Glucocorticoids and Postoperative Disease in Oral - Maxillofacial Surgery

CRISTIAN CONSTANTIN BUDACU[1], SORIN V. IBRIC CIORANU[2]*, IULIA CHISCOP[3], CONSTANTIN MIHAI[1]

[1]Grigore T. Popa University of Medicine and Pharmacy, Faculty of Dental Medicine, 16 Universitatii Str, 700115, Iasi, Romania

[2]Titu Maiorecu University of Medicine and Pharmacy, Faculty of Dental Medicine, Oral-Maxilofacial Surgery Department, 67A Gh.Petrascu Str., 031593, Bucharest, Romania

[2]Dunarea de Jos University of Galati, 47 Domneasca Str., 800008, Galati, Romania

Postoperative manifestations like pain, edema, affected oral functions provoke transitory morbidity in patients to a late recovery. Various classes of medicines are prescribed to prevent placing patients in such unpleasant situations. Both dexamethasone and methylprednisole can be used to reduce the manifestations of the postoperative disease. Although the state of local inflammation is precursory to healing, its exacerbation can lead to extremely painful severe local edema through tissue distention. In the initial phase of the inflammatory process, glucocorticoids act as producers of vein-active substances like prostaglandins and leukins, as dexamethasone has a recognised capacity of reducing COX-2, which is responsible for generating PGs which are produced within the inflammatory response. The efficiency of glucocorticoids is admitted in reducing the inflammatory state, lying at the top of oral maxillofacial surgeons´s choice in the therapy of postoperative manifestations. Our research was addressed to a lot of 68 patients to whom we performed interventions of oral and maxillofacial surgery at the Outpatient Clinic of Oral-Maxillofacial Surgery of Ia'i. Dexamethasone is a strong glucocorticoid with the following chemical formula: 90-fluoral-160 methylprednisole. The antiinflamatory effect of a 0.75 mg dosis of dexamethasone is equivalent to that produced by 5 mg of Prednison. Dexamethasone is more efficient than Medrol in the treatment of postoperative edema with complete remission of symptomatology.

Keywords: oral-maxillofacial surgery, glucocorticoids, dexamethasone, methylprednisole, postoperative disease

Any oral-maxillofacial surgery produces a traumatism which creates ripple effects, which is how three quarters of postoperative diseases are generated, being determined by nervous causes, rather than by chemical (toxic) causes. The best way to avoid them is to systematically use methods to block nervous extremities in order to guard them from vein-motoric posttraumatic disturbances provoked by surgeon's hand, even if operations are conducted mildly and without brutality. Operative traumatism challenges the global neural-hormonal balance of the organism in direct relationship with the intensity of the aggression and the reactive capacity of the relevant tissue through surgical intervention. As a consequence, patients set out by reflex a series of general and local changes with a defensive and compensatory role, whose occurrence, intensity and duration depend on the reactions of the organism, on its adapting power and its defence reserves [1,2].

Postoperative disease in oral-maxillofacial surgery has many clinic manifestations, some more frequent, others rarer, some milder, others more severe [3]. Postoperative edema results in interstitial liquid retention, which is clinically translated through tumefaction of the operated area and adjacent areas and by obstructing the lymphatics which drain the intervention site. This is explained through the richness of cellular tissue in some of the neighbouring regions: the genian, sub-mandibular region especially with overweight persons. Once installed, the edema creates a disharmonic aspect to the patient's physiognomy, stresses the intensity of the pain, determines the appearance of the trismus and can also alter the general state through a possible transitory bacteraemia and postpones the postoperative healing process [4,5].

Under these conditions, the necessity of knowing the prevention methods of the postoperative edema, which can be achieved first of all by avoiding the hurting of areas rich in conjunctive tissue by mild operative techniques.

Postoperative edema appears as a consequence of traumatising surgical manoeuvres or through intraoperative instrumental compressions; it is considered as the first phase of acute inflammation and in fact immediately after local-regional anaesthesia, a transitory vein constriction followed by vein dilation and lessening of the blood stream takes place.

Although normally cellular elements of the blood circulate through the centre of the sanguine stream, while plasma circulates at the periphery, in this case cellular elements circulate peripherally. Some authors claim that postoperative edema appears due to the fact that operative traumatism would produce histamine liberation [6-8].

In the appearance and development of postoperative edema, an important role is played by the allergic factor related to the individual responses to Ag-Ac reactions, leading to histamine liberation in the cells which respond to anaphylactic reactions. Other authors pay more attention to nervous phenomena, showing that vein mobility disturbances are produced locally on a neural-humoral path determining vein dilation, slowing down of circulation, local hyperaemia and a growth of vascular permeability with plasma extravasation and leukocyte inflow [9-11].

The anti-algetic and anti-inflammatory therapy of the postoperative edema targets the combating of the pain associated to tissue distension and local congestive phenomena. Pain occupies a very important place within the manifestations of the postoperative disease because it is the symptom which influences patients' state the most, as a more or less accepted daily reality. Some authors also

*email: isorin83@yahoo.com; Phone: (+40)748365320

insist on the reverse aspect of the issue, that is that paint induces anxiety, which however sets out muscular spasm in the area where the pain is localised, with vein constriction and the production of pain-promoting substances [12, 13]. They established that negative-type emotion is a good pain predictor and of course the way in which patients will accept therapy as well its success rate.

The efficiency of glucocorticoids is recognised as far as reducing the state of inflammation is concerned, lying at the top of oral maxillofacial surgeons regarding the therapy of postoperative manifestations.

These make up for a heterogeneous class of compounds which have a common action spectrum: painkilling, anti-inflammatory and antipyretic effect of various magnitudes. The inhibitors of the trombochsan (COX 2) and the consecutive reduction of the prostaglandins (PGs) explain the painkilling, antipyretic and antitrombotic activity.

Although to a lesser extent, inflammatory pain is especially susceptible to glucocorticoids and, these are less active than opioids, they can be as efficient under some conditions (postoperative pain). Glucocorticoids were developed in the 1940s and are used for treating stress-related disorders, as they are able to regulate stress responses. Glucocorticoids that may be used for reducing swelling and pain in orthognathic surgery, facial fractures, third molar removal and oncological reconstructive surgery include dexamethasone, hydrocortisone and methylprednisolone [14,15].

Patients undergoing general anesthesia for minor surgery such as dental procedures may receive 100 mg hydrocortisone intramuscularly. Major surgery requires 100 mg hydrocortisone before surgery, followed by a dose of 50 mg / 8 h for 48 h. Dexamethasone varies from 5 mg single-dose to a 116 mg total-dose. The total dose of dexamethasone used in orthognathic surgery, facial trauma surgery and reconstructive surgery ranges from 10 mg to 40 mg [16].

Pain control with injectable glucocorticoids can be achieved in cases of moderate to severe dental surgical procedures by reducing the nociceptive response of the operated tissue. Glucocorticoids limit swelling and pain by reducing the formation of COX-2 and phospholipases, which act as inflammation mediators [17].

Glucocorticoids reduce the permeability of the capillaries and of the vascular wall. Thereby, they prevent inflammatory mediators and fluids from entering the gingival tissues, so that they are also used in the therapy of postoperative edema. Glucocorticoids may ameliorate neurosensory disturbances such as the damage of the inferior alveolar nerve, which is a postoperative complication of maxillofacial surgery [18].

Due to the fact that glucocorticoids are stress relieving drugs, they have been also used in patients with dental anxiety. Oral or intravenous steroids are recommended in dental procedures, but frequent use may raise concern about the risk of disturbing the normal function of adrenal glands, especially in patients with comorbidities, such as Addison's disease. However, even if restorative dental treatment was found to increase salivary and urinary cortisol levels, they rise only 4 hours after surgery and return to the initial levels after 24 hours. Other glucocorticoid-related complications may involve muscular pain in patients who have received medication intramuscularly, but glucocorticoids rarely cause side effects. The only issue is that glucocorticoids alter the electrolyte and fluid balance and increase sodium and water retention [19]. Only one case of psychosis was reported in a 16-year old female patient with orthognathic surgery, after receiving first dose of 250 mg methylprednisolone intravenously, followed by three further doses of 250 mg / 6 h [20].

Glucocorticoids are rarely used in third molar surgery. Third molar surgery is considered a minor procedure performed under local anesthesia. Therefore, glucocorticoids are mostly used in orthognathic surgery [21].

Experimental part

Material and method

In the 1990s, a series of authors were proposing a method of evaluating the edema based on establishing an edematisation index resulting from measurements of the postoperative facial distension. Through numerous studies, specialty literature updates and recommends Carrillo's equation as an efficient method of assessing postoperative edema. Although the method does not constitute a novelty in the international practice of oral-maxillofacial surgery, we consider it useful in applying the treatment to the postoperative disease. Thus, the methods of comparative evaluation of the efficiency of the glucocorticoid therapy in the interventions of oral-maxillofacial surgery that we used in our studies were:

- measuring the facial distension caused by postoperative edema on the basis of anatomical references. We

Table 1

POSTOPERATORY MANIFESTATION	24 HOURS	48 HOURS	72 HOURS
EDEMA	E_C= 27.27 PRONOUNCED	E_C= 27.27 PRONOUNCED	E_C= 18.18 MODERATE
PAIN	Score 2	Score 2	Score 1

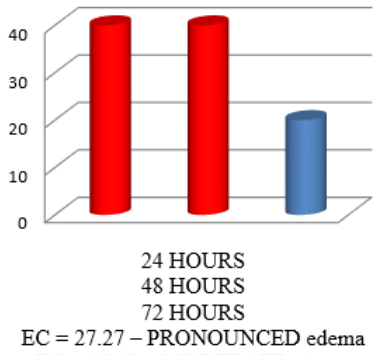


Fig.1 The evolution of the postoperative edema as modulated by the administration of preoperative Medrol

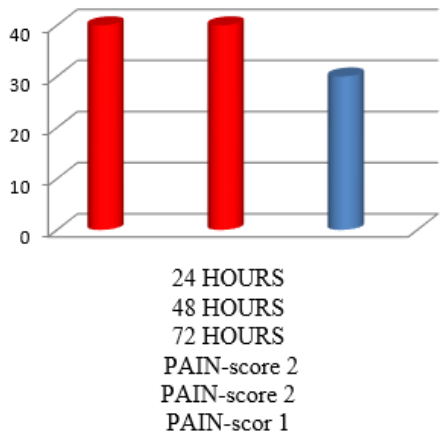
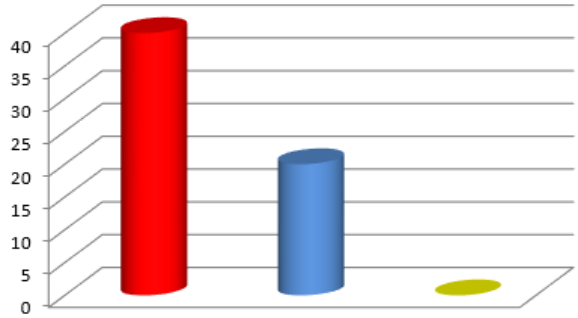


Fig.2. Evolution of postoperative pain modulated by preoperative administration of Medrol

POSTOPERATORY MANIFESTATION	24 HOURS	48 HOURS	72HOURS
EDEMA	E_C= 27.27 PRONOUNCED	E_C= 18.18 MODERATE	ABSENT
PAIN	Score 2	Score 2	Score 0

Table 2



24 HOURS
48 HOURS
72 HOURS
EC = 27.27 – PRONOUNCED edema
EC = 27.27 – PRONOUNCED edema
EC = 18.18 – MODERATE edema

Fig.3. Evolution of postoperative edema modulated by preoperative administration of Dexamethasone

Table 3

POSTOPERATORY MANIFESTATION 72 hours	DEXAMETHASONE	MEDROL
EDEMA	ABSENT	MODERATE
PAIN	Score 0	Score 1

measured the distance between the middle of the chin and the basis of the ear lobe on the same side with the help of Carrillo's modified formula, thus establishing the edematisation index as E_c: at 24 h postoperative, 48 h postoperative and 72 h postoperative respectively;

- we realised the evaluation of postoperative pain on the basis of the Postoperative Comfort Score.

The values of the edematisation index of the intensity of pain taken as points of reference in our study were:

The edematisation inde**x**

EC = POSTOPERATIVE distance – preoperative Distance X 100

PREOPERATIVE Distance(a reference value of the preoperative distance between the middle of the chin and the basis of the ear lobe on the same side = 11 cm)

For a distension of the facial profile by 1 cm ..... E_C = (12-11) : 11 X 100 = 9.09 ...MILD EDEMA

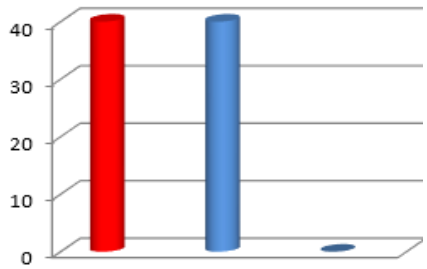
For a distension of the facial profile by 2 cm .....E_C = (13-11): 11 X 100 = 18.18 … MODERATE EDEMA

For a distension of the facial profile by 3 cm ..... E_C = (14-11) : 11 X 100 = 27.27 ... PRONOUNCED EDEMA

Pain intensity – Comfort score

Score 0 – absence of pain; score 1 –some minor or moderate pain complaints; Score 2 – moderate/major pain complaints; score 3 – major pain complaints

Departing from these items, our research envisioned the establishment of the therapeutic methods proposed as new. We thus planned a study with the goal to evaluate the efficiency of two representatives of the synthesis glucocorticoid class – Dexamethasone versus Medrol (Methylprednisolon) in preventing the manifestations of the edema-type postoperative disease and of pain. It follows



24 HOURS
48 HOURS
72 HOURS
PAIN-score 2
PAIN-score 2
PAIN-score 0

Fig.4. Evolution of postoperative pain modulated by preoperative administration of Dexamethasone

Table 4

	Chi-square	*p*
Chi-square (Pearson)	χ^2 = 18.13976	p=0.00590
Chi-square (M-L)	χ^2 = 20.44448	*p*=0.00231

that our research was addressed to a lot of 68 patients to whom we performed interventions of oral and maxillofacial surgery in the framework of day hospitalisations in the Oral-Maxillofacial Surgery Clinic Iasi.

Results and discussions

Dexamethasone is a synthesis glucocorticoid of high potency, with the following chemical formula: 90-fluoral-160 Methylprednisolone.

The anti-inflammatory effect of a 0.75 mg dose of Dexamethasone is equivalent to the one caused by 5 mg of Prednisone. As opposed to other corticosteroids, Dexamethasone does not have a practical effect of saline retention. The time of plasma halving is three hours; it has a long-lasting effect (36-54 h). Medrol or Methylprednisolone is a synthetic glucocorticoid derived from the carbon methylation in posture 6 of the prednisolone. It is available in 4, 16, 32, 40 mg doses.

In our study, 8 mg of dexametasone and 40 mg of Methylprednisolone were prescribed to patients (two equal 34-patient groups) an hour before the surgical procedure.

Edema and postoperative pain were detected comparatively in both groups on days 1, 2 and 3 of postoperative evolution. The Chi-square test was used to evaluate the significance between the study parameters.

The administration of 40 mg Medrol revealed the following findings:edema 24 h Ec =27,27 marked, edema 48 h Ec=27,27 marked, edema 72 h Ec=18,18 marked.

The evolution of postoperative pain as modulated by the administration of preoperative Medrol.

The administration of 40 mg of medrol showed the following results (table 1, fig. 1, 2).

The administration of 8 mg of dexamethasone showed the following results (table 2, fig. 3, 4).

The influence of preoperative glucocorticoid administration can be summarized in the table (table 3).

The correlation coefficient (Pearson) shows a close relationship between the variable of the preoperative administration of Dexamethasone and elimination of postoperative edema (table 4).

Conclusions

The maximum efficiency in the treatment of postoperative edema, with the complete remission of the symptoms after 72 h, is achieved through the administration of Dexamathasone as compared to Medrol.

Although no significant statistic differences were detected as concerns the level of postoperative pain, the patients to whom we administered Dexamethasone claimed to have a better postoperative comfort score and hence a lower level of pain.

References

1.BAXENDALE BR, VATER M, LAVERY KM. Dexamethasone reduces pain and swelling following extraction of third molar teeth. Anaesthesia 1993;48(11):961-4.

2.BJORNSSON G.A., HAANAES H.R. : Naproxen 500 mg bid versus acetaminophen 1000 mg qid: effect on swelling and other acute postoperative events after bilateral third molar surgery. J. Clin. Pharmac.,2005, 43(8):849-858

3. PATRASCU, Al., SAVIN, L., LUPESCU, O., MIHAILESCU, D., MIHAI, D.N., NICULAES, M., GRIGORESCU, V., GREIEROSU, C., BOTEZ, P., Rev. Chim. (Bucharest), **68**, no. 1, 2017, p. 200

4.BUCUR A., VILA C.N., LOWRY J.,: Oro-maxillofacial surgery compendium. 2009, Q Med Publishing house, Bucharest

5.CALVO A.M., SAKAI V. T.: Analgesic and anti-inflammatory dose–response relationship of 7.5 and 15 mg meloxicam after lower third molar removal: adouble-blind, randomized, crossover study. Int. J.Oral Maxillofac. Surg. ,2007, 36: 26–31

6.CARRICHES LC, GONZÁLEZ MJM, RODRIGUEZ DM. The use of methylprednisolone versus diclofenac in the pre-emptive effect of dexamethasone and methylprednisolone in the treatment of inflammation and trismus after surgical removal of lower third molars. Med Oral Patol Oral Cir Bucal 2006;11(5):E440-5.

7.DARAWADE DA, KUMAR S, MEHTA R, SHARMA AR, REDDY GS. In search of a better option: Dexamethasone versus methylprednisolone in third molar impaction surgery. J Int Oral Health 2014;6(6):14-7.

8.EBERSOLE J.L., CAPPELLI D.: Acute-phase reactants in infections and inflammatory diseases. Periodont.,2003, 23:19-49

9.FILHO, J.R.L., CAMARGO I.B.: The influence of cryotherapy on reduction of swelling, pain and trismus after third-molar extraction. A preliminary study. JADA,2005, 136 : 774-778

10. JENSEN MP, MARTIN SA, CHEUNG R. : The meaning of pain relief in a clinical trial. J. Pain. ,2005, 6: 400–406

11.JESKE A.H.: Selecting new drugs for pain control: evidence-based decisions or clinical impressions? J. Amer. Dent. Assoc.2005,,133:1052-1056

12.KIM K, BRAR P, JAKUBOWSKI J, KALTMAN S, LOPEZ E. The use of corticosteroids and nonsteroidal antiinflammatory medication for the management of pain and inflammation after third molar surgery: A review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2009;107(5):630-40.

13.KLONGNOI B, KAEWPRADUB P, BOONSIRISETH K, WONGSIRICHAT N. Effect of single dose preoperative intramuscular dexamethasone injection on lower impacted third molar surgery. Int J Oral Maxillofac Surg 2012;41(3):376-9.

14.LAUREANO FILHO JR, MAURETTE PE, ALLAIS M, COTINHO M, FERNANDES C. Clinical comparative study of the effectiveness of two dosages of Dexamethasone to control postoperative swelling, and pain . Med Oral Patol Oral Cir Bucal 2008;13(2):E129-32.

15.LENKA S, JAIN N, MOHANTY R, SINGH DK, GULATI M. Clinical comparison of three techniques of mandibular local anaesthesia. Adv Hum Biol 2014;4:13-9.

16.ONG K.S., SEYMOUR R.A.: The efficacy of preoperative versus postoperative rofecoxib for preventing acute postoperative dental pain: a prospective randomized crossover study using bilateral symmetrical oral surgery. Clin. J. Pain ,2007, 21:536-542

17.PEÑARROCHA M., GARCIA B.: Pain and swelling after periapical surgery in 60 patients. J. Oral Maxillofac. Surg.,2006,64:429-433

18.SANTANA H.G., PEÑARROCHA M.D. : Pain and inflammation in 41 patients following the placement of 131 dental implants. Med. Oral Patol. Oral Chir. Bucal ,2005, 10:258-263

19.SORTINO F, CICCIU M. Strategies used to inhibit postoperative swelling . Dent Res J (Isfahan) 2011;8(4):162-71.

20.USTUN Y, ERDOGAN O, ESEN E, KARSLI ED. Comparison of the effects of 2 doses of methylprednisolone on pain, swelling, and trismus after third molar surgery. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2003;96(5):535-9.

21.YUASA H., SUGIURA M.: Clinical postoperative findings after removal of impacted mandibular third molars: prediction of postoperative facial swelling and pain based on preoperative variables. Brit. J. Oral Maxillofac. Surg., 2007,42: 209–214

Manuscript received: 4.04.2017