissues regeneration after radical uranostaphyloplasty with support of traditional medical means, which are widely used in medical institutions of our country. Foreign colleagues [9, 10] note similar clinical and morphological characteristics of the wound process in the early postoperative period.

Conclusion

The study of the reparative regeneration state in the palatine soft tissues on the 13th-14th and the 29th-30th days after the radical uranostaphyloplasty by assessing the clinical situation and morphological structure of the palatine periosteal flaps permits to predict the probability of dense scar formation at early stages. It permits to deliberately influence this process by designing treatment and preventive and rehabilitation measures for individual treatment in this category of patients.

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Реферати

СТАН РЕПАРАТИВНОЇ РЕГЕНЕРАЦІЇ ТКАНИН ПІДНЕБІННЯ У ДІТЕЙ ПІСЛЯ РАДИКАЛЬНОЇ УРАНОСТАФІЛОПЛАСТИКИ

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Метою роботи стало вивчення стану репаративної регенерації м'яких тканин піднебіння після проведення радикальної ураностафілопластики шляхом оцінки клінічної ситуації і морфологічних структур піднебінних слизово-окісних клаптів. Комплекс взаємообумовлених порушень гомеостазу, який виникає після проведення ураностафілопластики, значно впливає на процес формування рубця і характер загоєння рани. Вивчення процесів репаративної регенерації м'яких тканин піднебіння на 13-14 і 29-30 добу після проведення радикальної ураностафілопластики дає можливість на ранніх етапах спрогнозувати ймовірність формування грубого рубця і вплинути на цей процес шляхом підбору індивідуального плану лікувально-профілактичних і реабілітаційних заходів для цієї категорії хворих.

Ключові слова: піднебіння, м'які тканини, діти, ураностафілопластика, репаративна регенерація.

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СОСТОЯНИЕ РЕПАРАТИВНОЙ РЕГЕНЕРАЦИИ ТКАНЕЙ НЁБА У ДЕТЕЙ ПОСЛЕ РАДИКАЛЬНОЙ УРАНОСТАФИЛОПЛАСТИКИ

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Целью работы стало изучение состояния репаративной регенерации мягких тканей нёба после проведения радикальной ураностафилопластики путём оценки клинической ситуации и морфологической структуры нёбных слизисто-надкостничных лоскутов. Сложный комплекс взаимообусловленных нарушений гомеостаза, который возникает после проведения ураностафилопластики, значительно влияет на процесс формирования рубца и характер заживления раны. Изучение процессов репаративной регенерации мягких тканей нёба на 13-14 и 29-30 сутки после проведения радикальной ураностафилопластики даёт возможность на ранних этапах спрогнозировать вероятность формирования грубого рубца и повлиять на этот процесс путём подбора индивидуального плана лечебно-профилактических и реабилитационных мероприятий для этой категории больных.

Ключевые слова: небо, мягкие ткани, дети, ураностафилопластика, репаративная регенерация.

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FREQUENCY AND STRUCTURE OF BENIGN SOFT TISSUE FORMATIONS IN THE MAXILLOFACIAL AREA

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The article considered our own observation results and retrospective analysis of archival material of the Maxillofacial Department of M.V. Sklifosovsky Poltava Regional Clinical Hospital and Surgical Department of the Poltava City Children's Clinical Hospital from 2008 to 2018. It was found that among adults the number of patients with benign soft tissue formations of the face and neck is 4.9%, and in children – 7.8% of the total number of inpatients. Most of them were bronchiogenic cysts of the lateral part of the neck (152 – 26.3%) and atheromatous plaques (147 – 25.4%). They mostly occurred at the age of 22 to 60 years, men suffered more often (205 - 35.5%). The largest number of discrepancies in the diagnosis at the prehospital phase were patients with epidermal cysts – 38 (7.9%). As for pediatric population, their number was 7.8% of the total number of inpatients. Neoplasms of dysontogenetic origin predominate, among which the most common were dermoid cysts – 92 patients (32.4%) and haemangiomas – 74 patients (26%). Less common were ranulae – 36 cases (12.7%), bronchiogenic cyst – 17 cases (6%) and atheromatous plaque – 16 cases (5.6%). They were found more often in the nursery age – from 1 to 3 years.

Key words: adults, children, benign formations, tumor-like formations, cysts of the maxillofacial area, soft tissues.

The work is a fragment of the research project "Integrative-differentiated substantiation of the choice for optimal methods of surgical interventions and scope of treatment in surgical pathology of the maxillofacial area", state registration No. 0116U003821.

According to various authors, the proportion of cystic lesions ranges from 25% to 40% in the structure of the maxillofacial area diseases, including within the Poltava region. Benign tumors and tumor-like neoplasms of the soft tissues of the face and neck account for 29% of all human tumors, of which 25% are cysts of the lateral surface of the neck. [1, 2, 4, 5].

There is no separate classification of maxillofacial tumors in the modern literature. Currently, oral and maxillofacial surgeons most often use O.O. Kolesov (primary tumors and tumor-like formations of