



GLOBAL JOURNAL OF MEDICAL RESEARCH: J
DENTISTRY & OTOLARYNGOLOGY
Volume 21 Issue 2 Version 1.0 Year 2021
Type: Double Blind Peer Reviewed International Research Journal
Publisher: Global Journals
Online ISSN: 2249-4618 & Print ISSN: 0975-5888

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

By D. M. Dusmukhamedov, A. A. Khadzhimetov, Z.K. Khakimova
& D. K. Dusmukhamedova

The Relevance of the Research- The provision of 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). In 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 surgical intervention in the dento-maxillary system causes disturbances in microcirculation, as well as 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 is worse. The interest in 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.

GJMR-J Classification: NLMC Code: WU 300



THE STATE OF THE LOCAL CYTOKINE STATUS AND ITS PATHOGENETIC SIGNIFICANCE WITH SECONDARY AND RESIDUAL DEFORMITIES OF THE PALATE AFTER URANOPLASTY IN CHILDREN

Strictly as per the compliance and regulations of:



RESEARCH | DIVERSITY | ETHICS

© 2021. D. M. Dusmukhamedov, A. A. Khadzhimetov, Z.K. Khakimova & D. K. Dusmukhamedova. This is a research/review paper, distributed under the terms of the Creative Commons Attribution-Noncommercial 3.0 Unported License (<http://creativecommons.org/licenses/by-nc/3.0/>), permitting all non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

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

D. M. Dismukhamedov^α, A. A. Khadzhimetov^σ, Z.K. Khakimova^ρ & D. K. Dismukhamedova^ω

I. THE RELEVANCE OF THE RESEARCH

The provision of 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). In 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 surgical intervention in the dento-maxillary system causes disturbances in microcirculation, as well as 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 is worse. The interest in 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. Recently, it is proved that the factors affecting wound healing, and cell interaction is the normal work of cells and cytokines. Consequently, the regeneration of tissues in 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 conducting various kinds and techniques of uranoplasty,

in particular arising from the secondary (SD) (post-operative) and residual defects (RD) of the palate in children, as well as difficulties in treating them do to date and the need for further study of their pathogenesis and improve the methods of treatment.

The aim of our study was- to evaluate with local cytokine status and its pathogenic role in secondary and residual defects of the palate after uranoplasty in children.

II. MATERIAL AND RESEARCH METHODS

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 CCLP who were treated in the department of pediatric surgical dentistry of the Andijan regional hospital in the period from 2010-2019. and pediatric maxillo - facial surgery clinic of the Tashkent State Dental Institute in the period 2010-2019 gg. To systematize residual and secondary defects and deformities of the upper lip, alveolar ridge and palate, the classification of E.N. Samara (1977, 1981), 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 you know, the results of uranoplasty largely depend on the completeness of the restoration of the anatomy of the palate and on the correct position of the pathologically altered muscles of the soft palate, which provide the palatopharyngeal 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 RD and SD of the palate after uranoplasty largely depends on the shape of the cleft and the method of uranoplasty, while 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 (RD) at the border of the hard and soft palate 18.5%. RDs of this localization, as a

Author ^{α σ ρ ω}: Tashkent State Dental Institute, Andijan State Medical Institute. e-mail: author.uzb@mail.ru

rule, develop due to the anatomical features of the cleft and technical errors of the operation. The results of a retrospective analysis of 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 in physical development from their peers. Consequently, secondary and residual defects, as well as deformation of the sky, are often the result of a defective examination and treatment of patients 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 = ...) - children with RD and SD of the palate after uranoplasty and group 3 (n = ...) - comparison group, children without pathology of the dentition. All studies were conducted with informed consent. The cytokines IL-1, IL-6, IL-8, TNF-a, and TGF-R were determined by enzyme immunoassay using "HUMAN" kits. Cytokines IL-1, IL-6, TNF-a, belonging to the group of pre-immune inflammation or primary pro-inflammatory cytokines. Secondary proinflammatory cytokines include chemokines, a large group of more than 50 proteins. In our study, this group is represented by IL-8. Anti-inflammatory cytokines: TGF- R. For the work, we used statistical methods of descriptive statistics, correlation analysis, 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 $M \pm m$ (mean value \pm standard error of its mean). Results with a significance level of <0.05 (95% confidence interval) were considered reliable.

III. RESEARCH RESULTS AND THEIR DISCUSSION

As it is known, in any phase of the surgical interference possibly a protracted course of healing of the wound process, with sluggish growth of granulation and delayed epithelization. Slowing down of wound healing occurs with a decrease in immunity indicators, 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 components of the extracellular matrix. In this situation, HA reduces the normal expression of proinflammatory cytokines, which is required for wound healing. The mechanism of action of glucocorticoids is inhibition of the transcription of certain genes, or in the suppression of the activation of NF -KB and. 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 reduction reepitelization wounds.

Considering that children with secondary and residual defects and deformations of the sky after uranoplasty in this area marked activation of a range of immunological mechanisms aimed at preventing the generalization of the pathologic process, we studied the local and general cytokine profile in this group of children with the purpose of determining their values in its flow. Informative in our opinion, is the study of cytokines in oral fluid and serum, which allows the system to evaluate the reaction of the organism in the presence of a pathological process in the oral tissues.

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)
Bloodserum			
IL-1 , pg / ml	6.85 \pm 0.54	8.81 \pm 0.61	5.29 \pm 0.38
IL-6, pg / ml	5.34 \pm 0.41	9.87 \pm 0.72	4.05 \pm 0.31
IL-8, pg / ml	2.60 \pm 0.24	6.28 \pm 0.53	1.74 \pm 0.13
TNF-a , pg / ml	2.45 \pm 0.22	20.99 \pm 1.28	1.89 \pm 0.15
TFR-r, pg / ml	4.01 \pm 0.26	4.96 \pm 0.35	3.71 \pm 0.26

Oralfuid			
IL-1 , pg / ml	120.05 ± 9.62	25.12 ± 2.52	139.72 ± 20.05
IL-6, pg / ml	55.86 ± 4.03	22.59 ± 7.93	41.58 ± 3.69
IL-8, pg / ml	47.55 ± 3.31	16.94 ± 9.98	39.87 ± 3.53
TNF-a , pg / ml	2.02 ± 6.84	0.29 ± 6.07	1.54 ± 0.11
TFR-r, pg / ml	2.82 ± 0.36	1.54 ± 0.37	3.68 ± 0.27

Note: * - reliability of differences $P < 0, 05$ relative to the comparison group

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 significance, 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.

Interestingly, the concentration of IL-1R was significantly lower in the oral fluid in children with defects. In POSSIBILITY, this is due to the depletion of the cytokine in connection with long-flowing 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 participates 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.

Presented studies indicate that in the oral fluid and blood serum of children surveyed come multidirectional changes in the concentration pro-

inflammatory cytokines and growth factors. Thus, there is a clear relationship between systemic cytokine pro Lemma and the process of healing wounds in children with secondary and residual defects of palate and strains after uranoplasty. The results of studies with one hand indicate values cytokines straight and wound healing that is of great interest of researchers , on the other of the SIC causes reduction epithelialization and dividing of wound healing and reduce e reparative processes in children with secondary and residual Defects and deformities of the palate after uranoplasty. Revealing the facts apparently due to a decrease m the production of IL -1 in the wound surface on a background of the use of glucocorticoids in early post operative period. Consequently, it can be concluded that disfunction production of cytokines, particularly IL-1 at the wound surface is one of the reasons of complicated wound healing in children with secondary and residual Defects sky and strains after uranoplasty.

BIBLIOGRAPHY

1. Blatun L.A. Local medical treatment of wounds. Problems and new opportunities for their solution // Consilium medicum. Surgery. 2007. No. 1. App. No. 1. S. 9-16.
2. 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.-- 172 p.
3. 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.
4. 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 CRHN. Collection of the scientific and practical international congress "Actual problems of dentistry and maxillofacial surgery." Tashkent, 30-32.
5. Dusmukhamedov MZ 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. - S. 60-62.
6. 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 - S. 20 -35.
 7. Ivanov A. A., Fedorov DN, Vasiliev A. Bed and. et al. The role of EGF -stimulated epidermis in the regulation of wound healing // Arch. patol. 2002. No. 1. S. 11-14.
 8. Mamedov A.A. (2002). Clinical and anatomical classification of congenital cleft of the upper lip and palate. Clinical presentation- anatomical classification of congenital cleft lip and palate. Hereditary pathology of the head, face and neck in children: topical issues of complex treatment, 155-157.
 9. 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. S. 89-95.
 10. Simbirtsev A.S. Cytokines - a new system of regulation of the body's defense reactions // Cytokines and inflammation. - 2002. - No. 1. - P. 9-16.
 11. Tolstyh M. P., Lutsevich OE et al. Theoretical and practical aspects of wound healing. M.: Deepak, 2007.96 p.
 12. Tolstyh M. P., Derbenev VA, Becher Yu. V. et al. Stimulation of healing and prevention of suppuration of postoperative wounds. M.: Deepak, 2007.96 p.
 13. Dusmuhamedov DM, Yuldashev AA, Dusmuhamedov MZ New approach of cheilopalatoplasty in children with unilateral congenital cleft lip and palate // European research: innovation in science, education and technology. 2018. - With. 62-64.
 14. 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.
 15. Rizaev Zh.A., Shamsiev R.A. Causes of dental caries in children with cleft lip and palate (review) // Vyunik problems byulogp i medicine. 2018. No. 2 (144).
 16. 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.
 17. 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.
 18. A biomarker that identifies senescent human cells inculture and in aging skin in vivo / GP Dimri [et al.] // Proc. Natl. Acad. Sci. USA. 2005. Vol. 92, No. 20. P.9363-9367.
 19. Altered intercellular communication in lung fibroblastcultures from patients with idiopathic pulmonary fibrosis / A. Trovato - Salinaro [et al.] // Respiratory Research. 2006. Vol. 7.P. 122-131.
 20. Galkowska H., Wojewodska U., Olszewski WL 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. - P. 558- 565.
 21. 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. - P. 98-105.
 22. Kishimoto T. Interleukin- 6: discovery of pleiotropic cytokine // Arthritis Res. Ther. - 2006. - V. 8. - Suppl. 2. - P. 2-14.
 23. Lawrence CM, Matthews JN, Cox NH The effect of ketanserin on healing of fresh surgical wounds // Br. J. Dermatol. 2005. V. 132. P. 580-586.
 24. Shleiffenbaum B. Regulation and selectivity of leukocyte emigration // J. Lab. Clin. Med. 2006. Vol. 127. P. 151-168.
 25. Proliferative capacity of venous ulcer wound fibroblasts in the presence of platelet - derived growthfactor / R. Vasquez [et al.] // Vasc. EndovascularSurg. 2004. Vol. 38, No. 4. P. 355 - 360.
 26. Telgenhoff D., Shroot B. Cellular senescence mechanisms inchronic wound healing // CellDeath and Differentiation. 2005. N 12.P. 695 - 698.
 27. Mesøe G., Richard G., White TW Gap Junctions: basic structure and function // Journal of Investigative Dermatology. 2007. Vol. 127. P. 2516-2524.
 28. Wei CJ, Xu X., Lo CW Connexins and cell signaling in development and disease // Annu. Rev. CellDev. Biol. 2004. Vol. 20.P. 811-838.