ANALGESIC EFFICACY OF MAXSULID™ AND IBUPROFEN AFTER LOWER MANDIBULAR THIRD MOLAR REMOVAL

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ABSTRACT

The objective of this paper was assessed the analgesic efficacy of Ibuprofen 600mg and Maxsulid™ (Nimesulid- Beta Cyclodextrin - Farmasa) 400mg 12/12 hours during 3 days after lower third molar removal. Twenty patients were selected of both sorts, with age ranges from 18 to 25 years, with both asymptomatic lower third molar. The patients were randomized divided in 2 groups: in the first one Maxsulid™ 400mg was managed in postoperative of 48 tooth and Ibuprofen 600mg in the postoperative of 38 tooth; in the second one Maxsulid™ 400mg was managed in the 38 and Ibuprofen 600mg in 48 and all surgeries were performed by the same surgeon. The pain index had been assessed by VAS scale during 3 days. The pain averages in the first, second and third day for Maxsulid™ and Ibuprofen was respectively: 0.92-1.12; 0.63-1.00; 0.42-1.02, with no statistical significant differences neither to patient pain index, nor to the use of the rescue medication. Maxsulid™ is higher clinical analgesic efficacy than Ibuprofen

KEYWORDS: Third molar, Maxsulid™, Ibuprofen, pain.

1. INTRODUCTION

O The third molar are the last teeth to burst in the buccal socket, presenting a high percentage of impelled[1,2]. Routinely all the impacted tooth must be extracted, except in cases with some against-indication.[1,2] The third molar extraction is the most common surgical procedure in Oral and Maxillofacial surgery, being indicated to prevent origin of infection, disease as tumor, cysts or damages to adjacent teeth. Pain is one of the main complications of this surgery which begins between 1 and 3 hours after procedure[3]. Its effective control is a great concern between surgeons[3], therefore about 63.5% of the patients whom submit to this procedure presented a high level of pain[4]. Ahead of this, it has been a good study model to evaluate the pharmacological control of postoperative pain in these surgical procedures, due to relatively uniform procedure that requires pharmacological agents helpful[3, 4, 5, 6, 7]. Due to this, the buccal surgeries have been used as model for analgesic medicine comparison on control of the painful symptoms[8,9]. These are relatively uniforms and produce moderate to severe pain levels which require pharmacological agents auxiliary[5,12].

Ibuprofen, a nonsteroidal anti-inflamatory drugs (NAIDs) derived from the acid propionic, has demonstrated to be effective in the control of chronic inflammatory[10, 12, 13, 14] and it was also revealed efficient as analgesic in chronic and acute pains, as the postoperative third molar extraction[10, 12, 13, 14]. Its action is based on the inhibition of the cyclooxygenase reducing the synthesis of prostaglandins[10, 12, 13, 14] and presents time of half life about two hours and quickly absorbed by the oral administration[10, 12, 13, 14]. The ibuprofen suffers a fast reduction in its plasmatic peak when managed together with aspirin and when associating with the Phenobarbital where increases in the hepatic metabolism[13]. It is cautious to evaluate the lapsing of Ibuprofen in patients with renal commitment, previous history of pectical ulcer[13] and its use is not indicated in pregnancy and lactifics[14]. The Ibuprofen is available in pills and granules for dissolution in water from 200 to 800 mg which the maximum daily dose can't exceed 2400mg[5, 10, 12, 14]. Some studies have shown that doses of 400mg and 600mg, in 6-6 hours or in 8-8 hours or in 12-12 hours are indicated

in pain control[5, 10, 12, 14].

Nimesulide is NAIDs belonging to the class of the sulfonamides used in Europe and Brazil with a high therapeutic indication[13, 14]. It is indicated in the treatment of acute pains and as analgesic, anti-inflammatory and anti-thermal postoperative medication, presenting few effect in gastrointestinal treatment[13 14, 15, 16]. It acts inhibiting the enzyme Cyclooxygenase-2, reducing the synthesis of prostaglandins related to the inflammation and also it neutralizes the formation of cytokine, cartilaginases, superoxide anion and other toxic substances derivatives of many types of cells as granulocytes, neutrophil, macrophages[14]. The nimesulide possess fast and extensive absorption when managed for oral mode, having a half life of about 3 hours, with peak plasmatic concentration between 1 and 2 hours[13,14]. The cyclodextrin are cyclical composites formed by few units of glucose. The most common types of dextrin are α (alpha), β (beta) and λ (gamma), constituted of 6, 7 and 8 units of glucose respectively (referencia). The Betacyclodextrin is the most commom dextrin used, having as characteristic to be a transmitted of molecules, insurance, no-toxic and endowed with excellent tolerance. *Maxsulid*™ (Nimesulide- Beta Cyclodextrin - Farmasa) is an association formed by Nimesulide and Betacyclodextrin, that creates an inclusion complex (Nimesulide-betacyclodextrin) resulting in a better absorption of Nimesulide, providing a fast beginning of action and greater gastrointestinal (gastrointestinal) tolerance[16]. *Maxsulid*™ presents beginning of action from 15 minutes while the isolated Nimesulide is about 30 minutes[16]. The fact of the inclusion complex be easily dissociated, the period after-absorption is similar to isolated Nimesulide with intense hepatic metabolism, being exit 70% in urine and 20% in excrements and only 13% are exit unchanged in urine. The indicated dosage of *Maxsulid*™ is 400mg twice a day that is equivalent 100mg of isolated Nimesulide two times a day[16]. In studies carried through patients with osteoarthritis showed that the *Maxsulid*™ complex was efficient in the pain control[15].

The objective of this study was to assess the analgesic efficacy of *Maxsulid*™ 400mg twice a day and compare with Ibuprofen 600mg analgesic efficacy twice a day after lower third molar removal.

2. MATERIAL AND METHODS

This study was submitted and approved for the research committee of ethics in human beings with seeming n º 270/2007 and carried through in the Department of Dentistry of the State University of Maringá-UEM, Maringá, Paraná, Brazil, being selected 20 patients, of both sorts, with age range between 18 and 25 years and indicated for lower third molar (LTM) removal, bilateral, asymptomatics and similar in the surgical difficulty according to Pell and Gregory (1933) position for the occlusal plane, , relation with the ascending ramus classifications about the space localization r[17, 18]. None of the patients of the study was using systemic medication or presented systemic disease. All patients was in agreement with the Free and Clarified Assent Term. The surgeries had always been carried through two trained dentist, being always the same operator.

The patients had been randomized divided in two groups so that each patient was submitted to two surgical procedures, that is, in the left lower third molar (LLTM) and in the right lower third molar (RLTM), waiting 30 days between each surgical procedure. The group 1 (n=10 patients) LLTM had been removed using as postoperative medication Ibuprofen 600mg (pills of 300mg), 2 pills each 12 in 12 hours during 3 days; and 30 days after, in RLTM surgery, was used *Maxsulid*™ 400mg, 1 pill each 12 hours during 3 days. In group 2 (n=10 patients), after LLTM surgery, *Maxsulid*™ 400mg was used as postoperative medication; and 30 days after, in RLTM surgery, Ibuprofen 600mg (pills of 300mg) was used. In case the patients had pain, sodium metamizole 2 pills of 500mg in 6-6 hours was used as rescue medication.

Assessment

After each surgical procedure, the patient received a form where the pain level was registered in each 4 hours, being based on a visual analogue scale (VAS) pain. The VAS presents numbers from 0 to 10, where the zero corresponds pain absence, 1 light pain, 5 moderate pain and 10 severe pain. In case that the patient needed the medication of rescue for pain control, he/she would write down in the form the day and the hour of the medication use[19].

Statistics analysis

The two groups of medicines were compared using statistics analysis was carried using the WILCOXON test, non-parametric test, of 5% significance (Tab. 1). This test was applied to avaluated how many times the sodium dipirone was taked (Fig. 1). For both medicine the average pain scale of all patients in each period was obtained through T-student test (Fig. 2) qui-squared. The program used for attainment of the results was STATISTICS 7[12]. Assessing the correlation between sodium metamizole and both medicines the Chi-square test was used.

3. RESULTS

From the total of 20 patients, 11 (55%) are feminine and 9 (45%) are masculine gender. The addition of pain scale in the three days for each medicine and each patient and the p-value of Wilcoxon test are represented by table 1 and schematized graphically for figures 1, 2 and

3 that they represent the values gotten to each day. For this variable it did not have significant statistical differences in none of the days.

Table 1. Addition of pain scale in three days for each medicine and the patient and the p-value of Wilcoxon test (p<0,05).

Pacient	First day (p = 0,6051)		Second day (p = 0,2845)		Third day (p = 0,0756)	
	Maxsulid	Ibuprofen	Maxsulid	Ibuprofen	Maxsulid	Ibuprofen
Pacient 1	0	0	0	0	0	0
Pacient 2	1	7	0	2	0	4
Pacient 3	11	37	29	43	19	42
Pacient 4	4	7	4	6	0	1
Pacient 5	7	4	6	3	1	4
Pacient 6	2	8	0	0	0	0
Pacient 7	7	5	12	4	7	6
Pacient 8	0	0	0	0	0	0
Pacient 9	18	4	5	2	0	4
Pacient 10	3	0	1	0	7	0
Pacient 11	6	21	0	27	4	41
Pacient 12	12	11	3	3	0	0
Pacient 13	8	12	7	11	6	14
Pacient 14	0	0	0	0	0	0
Pacient 15	6	0	0	0	0	0
Pacient 16	13	2	0	0	0	0
Pacient 17	4	5	0	0	0	0
Pacient 18	0	0	0	0	0	0
Pacient 19	1	5	0	11	0	0
Pacient 20	7	6	8	8	6	6

The values gotten referring to the use of sodium metamizole as rescue medication had been: of the 20 patients who had received *Maxsulid*™ as medication postoperative, 14 patients (70%) didn't use rescue medication, 4 patients (20%) had used only one time, 1 patient (5%) told he/she used twice, the same value was gotten for three administrations and no patient used four or more times. Of the 20 patients who had received the Ibuprofen with postoperative medication, 16 patients (80%) didn't use rescue medication, 1 patient (5%) used only once, 2 patients (10%) used twice and 1 patient (5%) used seven times. As well as in the previous item he/she was not possible to observe a higher trend for any of medicines due to the rescue medication use. The gotten data are schematized in figure 1.

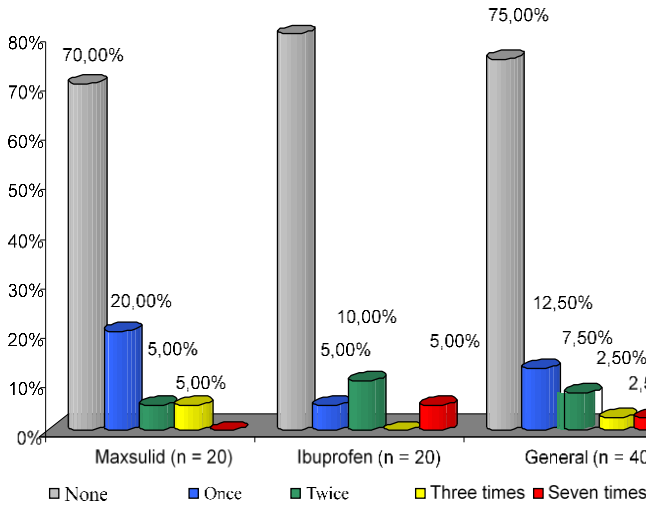

Figure 1. Frequency of metamizole sodium use with regard to the type of medicine used.

The postoperative of pain control was carried through 6 daily gauging, with aid of visual analogical scale to each 4 hours during 3 days, totalizing 72 hours of postoperative control. The averages of pain tried for the 20 patients to the medicine used are schematized by figure 2.

No patient presented any collateral effect in the administration of both medicines.

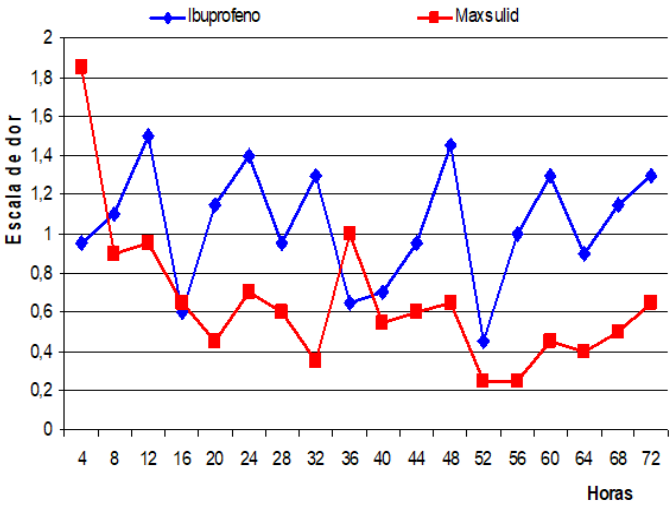

Figure 2: Average of pain scale to the 20 patients for each schedule verified in relation to the medicine used.

4. DISCUSSION

The LTM surgery is an efficient model of study to evaluate the pharmacological control of pain for allowing, the patient, a specific evaluation of the pain related to the procedure, which had the fact of relatively dealing with a located trauma and the operated technique is uniform for the majority of cases[3,4,5,7]. Patients who removal the third molar could try pain levels from moderate to severe, with fast beginning, with short duration, reaching its postoperative peak in 3 hours[3,5,7]. NAIDs has demonstrated great effectiveness in control of the resultant complications procedure and consists of a challenge for the surgeons, in the search of higher comfort for the patients[5,7,8,22].

Seymour et al. (1998)[12] evaluated the Ibuprofen 400mg and Aceclofenac100mg and got Ibuprofen significant statistical minors levels for the Aceclofenac, thus constituting an efficient and safe medicine for use in LTM surgery. Joshi et al. (2004)[10] when comparing analgesic efficacy of Ibuprofen 600mg with diclofenac 100mg and codeine 60mg associated with paracetamol 1g, had observed, that Ibuprofen, were presented as an effective medicine in the control of postoperative pain not having statistical significant differences.

Bocanegra et al. (2003)[7] had compared the analgesic effectiveness of Nimesulid (CN) 100mg with Nimesulid-betacyclodestrin (CB) 400mg in LTM surgery

and had evidenced that CB presented greater consequently absorption speed and time in the beginning of lesser action than CN. Concluding that as much Nimesulide how much the Nimesulid-betacyclodestrin had been efficient and safe for control of postoperative pain.

In our study *Maxsulid*™ did not present statistical significant difference in relation to Ibuprofen 600mg, but it was clinically superior when evaluating the results individually with aid of figure 1. The average of pain tried for the patients when receiving *Maxsulid*™ was higher in 2 periods of the 18 periods evaluated

5. CONCLUSION

According to the conditions of this study it can be concluded that both Ibuprofen and *Maxsulid* ™ have equal efficient in the control of postoperative pain and not having significant statistical differences between two medications, however *Maxsulid*™ was presented clinically superior to Ibuprofen.

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