Oral and Maxillofacial Surgery (2019) 23:395–405
https://doi.org/10.1007/s10006-019-00776-z

ORIGINAL ARTICLE

Evaluation of the impact of preoperative use of dexamethasone and cyclobenzaprine in surgical extraction of lower third molars on trismus by electromyographic analysis

Fernando Vagner Raldi[1] · Rodrigo Dias Nascimento[1] · Fábio Ricardo Loureiro Sato[1,2] · Lucio Murillo Santos[3] · José Benedito Oliveira Amorim[3] · Michelle Bianchi de Moraes[1]

Received: 22 October 2018 / Accepted: 2 May 2019 / Published online: 22 May 2019

Abstract

Purpose The aim of this study was to evaluate the influence of cyclobenzaprine and dexamethasone on the electrical activity of the masticatory muscles in patients who had undergone lower third molar surgery.

Methods Thirty bilateral impacted lower third molars with indication of extraction were randomised into three groups: the control group, the dexamethasone, and the cyclobenzaprine group. To obtain muscular electrical activity and mouth opening, an electromyographic device was used at mandibular rest and maximum voluntary contraction and compared pre- and post-operatively.

Results During muscle contraction, no significant difference was observed in the electromyographic records on the non-operated side. On the operated side, there was a reduction in electrical activity for both drugs pre-operatively and immediately post-operatively compared to the control group. All pharmacological agents promoted a higher mouth opening compared to control group.

Conclusion The results suggest that dexamethasone and cyclobenzaprine may be useful as an adjuvant in the prevention of motor dysfunctions in third molar surgery.

Keywords Muscle relaxants · Corticosteroid · Third molars · Electromyography

Introduction

Exodontia of impacted third molars is one of the most commonly performed procedures in the field of oral surgery and is often associated with post-operative morbidity that may be transient or permanent. Among the most common accidents and complications of these procedures are haemorrhages, alveolitis, pain, oedema, trismus, injury to the inferior alveolar nerve, infections involving facial spaces, and injuries in adjacent teeth. Of all of the complications that can occur, one of the most common is the alteration of the activity of the masticatory muscles, such as the trismus. Trismus refers to the difficulty of opening and closing of the mandible, ranging from mild to moderate, due to a muscular contracture located in the masticatory muscles. This result is observed due to an inflammatory process, which may spread and involve several muscles, primarily the masseter muscle[1,2]. It has been described that this muscular dysfunctional condition occurs approximately 56% of individuals who undergo this type of surgery during the post-operative phase. The trismus decreases gradually; it is verified that full capacity to open the mouth should be established between 10 and 14 days after the surgery [1–3]. Another complication that commonly occurs is exaggerated facial surgical swelling, which is one of the body's reactive responses to surgical aggression. Extensive facial swelling, as well as delaying the surgical wound repair process, is one of the main factors responsible for post-

✉ Fábio Ricardo Loureiro Sato
fabio.sato@ict.unesp.br

[1] Department of Surgery and Oral Diagnoses, College of Dentistry, State University of São Paulo – UNESP, São José dos Campos, Brazil

[2] Department of Oral and Maxillofacial Surgery, College of Dentistry, State University of São Paulo – UNESP, Av. Eng. Francisco José Longo, 777, São José dos Campos, SP 12245-000, Brazil

[3] Department of Bioscience and Oral Diagnoses, College of Dentistry, State University of São Paulo – UNESP, São José dos Campos, Brazil

operative pain [4]. Besides those two factors, oral muscular function is also affected by a reflex muscle spasm or the inflammatory process itself resulting from the removal of the third molars [5].

The use of anti-inflammatory drugs aims to control the inflammatory reactions without causing damage to the repair and healing processes and may prevent post-operative complications. In this context, many clinical research studies on the use of steroidal anti-inflammatory drugs (SAIDs) and non-steroidal anti-inflammatory drugs (NSAIDs) have been conducted to control post-operative inflammatory reactions, thereby alleviating inflammatory signs. The synthetic corticosteroids analogous to hydrocortisone, such as prednisone, methyl prednisolone, betamethasone, and dexamethasone, have attracted considerable attention [6–9], primarily betamethasone and dexamethasone, due to their excellent therapeutic qualities, low sodium retention (thus having little water retention) and low incidence of adverse reactions and side effects when used in single and higher doses [7–12].

Central myorelaxants are drugs that selectively depress the part of the central nervous system that controls muscle tone. These drugs are used to promote muscle relaxation in musculoskeletal spasms, which is useful for rest, psychotherapy, and other appropriate measures to treat localised painful musculoskeletal spasms [13]. Cyclobenzaprine, one of the most widely used myorelaxant drugs in daily doses of 75 to 150 mg, has been shown to be effective in treating depression but without offering advantages over existing agents [14]. Additionally, after limited success in the treatment of schizophrenia, anxiety, chronic headache, and rigidity caused by Parkinson's disease, cyclobenzaprine hydrochloride was introduced as an adjuvant in relieving muscle spasm associated with acute musculoskeletal pain [15].

Currently, cyclobenzaprine hydrochloride is used as a muscle relaxant, although the mechanism of action is not well-defined. It is known that this drug does not act directly on skeletal muscle relaxation and does not depress neural conduction or neuromuscular transmission [16]. However, this drug does act particularly in pain associated with skeletal muscle hyperactivity and sleep disorders associated with fibromyalgia [16, 17].

To observe the electrical activity through the presence of cyclobenzaprine and steroidal anti-inflammatories in the masseter muscle and temporal muscles, an electromyographic surface register could be used, which detects the action potentials of all motor units that work together [18, 19]. Because it is an easy-to-execute, high-sensitivity, non-invasive method, usage of surface electromyography (EMGs) has been increasing for monitoring the electrical activity of the muscles, such as the motor behaviour of the mandibular lifts during maximum masticatory effort [20], intraoral evaluations [21], masticatory force analysis [22], speech and swallowing disorders [23], pain evaluation in surgical procedures [24], and muscle spasm [25].

Thus, the present study evaluated the influence of the administration of the myorelaxant cyclobenzaprine (10 mg) and the steroidal anti-inflammatory dexamethasone (8 mg), through electromyographic EMG analysis in the activity of the masticatory muscles, comparing the electrical activity of the same muscle groups in patients who did not receive any type of medication. In addition, due to the impairment in the motor activity resulting from the invasive surgical procedure, the degree of incisal opening was evaluated through an electronic goniometer (EMG System do Brazil, São José dos Campos, SP, Brazil) coupled to the system.

The hypothesis is that both dexamethasone and cyclobenzaprine have a positive effect on the decrease in the electrical activity of masticatory muscles, with positive effects on the improvement of incisal opening. As a specific aim, it will be evaluated whether there is a difference between the use of dexamethasone or cyclobenzaprine pre-operatively in third molar surgeries.

Materials and methods

The sample consisted of 30 impacted lower third molars with indication for extraction with class II or position B impaction according to Pell and Gregory classification, without distinction of gender and with ages ranging between 20 and 30 years. Participants underwent routine pre-operative exams, such as blood pressure measurement, heart rate, bleeding time and coagulation, and blood glucose measurement. Elective surgeries were performed by a single surgeon in the morning (FVR), always requiring at least 48 h of alcohol withdrawal and 8 h of smoking. All surgeries were performed under local anaesthesia with the pterygomandibular anaesthetic technique to block the inferior alveolar and lingual and buccal nerves, with a total of two anaesthetic tubes (3.6 ml) of lidocaine 2% with 1:100,000 IU epinephrine. No anaesthesia was used in the masticatory muscles to avoid affecting the research data. The interval between the surgeries from one to side to the other in the same patient should be at least 30 days.

Inclusion criteria included

1. Free and informed consent for participation in the study, in accordance with the provisions of resolution of the National Health Council number 196/96,
2. Healthy patients who need to extract the impacted lower third molars and have no missing teeth until the second molar.

Exclusion criteria included

1. Patient with systemic alteration that did not allow the surgical procedure or the use of any of the medications,

2. Use of analgesics and anti-inflammatories in the last 10 days, and
3. Patients with temporomandibular joint dysfunction [26].

Randomised participants were divided into three groups, with 10 lower third molars participating in each group: control group (placebo medication); dexamethasone group (8 mg), and cyclobenzaprine group (10 mg). The selection of the group of each patient was done an hour before by another research (MBM) based on an aleatory distribution made previously of all patients though the groups.

The pharmacological agents were produced in identical packages and only the external researcher (MBM) could identify them to administer orally as a single dose 1 h before the surgical procedure. Neither the patient nor the surgeon knows to which group the patient belonged. In all groups, participants received the same surgical procedures performed by a single surgeon (FVR). If the patient reported that he had allergy to any of the drugs used as a protocol in the research, the patient was automatically excluded from the sample. No antibiotics were used in this research pre- or post-operatively, as no patient had the risk for bacterial endocarditis. As a post-operative medication, only dipyrone sodium (500 mg every 6 h) was prescribed as a rescue analgesic medication for all patients.

Obtaining electromyographic data

During the experimental phases, the volunteers were evaluated electromyographically. The EMG-800C electromyograph (EMG System do Brasil, São José dos Campos, SP, Brazil) was used to record the electromyographic signal of the anterior right (TD) and left (TE) temporal sides and a superficial part of the right (MD) and left (ME) masseters. The electromyograph was previously calibrated with a gain of total amplification of 20 times, common mode rejection > 100 dB, 16-bit analogue-to-digital (A/D) converter card with dynamic range resolution, communication with a microcomputer using 10 Mbps ethernet network with RJ45 connector (10BASE T) using the TCP/IP protocol; two-pole analogue *Butterworth* filter, low-pass (FPB) 500 Hz and high pass (FPA) 20 Hz; *software* for the acquisition and analysis of electromyographic signals, Windows Vista/XP platform, for simultaneous presentation of multi-channel signals and signal processing (RMS value, average, minimum, maximum, and standard deviation); and FFT (on line) with an acquisition rate (sampling) up to 2000 samples/s per channel to be programmed by the *software*. Six input channels with active electrodes with amplification gain of 20 times were used to collect the electromyographic signal. The corresponding channels of the studied muscles were channel 1—anterior portion of the left temporal muscle; channel 2—superficial portion of the left masseter muscle; channel 3—anterior portion of right temporal muscle; and channel 4—superficial portion of the right masseter muscle. Channel 5 was used for the mandibular goniometer coupled to the system.

To capture the action potentials of the evaluated muscles, surface electrodes were used for electromyography, which consisted of two Ag/AgCl discs (10 mm diameter) coupled in a polyethylene foam with a disposable hypoallergenic medical adhesive and with a solid adherent gel on the contact surface—Meditrace® (Kendall-LTP, Mansfield, MA, USA)—which captured the electrical activity of several motor units at the same time, providing a general approach to muscle dynamics. These electrodes were coupled to a 20-fold gain preamplifier that characterised a differential circuit. A reference electrode (ground) was placed on the forehead, which was anointed with an electroconductive gel to reduce an undesirable electrical noise in the electromyographic signal.

To measure the opening amplitude, in triplicate, a mandibular goniometer (EMG System do Brasil, São José dos Campos, SP, Brazil) coupled to the electromyograph was used, providing an electrical signal corresponding to the angular movement that was recorded during the experiment along with the electromyographic signals. This approach enabled a reading from 0 to 255° or 0 to 80 mm with a signal recording on the actual measurement unit (in degrees or millimetres).

Protocol

During the electromyographic evaluations, subjects were kept seated with their eyes open, natural posture and positioned with their heads oriented according to the Frankfurt horizontal plane without being able to visualise the records on the computer monitor. Electromyographic records were gathered by cleaning the skin with cotton soaked in 70% alcohol to reduce skin impedance and adequate placement of the surface electrodes oriented by the direction of the muscular fibres [27, 28]. Surface electrodes were fixed on the right and left masseter muscles and on the right and left anterior (right bundle) temporal muscles, observing the insertion of the electrodes (Fig. 1). The electrodes were positioned on the surface of the skin above the masseter muscle belly and anterior temporal muscle, parallel to the muscular fibres. For the masseter muscle, the belly was palpated during maximal intercuspation, and the electrodes were later fixed parallel to the fibres 2.5 cm above the angle of the mandible to avoid the influence of the motor point, whereas for the anterior temporal muscle, the belly was palpated during maximal intercuspidation (tightening), and the electrodes were later fixed along the anterior margin of the muscle 2 cm above the zygomatic arch. A disposable ground electrode was attached to the skin in the frontal region. A maximum inter-electrode distance of 20 mm (centre to centre) was used according to the recommendation of SENIAM (Enschede, The Netherlands) [29–32].

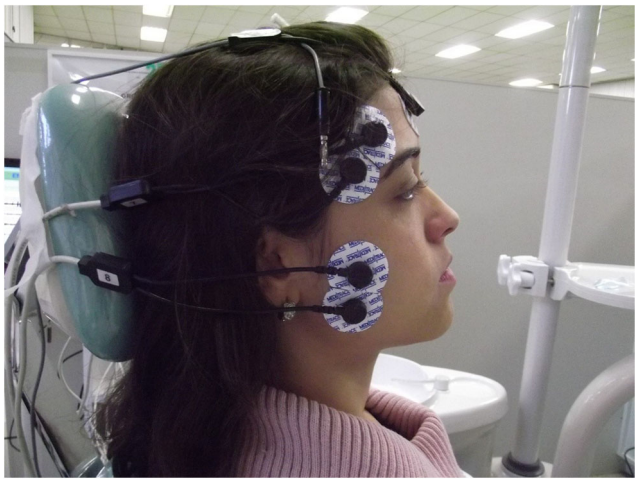

Fig. 1 The electrodes positioned on the surface of the skin above the masseter muscle belly and anterior temporal muscle for electromyographic registration

The electromyographic records began with the evaluation in a postural state at rest (basal) and later in the condition of maximum voluntary contraction (isometry) of the masseter and temporal muscles and concomitantly, with the mandibular goniometer, which measured the interocclusal distance of the central incisors (to evaluate the degree of oral opening of the patient). During the electromyographic data acquisition phase, the time required to gather data was 10 s (with repetition of three successive times and with a 1-min interval between each acquisition).

The collection of the electromyographic signals was performed by a single observer who was previously calibrated and monitored the collection and recording of the electromyogram obtained in real time. In the presence of any unwanted interference in the collection of the electrical potentials, such as an unsolicited movement, the examination was repeated, and the electromyographic signals were recorded and saved in computer files.

In this study, the electromyographic amplitude values were quantified through two measures (response variables): *root mean square* (RMS). The RMS is an electronic media that represents the square root of the mean square of the voltage of the electromyographic signal. It is recommended to represent the electromyographic amplitude of non-dynamic contractions, such as isometric, according to SENIAM (Enschede, The Netherlands) and ISEK (International Society of Electrophysiology and Kinesiology—Victoria, BC, Canada) [27, 33]. The RMS values were quantified in microvolts (μV) RMS [34–36].

The RMS values were calculated using *software* EMGLab V1.1 (EMG System do Brasil, São José dos Campos, SP, Brazil), in a specific binary language, providing all of the mathematical and statistical information in the time domain and in the frequency domain. It is also possible to export the gathered data to a numerical standard, known as ASCII, to be processed and analysed in software *MATLAB* (version 7.0 or higher). The gathered electromyographic data, referring to the temporal and masseter muscles, were predicted in six distinct phases (Table 1):

Statistical analysis

The gathered electromyographic data were submitted to analysis of variance (ANOVA) and Tukey test (GraphPad Prisma version 5.0 for Windows XP, GraphPad Software, San Diego, CA, USA). The level of significance was set at $p < 0.05$. Based on the collected data, using the variable transoperative electrical activity of the masseter muscle in the side of the procedure, using an alpha error of 5%, with a sample of 15 patients, the beta error of the sample power was 10%.

Results

The sample of 15 patients was composed of 7 males and 8 females with both lower third molars, mean age of 22.1 with a standard deviation of 4.4 years. The consumption of the dipyrone sodium as a rescue analgesic was 1.4, with a standard deviation of 1.6 doses.

Table 2 shows the averages of the electrical activity values of the muscle groups studied during the experimental phases gathered on the contralateral side (not operated), that is, on the opposite side to the procedure of the tooth removal surgery under maximum intercuspidation (maximum voluntary contraction). The electromyographic records that were measured did not vary significantly among the groups studied, although dexamethasone produced a greater reduction of electrical activity in the initial phases, during the immediate post-operative period and after 7 days of surgical procedure in the case of the masseter muscle. Cyclobenzaprine, in the same muscle, showed an increase in electrical activity just after 15 and 30 days, signalling a higher recruitment of motor units, but with no interference in the incisal opening though the periods (Fig. 2).

It should be noted that during the isometric contraction (centric occlusion), the masseter muscle acquires greater functional importance, whereas the anterior temporal muscle is related mainly to the mandibular postural position, determining the position of mandibular rest (Fig. 3). Thus, the motor behaviour after the surgical procedure was slightly better in the presence of the muscle relaxant cyclobenzaprine 7 days after surgery, due to a greater increment of fibres (increase of electrical potentials) when the patient was voluntarily requested to undertake maximum mandibular contractile effort.

Table 3 provides the mean values of the electrical activity values of the same muscle groups, during the same experimental phases, which were collected on the side of the third molar removal surgery in the condition of maximal

Table 1 Experimental model used for electromyographic evaluation of the masseter and temporal muscles

Initial phase	Phase 1	Phase 2	Phase 3	Phase 4	Phase 5	Phase 6
Before surgery and 1 h after taking the medication	After anaesthesia (3 min after local anaesthesia)	During surgery (after incision and detachment of the mucosa)	Immediately after surgery (just after the sutures)	Post-surgery 7 days	Post-surgery 15 days	Post-surgery 30 days

intercuspidation (maximal contraction). The electromyographic records that were measured varied between the groups studied. Both dexamethasone and cyclobenzaprine were effective in reducing the electrical activity of the masseter and temporal muscles in the initial and immediate post-operative periods when compared with the initial period, but the muscle relaxant apparently brought a benefit higher than the steroidal anti-inflammatory as the reduction of the electrical muscle activity remained longer (Figs. 4 and 5).

Whereas in the periods after the surgical procedure, a very similar motor behaviour occurred between the treated groups compared with the control group. It is possible that the presence of a local inflammatory process, due to the surgical procedure itself, causes swelling or even painful stimuli, which can lead to an increase in motor tone (trismus), with difficulty in mandibular movements and even with the reduction of the mouth opening, which is commonly observed in the literature during surgical procedures of this nature. In this regard, the authors performed a series of paired evaluations, aiming to determine the degree of mouth opening through an electronic goniometer coupled to the collection system (electromyograph). Such evaluations are useful in determining the presence of muscle spasms and the impact of the surgical procedure on patients' quality of life that result from invasive surgical procedures, such as the extraction of impacted teeth. Figure 5 shows that the pharmacological agents used in the present study provided a significant increase in the degree of buccal opening ($p < 0.05$) during the pre-, trans-, and post-operative periods compared with the control group. The muscle relaxant was more effective than anti-inflammatory steroid; although it should be noted that the activity of these drugs has a short-term effect, its influence may be related to a greater degree of muscle relaxation, less tissue damage, and less release of cellular-modulating agents that promote the increase of tonus of the mandibular lifting muscles and thus makes it difficult for the mouth to open in these patients (Fig. 6).

Discussion

Trismus, which is a change in oral motor activity, is a frequent complication in the post-operative period of extraction of impacted third molars and is due to several factors, including the magnitude of the surgical procedure, the surgical technique used and/or the ability of the surgeons who promote the release of local chemical mediators that activate the sensory (nociceptive) pathways that result in increased muscle tone (by increased gamma-motoneuron activity). The elevation of muscle tone causes problems in mandibular mobility, mouth opening and closing movements, as well as deglutition, verbal communication (phonation), and oral hygiene that leads to serious losses in the quality of life of individuals. It is

Table 2 Mean and standard deviation of the electrical activity of the anterior temporal and superficial masseter muscles gathered during the experimental phases in patients who underwent extraction of impacted third molars on the contralateral side of the surgical procedure in the condition of maximum voluntary contraction (MVC)

Periods	Control (10)		Cyclobenzaprine (10)		Dexamethasone (10)	
	Masseter	Temporal	Masseter	Temporal	Masseter	Temporal
Pre-surgical	144.24 ± 99.0[a]	214.67 ± 98.86[b]	175.24 ± 92.8[a]	230.90 ± 83.8[b]	133.65 ± 36.1[a]	198.69 ± 54.5[b]
Post-anaesthesia	145.90 ± 73.4[a]	248.71 ± 101.5[b]	151.98 ± 83.6[a]	210.39 ± 55.91[b]	121.11 ± 48.5[a]	194.77 ± 47.3[b]
Trans-surgical	130.517 ± 68.9[a]	223.92 ± 134.4[b]	139.7 ± 86.6[a]	187.333 ± 67.2[b]	117.23 ± 52.3[a]	206.47 ± 42.9[b]
Immediately after surgery	137.83 ± 71.15[a]	203.73 ± 108.7[b]	151.90 ± 101.6[a]	204.69 ± 83.24[b]	121.44 ± 69.2[a]	232.27 ± 101.3[b]
Post-operative 7 days	148.801 ± 89.9[a]	235.51 ± 84.4[b]	197.93 ± 87.40[a]	223.92 ± 79.34[b]	132.68 ± 43.35[a]	292.11 ± 233[b]
Post-operative 15 days	141.64 ± 85.6[a]	219.35 ± 75.0[b]	167.47 ± 64.3[a]	231.44 ± 77.8[b]	144.03 ± 62.4[a]	186.49 ± 43.9[b]
Post-operative 30 days	199.64 ± 98.9[a]	237.52 ± 128.2[b]	198.88 ± 92.2[a]	247.08 ± 85.6[b]	187.97 ± 126.9[a]	197.01 ± 50.5[b]

Means followed by the same letter ([a] or [b]) do not differ statistically from each other by the Tukey test at 5% probability

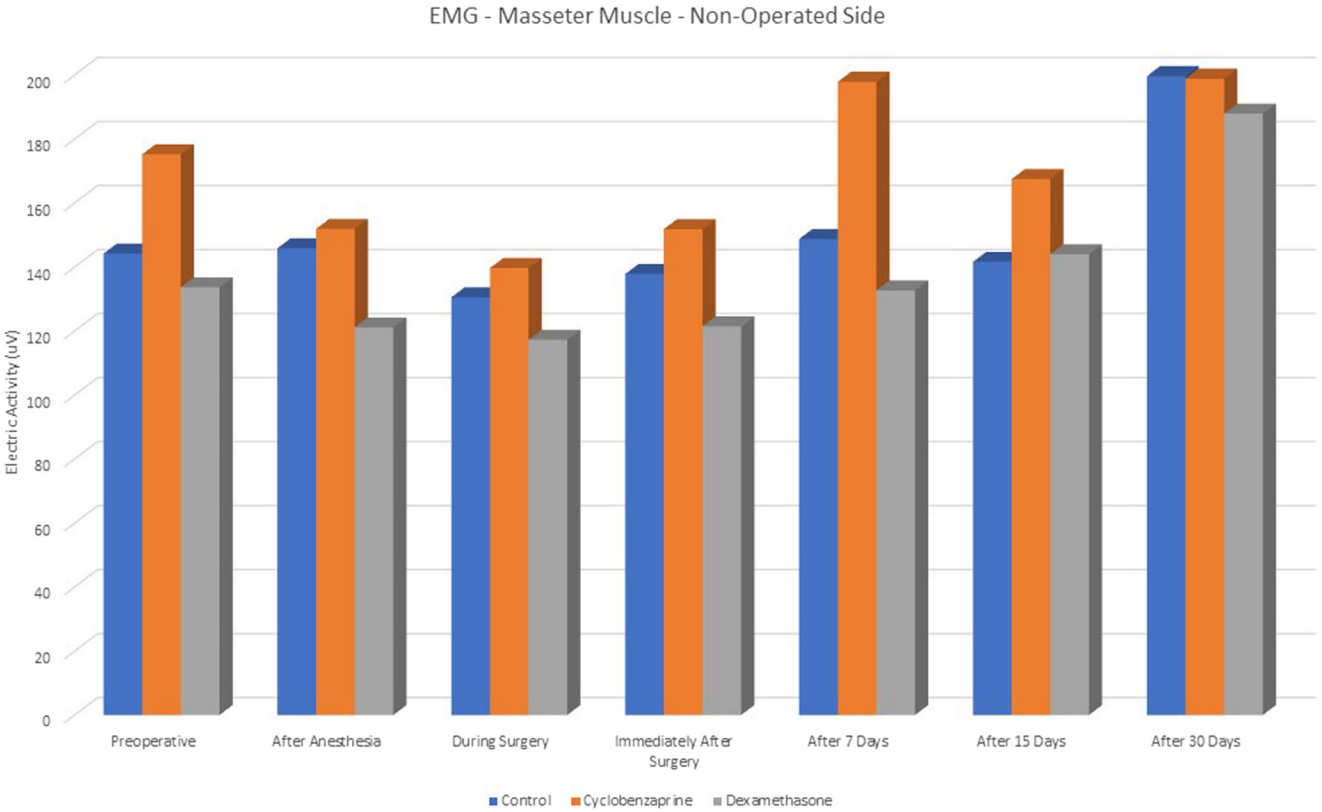

Fig. 2 Electrical activity of the temporal anterior and masseter muscles in the condition of maximum voluntary contraction (MVC) contralaterally to the surgical procedure of the removal of impacted third molars during the predicted phases of this research

estimated that the frequency of this type of complication is approximately 56% of the post-operative periods performed in this type of procedure [2, 37].

Thus, considering the dimension of the problems related to the extraction of impacted third molars, several researchers have investigated alternatives to prevent and often treat the onset of these oral complications. These alternatives include several measures, such as physiotherapeutic procedures, use of wet heat therapy, oral antiseptics, low power laser, cryotherapy/thermotherapy, and mainly the use of chemical agents modulating the inflammatory response that included nonsteroidal (NSAIDs), steroid (corticosteroids) analgesics, and nervous system depressants that involves an extensive list of biologically active drug agents (tricyclic antidepressants, benzodiazepines, and central nervous system depressants) [38]. However, there is still no consensus in the literature regarding the best protocol for drug control of pain and/or inflammation in this type of surgical procedure. Therefore, the authors decided to study the use of two pharmacological agents, with one being more widely used in the clinic (dexamethasone) and the other being part of a series of drugs that promote reduction of muscle tone without affecting the motor conscious activity, known as muscle relaxants, which includes cyclobenzaprine.

The decision to use of dipyrone sodium as a rescue medication was based on its main effect as an analgesic drug, with minimum spasmolytic and anti-inflammatory effects, that could interfere with the research results [39]. Also, the usage of dipyrone by the patients in the post-operative period was very low (less than 2 doses per patient).

The results of the study demonstrated that both drugs could reduce the electrical activity of muscle groups during the presurgical phase until the immediate post-operative period, especially in the masseter muscle on the operated side. This research presents a more important functional role in the development of mandibular force during isometric contraction, that is, during centric occlusion, with the purpose of fragmentation and formation of the alimentary bolus, unlike the anterior temporal muscle that has a larger role in determining the mandibular rest position. Regarding the post-operative period, that is, during the absence of action of the chemical agents used in this research, once its metabolism occurs at most after 2 days, a significant reduction was observed in the muscular electrical activity in the group (7 days). This reduction possibly resulted from the presence of increased swelling, inflammation, and pain in these patients, which was different from the values obtained in the experimental groups (cyclobenzaprine and dexamethasone) and allowed a greater recruitment of muscle fibres and therefore increased the electrical activity when compared with the control group (Fig. 3). Thus, the use of these agents suggests a preventive action in

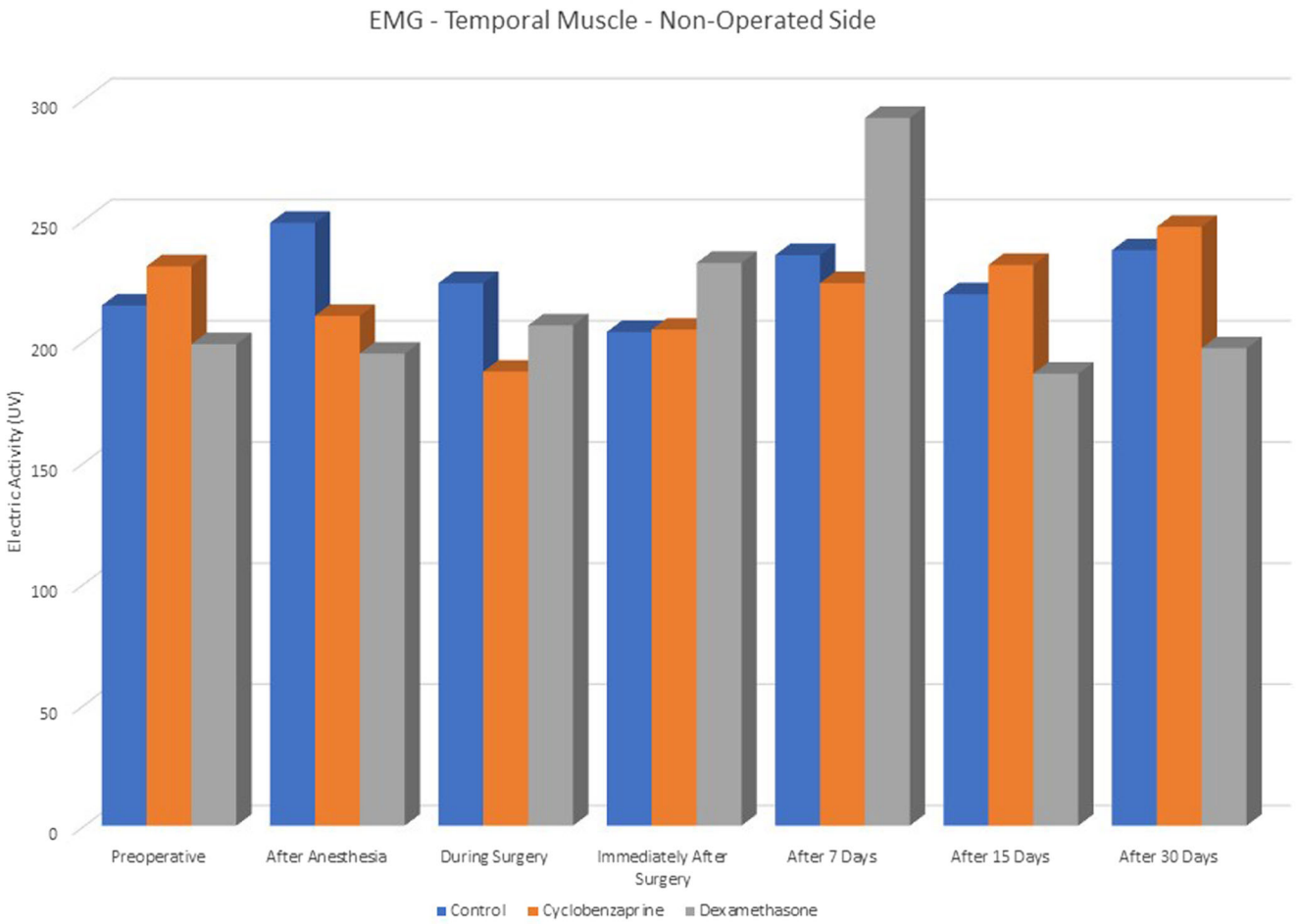

Fig. 3 Electrical activity of the temporal anterior and masseter muscles in the condition of maximum voluntary contraction (MVC) contralaterally to the surgical procedure of the removal of impacted third molars during the predicted phases of this research

triggering complications that result from invasive surgical procedures of third molar extraction.

When comparing cyclobenzaprine and dexamethasone, it was possible to observe a similar behaviour in terms of the reduction of electrical activity in the pre- and trans-surgical period. However, cyclobenzaprine showed a decline in the more constant activity for a longer time when comparing the two groups.

Table 3 Mean and standard deviation of the electrical activity of the anterior temporal and superficial masseter muscles gathered during the experimental phases in patients who underwent extraction of impacted third molars on the same side of the surgical procedure in the condition of maximum voluntary contraction (MVC)

Periods	Control (10)		Cyclobenzaprine (10)		Dexamethasone (10)	
	Masseter	Temporal	Masseter	Temporal	Masseter	Temporal
Pre-surgical	195.35 ± 208.9[a]	205.57 ± 154.0[b]	147.49 ± 51.1[a]	184.18 ± 73.3[c]	180.98 ± 59.1[a]	205.56 ± 35.2[b]
Post-anaesthesia	215.71 ± 224.8[a]	191.07 ± 83.2[b]	135.63 ± 41.8[a]	186.67 ± 70.5[c]	134.71 ± 38.9[a]	198.12 ± 34.0[b]
Trans-surgical	162.85 ± 125.9[a]	183.25 ± 98.2[b]	112.93 ± 30.0[a]	162.83 ± 74.1[c]	148.94 ± 58.5[a]	205.71 ± 55.9[b]
Immediately after surgery	175.29 ± 97.7[a]	215.21 ± 124.0[b]	144.41 ± 51.4[a]	149.64 ± 74.8[c]	174.20 ± 91.5[a]	210.99 ± 119.0[b]
Post-operative 7 days	103.12 ± 64.7[a]	215.65 ± 87.7[b]	155.15 ± 55.3[a]	193.40 ± 82.0[c]	161.105 ± 60[a]	215.42 ± 78.9[b]
Post-operative 15 days	193.30 ± 132.3[a]	204.65 ± 64.6[b]	161.5 ± 62.2[a]	188.38 ± 54.4[c]	167.37 ± 66.1[a]	197.93 ± 48.4[b]
Post-operative 30 days	202.56 ± 89.07.2[a]	225.93 ± 83.6[b]	172.35 ± 71.0[a]	207.26 ± 48.2[c]	142.90 ± 48.5[a]	210.35 ± 49.9[b]

Means followed by the same letter ([a] or [b]) do not differ statistically from each other by the Tukey test at 5% probability

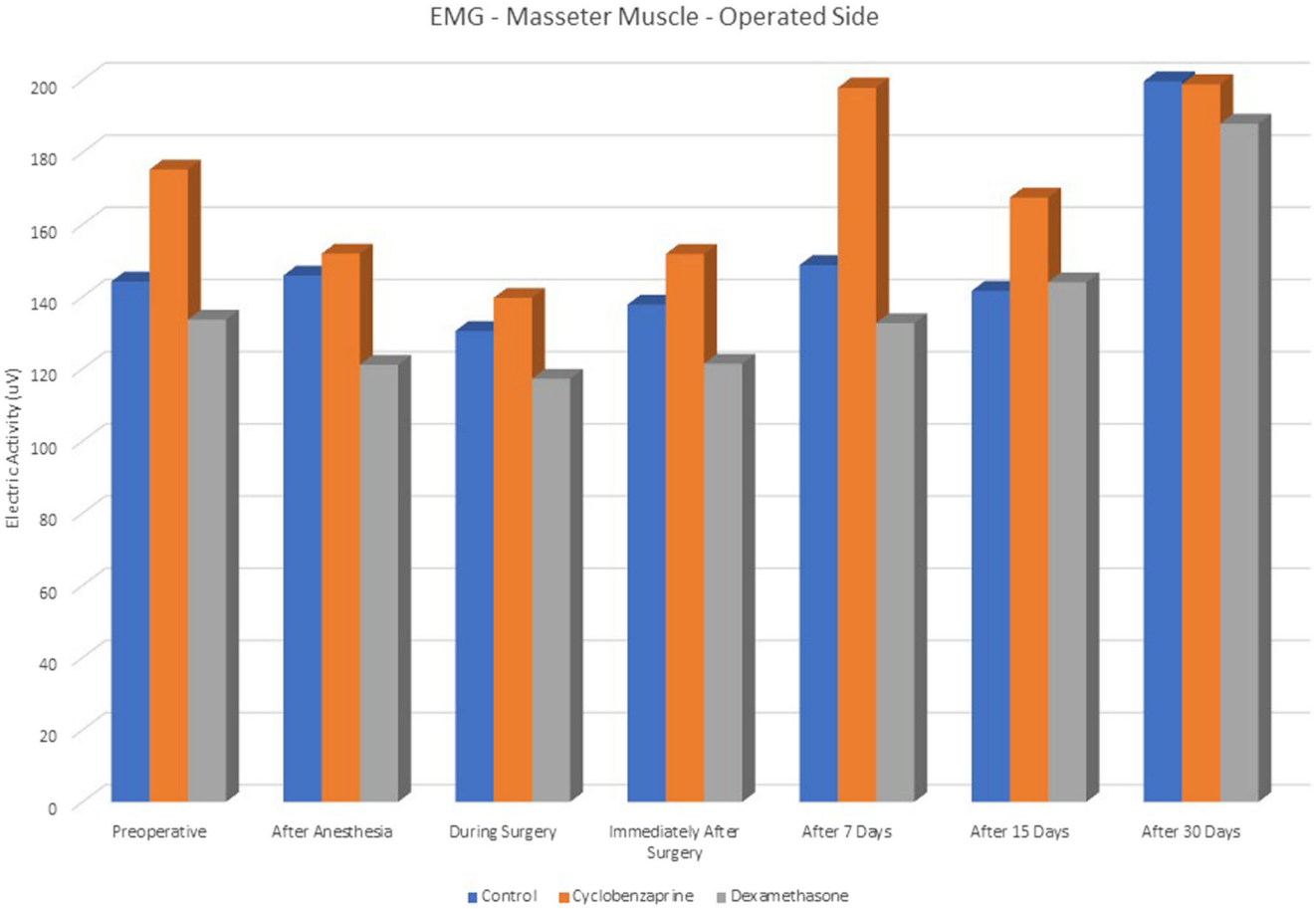

Fig. 4 Electrical activity of the temporal anterior and masseter muscles in the condition of maximum voluntary contraction (MVC) in the side of the surgical procedure of the removal of impacted third molars during the predicted phases of this research

Dexamethasone is a drug belonging to the corticosteroid class, acting to control the rate of protein synthesis. The primary effect of this medication is the profound alteration promoted in the lymphocytic immune response, due to an anti-inflammatory and immunosuppressive action that can prevent or suppress inflammatory processes of various natures. Known mechanisms of action involve inhibition of enzyme phospholipase A2. Inactivation of the same enzyme decreases the availability of arachidonic acid in the cell and causes a decrease in the metabolites of COX-2 (cyclooxygenase 2), thereby decreasing the symptomatic clinical manifestations. Dexamethasone's application in the dental clinic is extremely widespread. Dexamethasone is currently being used as a drug protocol for the prevention of inflammation, pain, and tissue injury [1, 6, 40–42]. Studies of systematic review of the literature have shown that the use of corticosteroids is effective both in the control of swelling and trismus in third molar surgery, being more effective when administered preoperatively [43, 44], regardless of the route of administration (oral, intravenous or submucosal) [45, 46]. Another advantage of dexamethasone is its long duration of action that last about 2.75 days. Its half-life plasma elimination is about 3 to 4.5 h, but its tissue (biological) half-life is 36 to 54 h [39].

Despite the already known effects of dexamethasone, the effect of this medication in a preventive way on oral motor complications by electromyographic analysis was not very clear until now [47, 48]. Thus, the authors attempted to evaluate a new agent that could add some of the pharmacological characteristics that favour the reduction of the motor activity, promoting greater relaxation of muscle fibres mainly during the surgical period and that would facilitate the prevention of trismus during the post-operative period, as is the example of cyclobenzaprine. Cyclobenzaprine is used mainly in the treatment of muscle spasms associated with acute pain and musculoskeletal aetiology (as in lumbago, torticollis, and fibromyalgia).

Cyclobenzaprine suppresses spasm of local skeletal muscle without interfering with muscle function. The action on the reticular formation (brainstem) reduces motor tone, influencing the motor and alpha motor system,

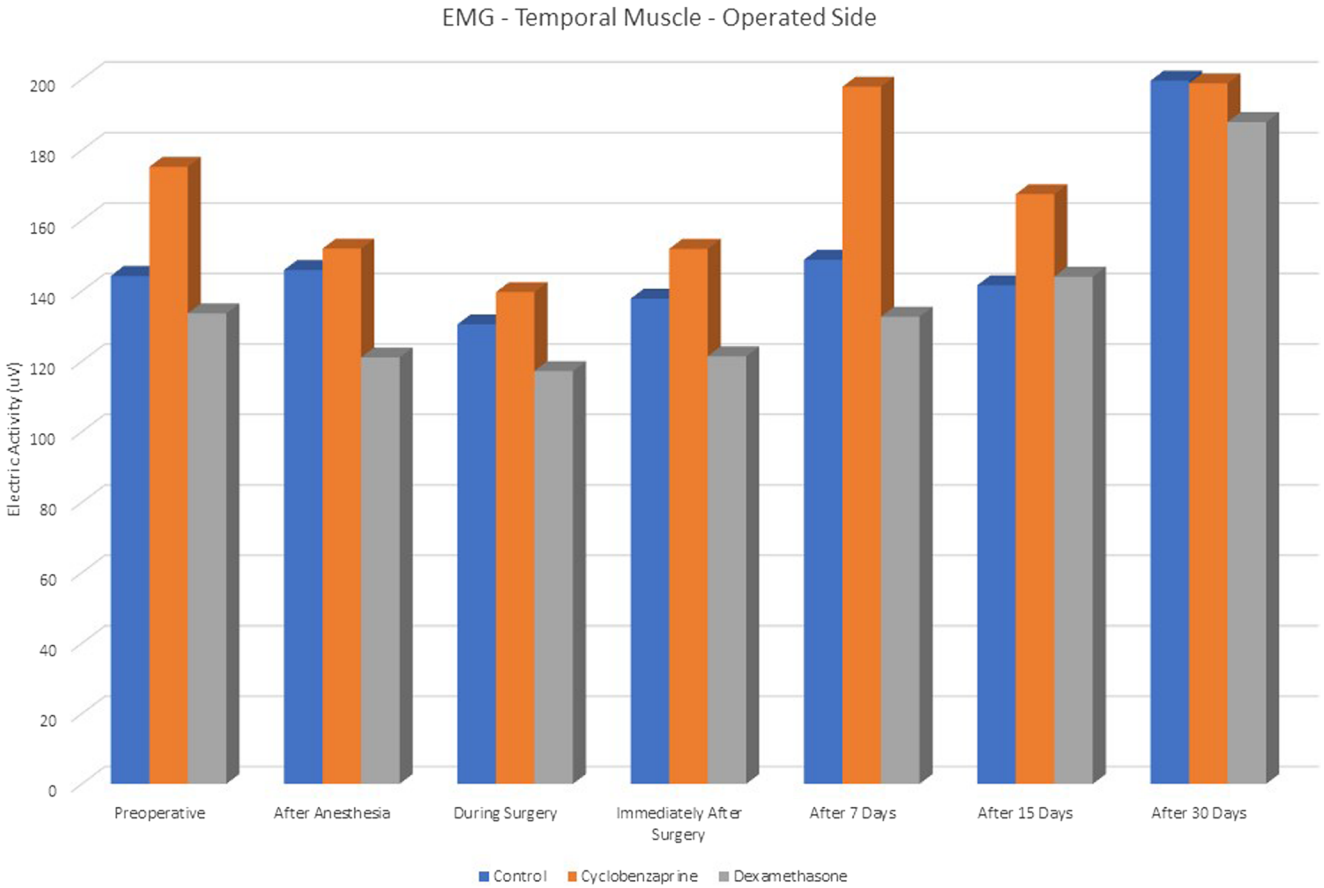

Fig. 5 Electrical activity of the temporal anterior and masseter muscles in the condition of maximum voluntary contraction (MVC) in the side of the surgical procedure of the removal of impacted third molars during the predicted phases of this research

without affecting the CNS or consciousness [16]. The plasmatic half-life is around 18 h, with tissue effects can last until 37 h [39]. Santos et al. [49] evaluated cyclobenzaprine in the extraction of third molars in three consecutive doses (1 day before the day of the surgery and 1 day after) in the same dosage used in the present study and did not observe a positive effect on pain reduction and/or prevention of trismus. However, the experimental model differs from that used by our laboratory, which consists of capturing the potentials generated by the fibre itself in real time (electromyography), whilst the authors used a method based on swelling, visual analogue scale, and mouth opening degree. Thus, with respect to these last two methodologies (VAS and interincisal distance), it was observed that VAS was not effective in solving the problem, since it presents a subjective character of somesthetic sensitivity, which varies according to climate, gender, general health condition, time of collection, and presence or absence of stressors. However, in relation to the interincisal distance or degree of buccal opening, it was possible to verify a significant effect in the presence of cyclobenzaprine and dexamethasone in all periods of data collection. The patients presented higher values of mouth opening degree when compared with the control group ($p < 0.05$). However, when the experimental groups were compared with each other, despite not achieving a significance level, the muscle relaxant promoted greater mouth opening, which suggests an immediate effect of the drug's action but favoured a posteriori motor behaviour observed after two post-operative days.

Other studies need to be developed to better understand the effects of medications on muscle activity. This work was a pilot study with some limitations as a small sample of 30 cases, that impacts, for example, in a large standard deviation ranges for the electromyographic variables evaluated.

Conclusions

Our findings suggest that cyclobenzaprine, as well as dexamethasone, may be useful in the therapeutic use of prevention of motor dysfunctions resulting from the

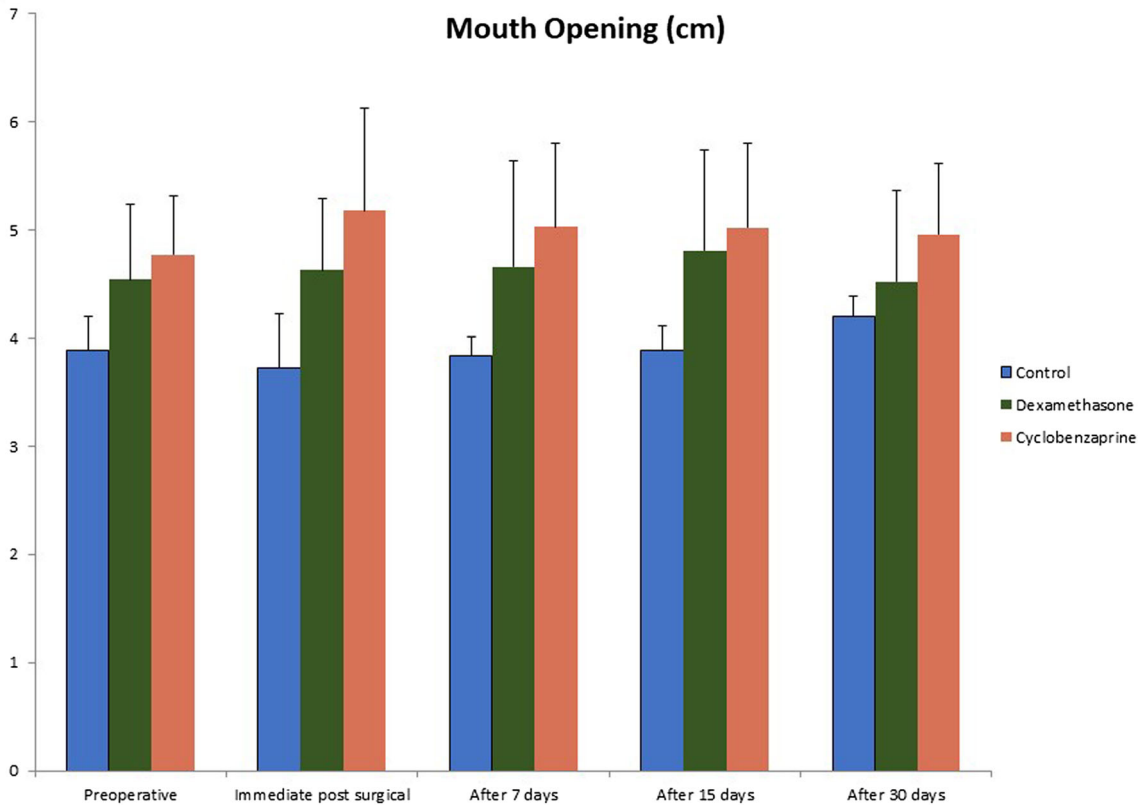

Fig. 6 Variation of the degree of buccal opening (mean values) obtained during the predicted periods of this research study

invasive removal procedures of impacted third molars. The authors believe that new systematic work should be performed in order to develop more effective, safer, and less collateral protocols, thereby reducing the number of post-operative complications, especially post-operative trismus.

Compliance with ethical standards statement

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the local ethics committee.

Informed consent Informed consent was obtained from all participants.

References

1. Raldi FV, Moraes MB, Nascimento RD, Santamaria MP, Amorim JBO, Paula FA (2011) The role of electromyography in dentistry. Braz Dent Sci 14:60–65
2. Rossi-Junior WC, Esteves A, Bérzin F, Couto Filho CEG, Nogueira DA, Villela GA Jr (2011) Masseter and extraction of third molars: electromyographic evaluation. Rev Cir Traumatol Buco-Maxilo-Fac 11:101–108
3. Flores JA, Machado E, Machado P, Flores FW, Mezomo MB (2007) Avaliação da prevalência de trismo em pacientes submetidos a exodontia de terceiros molares. RGO 55:17–22
4. Souza JA, Consone DP (1992) Método para medida do edema facial. RGO 40:137–139
5. Boer PJ, Raghoebar GM, Stegenga B, Schoen PJ, Boering G (1995) Complications after mandibular third molar extraction. Quintessence Int 26:779–784
6. Weber CR, Griffin JM (1994) Evaluation of dexamethasone for reducing postoperative edema and inflammatory response after orthognathic surgery. J Oral Maxillofac Surg 52:35–39
7. Raldi FV, Sá-Lima JR, Zanotti GG, Moraes MB (2006) Avaliação da eficácia da dexametasona no pós-operatório de terceiros molares. Revista Internacional de Cirurgia e Traumatologia Bucomaxilofacial 4:251–257
8. Delegado JHO, Fernandes JMT, Salinas BB (1997) Estudio comparativo entre ibuprofeno, dexametasona y betametasona em el control del edema postoperatorio em cirurgia de terceros molares retenidos. Revista ADM 2:88–91
9. Ensen E, Tasar F, Akhan O (1999) Determination of the anti-inflammatory effects of methylprednisolone on the sequelae of third molar surgery. J Oral Maxillofac Surg 57:1201–1206
10. Lima CA, Favarini V, Torres AM, Silva RA, Sato FRL (2017) Oral dexamethasone decreases postoperative pain, swelling, and trismus more than diclofenac following third molar removal: a randomized controlled clinical trial. Oral Maxillofac Surg 21:321–326
11. Yuasa H, Sugiura M (2004) Clinical postoperative findings after removal of impacted mandibular third molars: prediction of post-operative facial swelling and pain based on preoperative variables. Br J Oral Maxillofac Surg 42:209–214
12. Benediktsdóttir IS, Wenzel A, Petersen JK (2004) Mandibular third molar removal: risk indicators for extended operation time, postoperative pain, and complications. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 97:438–446
13. Korokolvas A (2015) Dicionário Terapêutico Guanabara. Guanabara-Koogan, Rio de Janeiro

14. Linden CH, Mitchiner JC, Lindzon RD (1983) Cyclobenzaprine overdosage. J Toxicol Clin Toxicol 20:281–288
15. Katz WA, Dube J (1988) Cyclobenzaprine in the treatment of acute muscle spasm: review of a decade of clinical experience. Clin Ther 10:216–228
16. Yagiela JA, Dowd FJ, Johnson BS, Mariotti A, Neidle E (2010) Pharmacology and therapeutics for dentistry. Mosby, Maryland
17. Merletti R (1999) The standards for reporting Emg data. J Electromyogr Kinesiol 9:3–4
18. Ahlgren JG, Ingerval BF, Thilander BL (1985) Surface and intramuscular EMG from the temporales muscle. A study of methods. Electromyogr Clin Neurophysiol 25:353–357
19. Portney LG, Roy SH (2004) Eletromiografia e testes de velocidade de condução nervosa. In: O'Sullivan S, Schmitz JT (eds) Fisioterapia – Avaliação e Tratamento. Manole, São Paulo
20. Pignataro Neto G, Berzin F, Rontani RMP (2004) Identificação do lado de preferência mastigatória através do exame eletromiográfico comparado ao visual. R Dent Press Ortodon Ortopedi Fac 9:77–85
21. Jung JW, Song KH, Chee Y (2010) Eletromyographic activity of the masseter muscle after radiofrequency therapy in an animal model. Oral Maxillofac Surg 14:35–41
22. Borrini CB. (2005) Analise da atividade eletromiografica de musculos mastigatorios em portadores de disfunção temporomandibular durante a mastigação. Piracicaba, 134p. Dissertação (Mestrado em Odontologia) – Faculdade de Odontologia de Piracicaba, Universidade Estadual de Campinas
23. Pontes RT, Orsini M, Freitas MRG (2008) Alterações Da Fonação E Deglutição Na Esclerose Lateral Amiotrófica: Revisão de Literatura. Revista Neurociência 18:69–73
24. Seymour RA, Walton JG (1984) Pain control after third molar surgery. J Oral Surg 13:457–485
25. Ferrario VF, Sforza C, Zanotti G (2004) Maximal bite forces in healthy young adults as predicted by surface electromyography. J Dent 32:451–457
26. Ahmad M, Hollender L, Anderson Q (2009) Research diagnostic criteria for temporomandibular disorders (RDC/TMD): development of image analysis criteria and examiner reliability for image analysis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 107: 844–860
27. Hermens HJ (1999) European recommendations for surface electromyography – results of the SENIAM project. Roessingh Research and Development, Netherlands, pp 1–3
28. Hermens HJ, Freriks B, Disselhorst-Klug C (2000) Development of recommendations for SEMG sensor and sensor placement procedures. J Electromyogr Kinesiol 10:361–374
29. Castroflorio T, Icardi K, Torsello F (2005) Reproducibility of surface EMG in the human masseter and anterior temporalis muscle areas. Cranio 23:130–137
30. Hermens HJ, Merletti R, Freriks B. (1999) The state of the art on signal processing methods for surface EletroMyoGraphy, deliverable of the SENIAM project. Roessingh Research and Development, p 17–19
31. Soderberg GL, Knutson LM (2000) A guide for use and interpretation of kinesiologic electromyographic data. Phys Ther 80:485–498
32. Albornoz M, Ogalde A, Aguirre M (2009) Estudio radiográfico y electromiográfico de los músculos masetero y temporal anterior em indivíduos com maloclusion tipo II, 1 de angle y controles. Int J Morphol 27:861–866
33. Ernberg M, Schopka JH, Fougeront N (2007) Changes in jaw muscle EMG activity and pain after third molar surgery. J Rehabil 34: 15–26
34. Bérzin, F. (2001) Estudo eletromiográfico da hipoatividade de músculos da mastigação em pacientes portadores de desordem cranio-mandibular (DCM), com dor miofacial. In: Anais do 5° Simpósio Brasileiro e Encontro Internacional sobre Dor, São Paulo, 292
35. Amorim MM, Borini CB, Lopes SLPC, Haiter Neto F, Berzin F, Caria PHF (2008) Relationship between the inclination of the coronoid process of the mandible and the electromyographic activity of the mandible and the electromyographic activity of the temporal muscle in skeletal class I and II individuals. J Oral Sci 50:293–299
36. Kroll CD. (2009) Avaliação da Ansiedade e da atividade eletromiografica dos músculos elevadores da mandibula em mulheres com disfunção temporomandibular [Tese] Piracicaba UNICAMP/FOP
37. Sato FRL, Asprino L, de Araújo DE, Moraes M (2009) Short-term outcome of postoperative patient recovery perception after surgical removal of third molars. J Oral Maxillofac Surg 67:1083–1091
38. Mehra P, Reebye U, Nadershah M (2013) Efficacy of anti-inflammatory drugs in third molar surgery: a randomized clinical trial. Int J Oral Maxillofac Surg 42:835–842
39. Brunton L, Knollmann B, Hilal-Danda R (2017) Goodman and Gilman's the pharmacological basis of therapeutics. McGraw-Hill Education, New York
40. Baxendale BR, Vater M, Lavery KM (1993) Dexamethasone reduces pain and swelling following extraction of third molar teeth. Anaesthesia 48:961–964
41. Dan AEB, Thygesen TH, Pinholt E (2010) Corticosteroid administration in oral and orthognathic surgery: a systematic review of the literature and meta-analysis. J Oral Maxillofac Surg 68:2207–2220
42. Nesi H, Vicente A, Loffi (2013) Uso de corticosteroide no pré-operatório em cirurgia de terceiros molares. Rev Bras Odontol 70: 22–27
43. Herrera-Briones FJ, Prados Sánchez E, Reyes Botella C, Vallecillo Capilla M (2013) Update on the use of corticosteroids in third molar surgery: systematic review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol 116:342–351
44. Ngeow WC, Lim D (2016) Do corticosteroids still have a role in the management of third molar surgery? Adv Ther 33:1105–1139
45. Lim D, Ngeow WC (2017) A comparative study on the efficacy of submucosal injection of dexamethasone versus methylprednisolone in reducing postoperative sequelae after third molar surgery. J Oral Maxillofac Surg 75:2278–2286
46. Chugh A, Singh S, Mittal Y, Chugh V (2018) Submucosal injection of dexamethasone and methylprednisolone for the control of postoperative sequelae after third molar surgery: randomized controlled trial. Int J Oral Maxillofac Surg 47:228–233
47. Mathias IF, Campos MA, Amorim JBO, Moraes MB, Nascimento RD, Santamaria MP, Raldi FV (2013) The influence of single-dose dexamethasone on masseter and temporal muscles after impacted lower third molar extraction. Pilot study through electromyography evaluation. Braz Dent Sci 16:65–76
48. Grossi GB, Maiorana C, Garramone RA, Borgonovo A, Beretta M, Farronato D, Santoro F (2007) Effect of submucosal injection of dexamethasone on postoperative discomfort after third molar surgery: a prospective study. J Oral Maxillofac Surg 65:2218–2226
49. Santos TS, Calazans ACM, Martins-Filho PRS (2011) Evaluation of the muscle relaxant cyclobenzaprine after third-molar extraction. JADA 142:1154–1162