



Effectiveness of submucosal, oral, and intramuscular routes of dexamethasone administration in trismus, swelling, and pain reduction after the third lower molar surgery

Efikasnost submukozne, oralne i intramuskularne primene deksametazona u redukciji trizmusa, otoka i bola nakon hirurgije donjih trećih molara

Filip Djordjević*, Marija Bubalo[†], Dejan Perić*, Djordje Mihailović*,
Zoran Bukumirić[‡], Dejan Dubovina*

*University of Priština/Kosovska Mitrovica, Faculty of Medical Sciences, Department of Oral Surgery, Kosovska Mitrovica, Serbia; [†]Military Medical Academy, Dentistry Clinic, Belgrade, Serbia; [‡]University of Belgrade, Faculty of Medicine, Belgrade, Serbia

Abstract

Background/Aim. Surgical extraction of impacted lower third molars is inevitably followed by the postoperative occurrence of trismus, swelling, and pain sensations to some degree. Corticosteroids (dexamethasone in particular) are commonly used drugs in the prevention of these complications. The aim of this study was to determine the effectiveness of dexamethasone in the prevention of postoperative complications, edema, trismus, and pain after the surgical extraction of impacted lower third molars, depending on the method of its administration. **Methods.** This prospective study involved 30 healthy patients, aged 18 years and above, of both sexes, with fully impacted lower third molar – class I or II and position B or C, according to Pell and Gregory classification system and vertical position according to Winter classification. All patients were divided randomly into three groups depending on the way of dexamethasone administration: oral – dexamethasone administered in the form of oral tablets in a dose of 4 mg one hour before the surgery; submucosal – dexamethasone solution administered submucosally in a dose of 4 mg in the area of the buccal

sulcus, after the inferior alveolar nerve block anesthesia and additional anesthesia for the buccal nerve; intramuscular – dexamethasone solution administered intramuscularly in a dose of 4mg into the area of the deltoid muscle, right before the intervention. Preoperatively and at every follow-up (on the first, second, and seventh day postoperatively), interincisal distance, the degree of edema, and the level of pain with the use of a visual analog scale (VAS) were measured. On the seventh postoperative day, the total number of analgesics taken by the patients was recorded. **Results.** In the postoperative period, there was no statistically significant difference between the examined groups in terms of effectiveness in swelling, trismus, and pain reduction ($p > 0.05$). **Conclusion.** There is no significant difference in dexamethasone effectiveness in postoperative trismus, swelling, and pain reduction after the third lower molar surgery, regarding the route of administration – oral, intramuscular, or local submucosal.

Key words: dexamethasone; drug administration routes; molar, third; oral surgical procedures; trismus.

Apstrakt

Uvod/Cilj. Hirurška ekstrakcija impaktiranih donjih trećih molara je, u izvesnom stepenu, neizbežno praćena postoperativnom pojavom trizmusa, otoka i osećaja bola. Kortikosteroidi (naročito deksametazon) su lekovi koji se najčešće koriste u prevenciji tih komplikacija. Cilj rada bio je da se utvrdi efikasnost deksametazona u prevenciji postoperativnih komplikacija, edema, trizmusa i bola, nakon hirurške ekstrakcije impaktiranih donjih trećih molara, u zavisnosti od načina njegove administracije. **Metode.**

Prospektivnom studijom obuhvaćeno je 30 zdravih pacijenata, starijih od 18 godina, oba pola, sa potpuno impaktiranim donjim trećim molarom – klase I ili II i pozicije B ili C, prema klasifikaciji Pell-a i Gregory-ja, i vertikalne pozicije prema klasifikaciji Winter-a. Svi pacijenti su nasumično podeljeni u tri grupe u zavisnosti od načina primene deksametazona: oralno – deksametazon primenjen u obliku oralnih tableta, u dozi od 4 mg, sat vremena pre operacije; submukozno – rastvor deksametazona primenjen submukozno, u dozi od 4 mg, u predelu bukalnog sulkusa, nakon sprovedne anestezije za donji alveolarni nerv i

dotatne anestezije za bukalni nerv; intramuskularno – rastvor deksametazona primenjen intramuskularno, u dozi od 4 mg, u predelu deltoidnog mišića, neposredno pre intervencije. Preoperativno i pri svakoj kontrolnoj poseti (prvog, drugog i sedmog dana postoperativno) određivani su interincizalno rastojanje, stepen edema i stepen bola primenom vizuelno analogne skale (VAS). Sedmog postoperativnog dana evidentiran je ukupan broj analgetika koje su pacijenti uzimali. **Rezultati.** U postoperativnom periodu nije bilo statistički značajne razlike između

ispitivanih grupa u pogledu efikasnosti u smanjenju otoka, trizmusa i bola ($p > 0,05$). **Zaključak.** Nema značajne razlike u efikasnosti deksametazona u odnosu na način primene – oralno, intramuskularno ili lokalno submukozno, u redukciji postoperativnog trizmusa, otoka i bola nakon hirurškog lečenja impaktiranog donjeg trećeg molara.

Ključne reči:
deksametazon; lekovi, putevi primene; molar, treći; hirurgija, oralna, procedure; trismus.

Introduction

Surgical extraction of impacted lower third molars is one of the most frequent procedures in oral surgery. Tissue trauma, made during the operation, causes a response in the form of hyperemia, vasodilation, increased vascular permeability, as well as granulocyte and monocyte migration^{1, 2}. That is followed by the appearance of pain sensations, swelling, and trismus, which negatively impact a patient's quality of life in the early postoperative period³. Besides the physical methods (placement of a rubber drain or the use of photodynamic therapy), corticosteroids are commonly used in the treatment of these postoperative complications^{4, 5}.

Administration of corticosteroids in order to prevent postoperative complications after surgical extraction of the impacted lower third molars is a common and very effective pharmacological method⁴⁻⁶. There are two main classes of corticosteroids: mineralocorticoids and glucocorticoids. Due to their anti-inflammatory potential, glucocorticoids are used in oral surgery. Based on the duration of action and anti-inflammatory potency, this group of drugs can be classified into: short-acting, including hydrocortisone and cortisol, with a duration of action of up to 12 hrs and anti-inflammatory potential 1; medium-acting, which includes methylprednisolone, with a duration of action from 12 to 36 hrs and anti-inflammatory potential 4; long-acting, which includes dexamethasone and betamethasone, with a duration of action of over 36 hrs and anti-inflammatory potential 25⁷. Glucocorticoids reduce inflammation in several ways. They inhibit the activity of the enzyme phospholipase A2, block the synthesis of prostaglandins and leukotrienes, which are considered mediators of inflammation, stabilize the cell membrane and thus reduce the release of inflammatory mediators, blood vascular permeability, and formation of bradykinin, which has a pronounced vasodilator effect⁸.

Dexamethasone is one of the most frequently studied and most commonly used types of corticosteroids in oral and maxillofacial surgery today. Numerous studies indicate its positive effect on swelling, pain, and trismus reduction after the third molar surgery^{6, 9-12}. In that sense, it can be administered *via* the local route – endoalveolar or submucosal administration, and *via* the systemic route – oral, intravenous, and intramuscular administration. There is still no consensus on the best route of its administration in order to prevent postoperative sequelae^{9, 10}.

The better effect of dexamethasone in postoperative complications prevention compared to other types of corticosteroids is well documented in literature^{8, 13, 14}. Furthermore, the fact that the effect of dexamethasone can be observed for up to three postoperative days allows the use of this medication in only one dose for preventing postoperative trismus, pain, and swelling. Regarding the dosing regimen, the literature states a wide range of doses in which dexamethasone can be administered to prevent postoperative complications, but it can be said that its minimum effective dose is 4 mg. Several studies indicate that there is no statistically significant difference in the effect of dexamethasone among different dose usages¹⁵⁻¹⁷. The aim of this study was to compare the effectiveness of dexamethasone for the prevention of postoperative complications, edema, trismus, and pain after the surgical extraction of impacted lower third molars, depending on the method of its administration.

Methods

The protocol of this study was approved by the Ethics Committee of the Faculty of Medical Sciences in Priština/Kosovska Mitrovica with protocol No. 09-453, from March 03, 2021. The study was conducted as a prospective study, involving a total of 30 patients, aged 18 years and above, of both sexes, with fully impacted lower third molar – class I or II and position B or C, according to Pell and Gregory¹⁸ classification system and vertical position according to Winter classification¹⁹. All patients were divided randomly into three groups depending on the way dexamethasone was administered: oral – dexamethasone administered in the form of oral tablets in a dose of 4 mg (Dexason[®] tab. 0.5 mg, Galenika, Serbia) one hour before the surgery ($n = 10$); submucosal – dexamethasone solution administered submucosally, in a dose of 4 mg (Dexason[®] amp 4 mg/mL, Galenika, Serbia), in the area of the buccal sulcus, at the site where the future flap will be formed, after the inferior alveolar nerve block anesthesia and additional anesthesia for the buccal nerve ($n = 10$); intramuscular – dexamethasone solution administered intramuscularly, in a dose of 4 mg (Dexason[®] amp 4 mg/mL, Galenika, Serbia), into the area of the deltoid muscle, right before the intervention ($n = 10$). Patients with systemic diseases, gastric ulcers, pregnant and lactating women, and people allergic to the drugs used in the study were not included. Furthermore, surgical procedures lasting longer than 60 min, as well as the occurrence of severe surgical

complications like infection or alveolar osteitis, were some of the reasons for exclusion from the study.

Preoperatively, the position of the impacted mandibular third molar was analyzed using an orthopantomogram according to Winter¹⁹ classification and Pell and Gregory¹⁸ classification. In addition, clinically, before the procedure, the distance between the cutting edges of the upper and lower incisors was measured, together with the parameters that would be used as a reference for determining the degree of postoperative edema. Surgical extractions were performed under local anesthesia – inferior alveolar nerve block with the additional plexus anesthesia for the *nervus buccalis* (Ubistesin forte[®], 1:100,000, Ultradent, Germany), using a buccal triangular flap. Alveolotomy and, if necessary, separation of the crown and roots of the impacted teeth were performed. After the surgical extraction, patients were advised to apply ice packs for the first six hours after surgery and use the analgesic Paracetamol at a dose of 500 mg in combination with Caffeine 65 mg (Panadol extra[®] tab. 500 mg + 65 mg, GlaxoSmithKline, Republic of Ireland), as needed, up to a maximum of four tablets daily. Patients were asked to keep a record of the total number of analgesics they used until the seventh postoperative day. Patients were prescribed antibiotic therapy (Erythromycin[®] 0.5g – Hemofarm AD, Vršac, Serbia) every six hours for five days.

Postoperative follow-up was performed on the first, second, and seventh postoperative day in order to record the degree of edema, trismus, and pain.

Assessment of the degree of edema was measured according to the method of Schultze-Mosgau et al.²⁰, which involves measuring the distance between the tragus and the corner of the lips, tragus and pogonion, as well as the lateral angle of the eye and the mandible angulus. For this purpose, a silk thread was used to measure the distance between two points, and then those measurements were transferred to a millimeter ruler. The arithmetic mean values of these three variables were calculated for each patient. Obtained data were then compared with the measures obtained in the preoperative period.

The degree of trismus was determined by the distance between the incisal edges of the upper and lower central incisors on the maximal mouth opening, measured in millimeters with a ruler, and it was also compared to the preoperatively collected data.

The level of pain was determined on every follow-up visit, measured with a visual analog scale (VAS), graded in centimeters from 0 to 10, where 0 was the lowest notch marking the “absence of pain” while notch 10 marked “unbearable pain”. The degree of pain was additionally evaluated by the total number of analgesic drugs consumed by the patient in the period of seven days.

According to the type of variables and the normality of the distribution, the data description is shown as n (%), mean \pm standard deviation (SD), or median (min-max). Repeated measures analysis of variance (ANOVA) and linear mixed models (LMNMS) were used to model the correlation between the size of the swelling, trismus, and VAS pain scale over time as dependent variables in relation to the type of corticosteroid administration (submucosal, oral, intramuscular) (Table 1). The level of statistical significance was set at 0.05.

All data were processed using IBM SPSS Statistics 22 (SPSS Inc., Chicago, IL, USA) software package and R-3.6.3 software environment (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Swelling

Preoperatively, the arithmetic mean and SD of the swelling volume was 12.4 ± 1.8 cm in the submucosal group, 11.6 ± 0.7 cm in the oral group, while in the intramuscular group, it was 12.0 ± 1.5 cm, which is not a statistically significant difference ($p = 0.426$). The distribution of patients among groups was valid (Table 2).

Overall, there was a significant reduction in the size of the swelling in the examination period ($p < 0.001$) among all

Table 1
Total number of respondents and their distribution according to the method of administration

Parameter	Frequency	%	Valid %	Cumulative %
Submucosal	10	33.3	33.3	33.3
Oral	10	33.3	33.3	66.7
Intramuscular	10	33.3	33.3	100.0
Total	30	100.0	100.0	

Table 2

Mean values and variations in the variable values specified for the size of the swelling among groups during the examination period

Swelling (cm)	Groups			<i>p</i> -value between groups
	submucosal	oral	intramuscular	
1st day	13.1 ± 1.8	12.27 ± 0.8	12.88 ± 1.5	0.419
2nd day	13.04 ± 1.8	12.26 ± 0.8	12.86 ± 1.4	
7th day	12.39 ± 1.8	11.61 ± 0.7	12.2 ± 1.4	
<i>p</i> -value in time series	< 0.001			

Results are expressed as mean \pm standard deviation.

three groups. There was no statistically significant difference in the size of swelling between the groups ($p = 0.419$) in any examination period (Table 2).

Trismus (interincisal distance)

Preoperatively, the arithmetic mean and SD of the interincisal distance was 3.9 ± 0.5 cm in the submucosal group, 4 ± 0.5 cm in the oral group, while in the intramuscular group, it was 4 ± 0.7 cm, which is not a statistically significant difference ($p = 0.787$). The distribution of patients among groups was valid.

Overall, there was a significant increase in the interincisal distance in the examination period ($p < 0.001$) among all three groups. There was no statistically significant difference in the interincisal distance between the groups ($p = 0.939$) in any examination period (Table 3).

Visual analog scale

Overall, there was a significant decrease in pain levels in the examination period ($p < 0.001$) among all three groups. There was no statistically significant difference in pain levels between the groups ($p = 0.725$) in any examination period (Table 4).

Number of analgesics

There was no statistically significant difference in the number of analgesic drugs taken by patients between the groups ($p = 0.069$) (Table 5).

Discussion

In order to prevent the occurrence of postoperative complications after surgical extraction of the impacted lower third molars, dexamethasone can be used locally, most often submucosally or systemically, intramuscularly, intravenously, or orally. Although the intravenous drugs administration provides the rapid achievement of high plasma concentrations, and thus the immediate effect, this route of the administration of dexamethasone is rarely used in outpatient settings because it is more difficult to perform, more unpleasant for the patient and has a higher rate of the possible complications after the administration. In addition, some studies show that a significant benefit cannot be achieved with the intravenous administration route compared to other routes of dexamethasone administration^{9,10}.

In this study, three routes of dexamethasone administration were used to prevent postoperative complications of trismus, pain, and swelling. The analysis of the obtained results did not reveal a statistically significant difference in the effect of dexamethasone in relation to all three examined parameters of submucosal, intramuscular, or oral administration. These results can be compared with other similar studies²¹⁻²³.

The submucosal route of dexamethasone administration, locally in the buccal sulcus area, is a relatively newer route of its administration that has shown high efficacy in the prevention of the postoperative complications of surgery of the impacted lower third molars in numerous studies²⁴⁻²⁶. However, similar studies have not shown statistically significant benefits of this route of administration compared to oth-

Table 3

Mean values and variations of interincisal distance (trismus) among groups during the examination period

Trismus (cm)	Groups			<i>p</i> -value between groups
	submucosal	oral	intramuscular	
1st day	3.54 ± 0.5	3.32 ± 0.6	3.4 ± 0.7	0.939
2nd day	3.57 ± 0.5	3.42 ± 0.7	3.49 ± 0.7	
7th day	3.89 ± 0.5	3.98 ± 0.5	3.97 ± 0.7	
<i>p</i> -value in time series	< 0.001			

Results are expressed as mean \pm standard deviation.

Table 4

Mean values and variations of pain levels among groups during the examination period

Visual analog scale	Groups			<i>p</i> -value between groups
	submucosal	oral	intramuscular	
1st day	3 (range, 1–7)	4 (range, 3–8)	3.5 (range, 1–7)	0.725
2nd day	2.5 (range, 0–8)	3 (range, 1–8)	4 (range, 0–7)	
7th day	0 (range, 0–1)	0 (range, 0–2)	0 (range, 0–2)	
<i>p</i> -value in time series	< 0.001			

Table 5

Total number of analgesics consumed during the examination period according to the route of administration

Parameter	Groups		
	submucosal	oral	intramuscular
Number of analgesics	4 (range, 1–8)	6.5 (range, 2–10)	4.5 (range, 2–6)
<i>p</i> -value between groups	0.069		

ers. In their study, Noboa et al.²¹ state that the effect of the submucosal administration of dexamethasone does not show a statistically significant difference in the prevention of these complications compared to the oral route of administration. Although it is a systemic route of administration in relation to the local application, this can be explained by the fact that the resorption of dexamethasone in the digestive tract is very good, followed by its very high concentration in plasma.

In a comparative analysis of the effect of dexamethasone administration on the degree of postoperative complications, Majid and Mahmood²² did not notice a statistically significant difference between submucosal and intramuscular administration. Likewise, Gopalakrishnan et al.²³ did not notice in their analysis a difference in the prevention of trismus, pain, and swelling *via* the intramuscular route of administration compared to the submucosal route of dexamethasone administration. On the other hand, Antunes et al.²⁷ have examined the effects of intramuscular and oral administrations of dexamethasone and did not find a statistically significant difference. Boonsirirath et al.²⁸ conducted almost the same study with the same conclusion. The only difference between these two studies is that for the intramuscular application of dexamethasone, the area of the masseter muscle was used in the first one, and in the second one, the area of the deltoid muscle was used. That may indirectly indicate that intramuscular administration of dexamethasone at local and remote sites has the same effect.

Considering the results of this study and similar studies of other authors, it can be said that the use of corticosteroids, especially dexamethasone, leads to a significant drop in swelling, trismus, and pain after the surgical extraction of the impacted lower third molars. In addition, the route of administration of dexamethasone does not lead to a statistically significant difference when it comes to the prevention of mentioned complications. Choosing the route of administration depends exclusively on the affinity of the therapist as well as the characteristics of each patient as an individual. The intramuscular route of administration, although undoubtedly effective, according to the authors of this study,

causes moderate discomfort in the form of pain or tingling at the site of the application when administered in the area of the deltoid muscle. In addition, this route of administration is particularly inconvenient for patients suffering from symptoms of trypanophobia. Finally, the intramuscular route of administration may be problematic in some patients for religious and cultural reasons. All these disadvantages can be avoided by oral or submucosal administration of dexamethasone. However, the oral route, due to the mode of absorption and the need to achieve the optimal concentration of the drug in the blood during and after the operation, requires administration usually one hour before the beginning of the intervention. In addition, the minimum effective dose of dexamethasone mentioned in the literature that should be used in order to prevent postoperative complications is 4 mg, depending on the manufacturer. That requires taking more tablets at the same time, which in some cases, causes confusion and doubt. According to our experience, the submucosal route of administration can be considered the most appropriate because the therapeutic dose can be achieved using only one ampoule of dexamethasone. In addition, for people suffering from needle phobia, this route of administration is more acceptable than the intramuscular; it causes no sensations because the medication is applied submucosally in the buccal sulcus region of the impacted lower third molars after the local anesthesia has already been given.

Limitations of the study

The main limitation of this study might be an insufficient sample size that could be enlarged in future studies.

Conclusion

Within the limitations of this study, it can be concluded that there is no significant difference in dexamethasone effectiveness in postoperative trismus, swelling, and pain reduction after the third molar surgery, regarding the route of administration – oral, intramuscular, or local submucosal.

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