Volatiles & Essent. Oils, 2021; 8(5):11869-11874

NVEO
Natural Volatiles & Essential Oils

The State of the Local Cytokine Status and Its Pathogenetic Significance with Secondary and Residual Palatal Deformities after Uranoplasty in Children

Khakimova Zilolaxon Kahramonjonovna[1], Dusmukhammedov Dilshod Mahmudovich[2], Khodjimetov Abdugaffur Axatovich[3], Dusmuxamedova Dilnavoz Karamalievna[4]

[1] Head of the Department of Propaedeutics of Dental Diseases Andijan State Medical Institute

[2] Professor of the Department of Pediatric Surgical Dentistry of the Tashkent State Dental Institute

[3] Professor of the Department of Biochemistry of the Tashkent State Dental Institute

[4]Assistant of the Department of Advanced Training in Orthopedic Dentistry, Tashkent State Institute of Dentistry

Abstract

Providing qualified care to patients with congenital cleft of the upper lip and palate (CCLP), accompanied by dentoalveolar anomalies and nasal deformities is one of the most difficult tasks of modern dentistry and maxillofacial surgery. According to various authors, complications after reconstructive operations range from 8 to 32% (4,5,8,13,14). With this pathology, the quality of the postoperative scar depends on the general condition of the body, the nature of the disease, the experience of the surgeon, the type of suture material and many other factors. Any kind of surgical intervention in the dental-jaw system causes disturbances in microcirculation, as well as in the blood circulation of tissues around the wound, which leads to an inflammatory reaction. Even with the initial wound healing, accompanied by a decrease in blood supply, the scar forms and matures more slowly, and its quality becomes worse. The interest to the problem of postoperative wound healing is explained by the fact that inflammation plays a leading role in the course of any wound process, which determines the path along which wound healing will go. Considering the medical and social significance of the problem of healing postoperative wounds in the tissues of the maxillofacial area, the development of methods aimed at optimizing the healing process of postoperative wounds, reducing the number of complications and improving the appearance of scars remains an urgent problem in surgical dentistry. It has recently been proven that one of the factors influencing wound healing is cellular interaction and adequate work of cells and cytokines. Consequently, the regeneration of the tissues of the oral cavity depends on adequate cellular cooperation. Growth factors play an important role in the development of scars. Growth factors are polypeptides that release various activated cells at the site of injury. They stimulate cell proliferation and chemoattraction of new cells. The variety of clinical manifestations after various types and techniques of uranoplasty, in particular the emerging secondary (SD) (postoperative) and residual defects (RD) of the palate in children, as well as the difficulties of their treatment, make it relevant and necessary to further study their pathogenesis and improve the methods of treatment.

The aim of our research was to assess the state of the local cytokine status and its pathogenetic significance in secondary and residual palatal deformities after uranoplasty in children.

Introduction

The relevance of research. Providing qualified care to patients with congenital cleft of the upper lip and palate (CCLP), accompanied by dentoalveolar anomalies and nasal deformities is one of the most difficult tasks of modern dentistry and maxillofacial surgery. According to various authors, complications after reconstructive operations range from 8 to 32% (4,5,8,13,14). With this pathology, the quality of the postoperative scar depends on the general condition of the body, the nature of the disease, the experience of the surgeon, the type of suture material and many other factors. Any kind of surgical intervention in the dental-jaw system causes disturbances in microcirculation, as well as in the blood circulation of tissues around the wound, which leads to an inflammatory reaction. Even with the initial wound healing, accompanied by a decrease in blood supply, the scar forms and matures more slowly, and its quality becomes worse. The interest to the problem of postoperative wound healing is explained by the fact that inflammation plays a leading role in the course of any wound process, which determines the path along

which wound healing will go. Considering the medical and social significance of the problem of healing postoperative wounds in the tissues of the maxillofacial area, the development of methods aimed at optimizing the healing process of postoperative wounds, reducing the number of complications and improving the appearance of scars remains an urgent problem in surgical dentistry. It has recently been proven that one of the factors influencing wound healing is cellular interaction and adequate work of cells and cytokines. Consequently, the regeneration of the tissues of the oral cavity depends on adequate cellular cooperation. Growth factors play an important role in the development of scars. Growth factors are polypeptides that release various activated cells at the site of injury. They stimulate cell proliferation and chemoattraction of new cells. The variety of clinical manifestations after various types and techniques of uranoplasty, in particular the emerging secondary (SD) (postoperative) and residual defects (RD) of the palate in children, as well as the difficulties of their treatment, make it relevant and necessary to further study their pathogenesis and improve the methods of treatment.

The aim of our research was to assess the state of the local cytokine status and its pathogenetic significance in secondary and residual palatal deformities after uranoplasty in children.

Material and Research Methods

In order to clarify the frequency, localization and mechanisms of development of secondary and residual palate defects in connection with the use of various uranoplasty techniques, we studied 47 archival case histories of children with congenital cleft of the upper lip and palate (CCLP), who were treated in the pediatric surgical dentistry department of the Andijan regional hospital in the period from 2010 to 2019 and the department of pediatric maxillofacial surgery in the clinic of the Tashkent State Dental Institute in the period from 2010 to 2019. For systematization of residual and secondary defects and deformities of the upper lip, alveolar bone and palate, the classification of E.N. Samara (1977, 1981) was used, where the author identifies the following forms: defects of hard, hard and soft, soft, connected defects. In terms of size, defects can be: small (up to 1 cm), medium (up to 2 cm), large (more than 2 cm)

As it is known, the results of uranoplasty largely depend on the completeness of the restoration of the anatomy of the palate and in the correct position of the pathologically altered muscles of the soft palate, which ensure the otopharyngeal closure. Our retrospective analysis of the case histories of patients with secondary (SD) and residual defects (RD) of the palate in children with CCLP shows that they have a peculiar clinical picture. The clinical picture of the SD and RD of the palate after uranoplasty largely depends on the shape of the cleft and the method of uranoplasty, where the SD and RD of the palate have the most common favorite localizations: they were located along the former cleft, had a different shape and size, from 3 to 22 mm. The most common complications of uranoplasty is the discrepancy of the sutures (SD) at the border of the hard and soft palate 18.5%. SDs of this localization, as a rule, develop due to the anatomical features of the cleft and technical errors of the operation. The results of a retrospective analysis of the case histories showed that 41 (87.2%) patients in the preoperative period had a severe somatic background - as prescribed by the pediatrician, they received antianemic treatment for several months, often received anti-inflammatory drug therapy and were somewhat lagging behind their peers in physical development. Consequently, secondary and residual defects, as well as deformities of the palate, are often the results of inadequate examination and treatment of the patient in the preoperative and postoperative periods. To study the state of local immunity in children with secondary and residual palatal deformities after uranoplasty, we selected patients after diagnosis, depending on the result of primary uranoplasty, and were divided into the following groups: group 1 (n = ...) consisted of children without local complications after uranoplasty; group 2 (n = ...) was related to children with SD and RD of the palate after uranoplasty and group 3 (n = ...) was about comparison group, children without pathology of the dentition. All studies

were conducted with informed consent. Cytokines IL-1, IL-6, IL-8, TNF-a, TGF-R were determined by enzyme-linked immunosorbent assay using kits from the firm "HUMAN". Cytokines IL-1, IL-6, TNF-a are that cytokines belonging to the group of pre-immune inflammation or primary pro-inflammatory. Secondary proinflammatory cytokines include chemokines that is a large group of more than 50 proteins. In our study, this group is represented by IL-8. Anti-inflammatory cytokines are TGF-R. For the work, statistical methods of descriptive statistics, correlation analysis were used establishing the reliability of the difference between data in the main and control groups on the basis of calculating the Student's test. Data in the text and tables are given as M ± m (mean ± standard error of the mean). The results with a significance level of <0.05 (95% confidence interval) were considered reliable.

Research Results and their Discussion

As it is known, a protracted course of wound healing with sluggish growth of granulations and delayed epithelization is possible in any phase of surgical intervention. Slowdown of wound healing occurs when immunity indicators decrease, for example, caused by a prolonged increase in the level of steroid hormones. The use of glucocorticoids (GCs) in the early postoperative period causes a significant decrease in the number and functions of immunocompetent cells, inhibition of angiogenesis, fibroblast proliferation and synthesis of extracellular matrix components. In this situation, GC reduces the normal expression of proinflammatory cytokines, which is required for wound healing. The mechanism of action of glucocorticoids is to inhibit the transcription of certain genes or to suppress the activation of NF-kB. Glucocorticoids inhibit the synthesis of proinflammatory cytokines, in particular IL-1, as well as the expression of the growth factors TGF-P and their receptors, which is reflected in the slowing down of the maturation of granulation tissue, which induces the synthesis of KGF in fibroblasts. Tumor necrosis factor (TNF-a), produced by macrophages, is a pro-inflammatory cytokine and plays a role in collagen synthesis. All this leads to a decrease in the re-epithelialization of wounds.

Taking into consideration that in children with secondary and residual defects and deformities of the palate after uranoplasty in this area, there is an activation of a number of immunological mechanisms aimed at preventing the generalization of the pathological process, we studied the local and general cytokine profile in this contingent of children in order to determine their meanings in its course. In our opinion, studies of cytokines in the oral fluid and serum are informative, which makes it possible to assess the systemic response of the body in the presence of a pathological process in the tissues of the oral cavity.

Table 1: Cytokine profile of blood serum and oral fluid in children with secondary and residual defects and deformities of the palate after uranoplasty

Indicator	I- group (n=16)	II- group (n=22)	III- group (n=24)
Blood serum			
IL-1, pg/ml	8,81±0,61*	6,85±0,54	5,29±0,38
IL-6, pg/ml	9,87±0,72*	5,34±0,41	4,05±0,31
IL-8, pg/ml	6,28±0,53*	2,60±0,24	1,74±0,13
TNF-a, pg/ml	20,99±1,28*	2,45±0,22	1,89±0,15
TGF-p, pg/ml	4,96±0,35*	4,01±0,26	3,71±0,26

Oral fluid			
IL-1, pg/ml	25,12±2,52*	120,05±9,62	139,72±20,05
IL-6, pg/ml	22,59±7,93*	55,86±4,03	41,58±3,69
IL-8, pg/ml	16,94±9,98*	47,55±3,31	39,87±3,53
TNF -a, pg/ml	0,29±6,07*	2,02±6,84	1,54±0,11
TGF-p, pg/ml	1,54±0,37*	2,82±0,36	3,68±0,27

Note: * - reliability of differences P <0.05 is relative to comparison groups

As can be seen from the presented research results (table 1), as a result of a decrease in the microbial load in the examined children, changes in the cytokine profile of blood serum occur, which are difficult to interpret, but from the point of view of their functional value, IL-1,6,8, TNF-a , that is, all pro-inflammatory cytokines, as well as TGF-R, which is necessary for the induction of regeneration processes, activation of fibroblasts, cells that are producers of collagen, elastin, proteoglycans. At the same time, TGF-R promotes the growth of blood vessels during reparative regeneration. With regard to the immune response in general, TGF-R manifests itself as an immunosuppressive agent. The importance of TGF-R is confirmed by the fact that it is one of three cytokines that is always detected in blood serum. Perhaps, this is due to the fact that the processes of cell death and their restoration are always parallel in the body.

Remarkably, the concentration of IL-1R was significantly lower in the oral fluid in children with defects. Possibly this is due to the depletion of the cytokine in connection with a long-term chronic inflammatory process. This assumption is indirectly confirmed by the fact that the use of antimicrobial therapy, due to which the microbial load decreases and, consequently, the inflammatory potential decreases, does not significantly increase the level of IL-1R, but, on the contrary, decreases it. The explanation for the findings of the study is that Porphyromonas gingivalis leads to a decrease in the production of IL-1R (3). It is known that IL-10 is a potent inhibitor of macrophages and their antigen-presenting function, and also inhibits the production of cytokines of active T-lymphocytes, namely, they synthesize TGF-R, one of the main participants in regeneration. It turned out that the level of serum TNF was significantly increased, while in the oral fluid it was significantly reduced. TNF takes part in the formation of a focus of local inflammation, creating barriers that can preserve the localization of the pathogen, and also induces the synthesis of IL-1 and IL-6, the main participants in the full response of the acute phase, which is necessary for the adequate course of all stages of inflammation and their full regeneration.

The presented research results indicate that in the oral fluid and blood serum of the examined children, there are multidirectional changes in the concentration of pro-inflammatory cytokines and growth factors. At the same time, there is a clear connection between the systemic cytokine profile and the process of wound healing in children with secondary and residual defects and deformities of the palate after uranoplasty. The obtained research results, on the one hand, indicate the values of cytokines in wound healing, which stimulates great interest of researchers, on the other hand, the main reasons are a decrease in epithelialization and delayed wound healing, as well as a decrease in reparative processes in children with secondary and residual defects and deformities of the palate after uranoplasty. The revealed fact is apparently due to a decrease in the production of IL-1 in the wound surface against the background of the use of glucocorticoids in the early postoperative period. For that reason, it can be concluded that disturbances in the production of cytokines, especially IL-1 in the wound surface, are one of the reasons for the complicated course of wound healing in children with secondary and residual defects and deformities of the palate after uranoplasty.

REFERENCES

Bessonov S.N. (2007). Surgical treatment of congenital and secondary deformities of the face with clefts of the upper lip and palate: Dis ... Dr. med. sciences. Smolensk, 2007. - p. 172.

Blasco-Baque V. Periodontitis induced by Porphyromonas gingivalis drives periodontal microbiota dysbiosis and insulin resistance via an impaired adaptive immune response / Garidou L., Pomie C., Escoula Q., et. al. // Gut. February, 2016, DOI: 10.1136

Blatun L.A. Local drug treatment of wounds. Problems and new opportunities for their solution // Consilium medicum. Surgery. 2007. No. 1. App. No. 1. - pp. 9-16.

Demyanov A.V., Kotov A.Yu., Simbirtsev A.S. Diagnostic value of the study of cytokine levels in clinical practice // Cytokines and inflammation. - 2003. - T. 2. - No. 3 – pp. 20 -35.

Dusmuhamedov D. M., Yuldashev A. A., Dusmuhamedov M. Z. New approach of cheilo- palatoplasty in children with unilateral congenital cleft lip and palate //European research: innovation in science, education and technology. 2018. – pp. 62-64.

Dusmukhamedov Dilshod Makhmudjanovich, Murtazayev Saidmurodxon Saida'Loevich, Yuldashev Abduazim Abduvalievich, Dusmukhamedova Dilnavoz Karamalievna, and Mirzayev Abdukadir. "Characteristics of morphometric parameters of the maxillo-facial region of patients with gnatic forms of occlusion abnormalities" European science review, vol. 2, no. 1-2, 2019. -pp. 95-99.

Dusmukhamedov M.Z. et al. Long-term results of bone grafting of the alveolar ridge defect in patients with cleft lip and palate // Ukrainian Journal of MRRGP. - 2013. - No. 2. – pp. 60-62.

Dusmukhamedov, D. M., Yuldashev, A. A., Dusmukhamedova, D. K., & Shamsiev, R. A. (2018). Comparative analysis of the results of microbiological and immunological studies in the long-term treatment of children with CCLP. Collection of scientific and practical international congress “Actual problems of dentistry and maxillofacial surgery.” Tashkent. – pp. 30-32.

Ivanov A. A., Fedorov D. N., Vasiliev A. B. et al. The role of EGF-stimulated epidermis in the regulation of wound healing // Arch. patol. 2002. No. 1. – pp. 11-14.

Mamedov A.A. (2002). Clinical and anatomical classification of congenital cleft of the upper lip and palate. Hereditary pathology of the head, face and neck in children: topical issues of complex treatment. –pp. 155-157.

Pogodina M.A., Abalmasov K.G., Shekhter A.B. Experimental substantiation of plasmodynamic therapy of non-healing wounds with exogenous nitric oxide // Annals of plastic, reconstructive and aesthetic surgery. 2007. No. 2. –pp. 89-95.

Rizaev Zh.A., Shamsiev R.A. The reasons for the development of caries in children with congenital clefts of the lip and palate (review of the literature) // Vyunik Problems of the Bulletin of Medicine. 2018. No. 2 (144).

Shamsiev Ravshan Azamatovich, Rizayev Zhasur Alimdzhanovich The functional State of platelets in children with congenital cleft palate with chronic foci of infection in the nasopharynx and lungs // International scientific review. 2019.

Simbirtsev A.S. Cytokines - a new system of regulation of the body's defense reactions // Cytokines and inflammation. - 2002. - No. 1. - pp. 9-16.

Tolstykh M. P., Derbenev V.A., Bekher Yu. V. et al. Stimulation of healing and prevention of suppuration of postoperative wounds. M .: Deepak, 2007. –p. 96.

Tolstykh M. P., Lutsevich O.E. et al. Theoretical and practical aspects of wound healing. M .: Deepak, 2007. –p. 96.

Vokhidov Utkirbek Nuridinovich. "Estimation of an average face zone after the primary cleft lip repair with congenital cleft upper lip and palate" European science review, no. 1-2, 2017. - pp. 55-56.

A biomarker that identifies senescent human cells inculture and in aging skin in vivo / G. P. Dimri [et al.] //Proc. Natl. Acad. Sci. USA. 2005. Vol. 92, N 20. – pp. 9363-9367.

Altered intercellular communication in lung fibroblastcultures from patients with idiopathic pulmonary fibrosis/ A. Trovato- Salinaro [et al.] // Respiratory Research. 2006. Vol. 7. – pp.122-131.

Galkowska H., Wojewodska U., Olszewski W.L. Chemokines, cytokines, and growth factors in keratinocytes and dermal endothelial cells in the margin of chronic diabetic foot ulcers // Wound Repair Regen.- 2006. - V. 14. - pp. 558-565.

Ghazizadeh M., Tos M., Shimizu H. Et al. Functional implication of the IL-6 signaling pathway in keloid pathogenesis // J. Invest. Dermatol. - 2007. - V. 127. - pp. 98-105.

Kishimoto T. Interleukin-6: discovery of pleiotropic cytokine // Arthritis Res. Ther.- 2006. - V. 8. - Suppl. 2. - pp. 2-14.

Lawrence C. M., Matthews J. N., Cox N. H. The effect of ketanserin on healing of fresh surgical wounds // Br. J. Dermatol. 2005. V. 132. – pp. 580-586.

Mesëe G., Richard G., White T. W. Gap Junctions: basic structure and function // Journal of Investigative Dermatology. 2007. Vol. 127. – pp. 2516-2524.

Proliferative capacity of venous ulcer wound fibroblasts in the presence of platelet - derived growthfactor / R. Vasquez [et al.] / / Vasc. Endovascular Surg. 2004. Vol. 38, N 4. – pp. 355-360.

Shleiffenbaum B. Regulation and selectivity of leukocyte emigration // J. Lab. Clin. Med. 2006. Vol. 127. – pp.151-168.

Telgenhoff D., Shroot B. Cellular senescence mechanisms inchronic wound healing // CellDeath and Differentiation. 2005. N 12. – pp. 695-698.

Wei C. J., Xu X., Lo C. W. Connexins and cell signaling in development and disease // Annu. Rev. Cell Dev. Biol. 2004. Vol. 20. – pp. 811-838.