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Analgesic efficacy of Lysine Clonixinate, paracetamol and dipyrone in lower third molar extraction. A randomized controlled trial

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Abstract

Objective: The purpose of this study is to compare the analgesic effect of lysine clonixinate, paracetamol and dipyrone after lower third molar extraction.

Material and Methods: The sample consisted of 90 individuals, with clinical indication for inferior third molars extraction. The mean age of the sample was 22.3 years (DP±2.5). The individuals received the medication in unidentified bottles along with the intake instructions. The postoperative pain parameters were measured according to Visual Analogical Scale (VAS) and the data was evaluated using the Kruskal-Wallis Test and Friedman Test, with the latter used to test different time intervals for each one of the drugs.

Results: The final sample consisted of 64 individuals, including 23 males (45.9%) and 41 females (64.1%) The mean age of the entire sample was 22.3 years (±2.5). The average length of the procedures was 33.9 minutes (±9.8). The distribution of mean values for this variable showed little variance for the different drugs (p=0.07).

Conclusion: Lysine Clonixinate did not show any substantial impact on the postoperative pain control when compared to other drugs.

Key words: *Lysine Clonixinate, paracetamol, dipyrone, postoperative pain, impacted third molar.*

Introduction

Surgical extraction of third molars is a very usual clinical procedure for controlling problems caused by impacted tooth and usually is followed by postoperative pain (1). As a result, several studies have been published comparing the drugs used to control postoperative pain after surgical removal of third molars (1-4).

Lysine Clonixinate is an analgesic that inhibits prostaglandin synthesis. A study comparing Lysine Clonixinate with Paracetamol on the oral postoperative pain did not find any significantly difference between them (5). In animals, Lysine Clonixinate showed a life span of 3 hours, and it is recognized as a non-steroid anti-inflammatory with the shortest life span when compared to other drugs of its category (6).

It bonds to plasma proteins in up to 96-98% and its metabolism takes place in the liver, four different inactive metabolites being derived. Seventy-four percent of its excretion is renal and 25%, fecal (7). It holds an excellent bio-tolerance and low incidence of collateral effect in the treatment of painful syndrome such as renal, neurogenic, muscular and tooth pain (8,9) and migraine (7).

The Visual Analogical Scale (VAS) is considered the best and easiest instrument to measure this type of pain. The parameters used by VAS determine the intensity of pain as following: no pain, mild pain, moderate pain and severe pain (10-12). The postoperative pain in dentistry should be controlled even before the surgical procedure itself. For that, many studies suggest the prescription of anti-inflammatory drugs, steroids or not, or analgesic drugs with some level of anti-inflammatory properties (13,14).

Paracetamol is a safe, effective drug for the treatment of postoperative pain following the surgical removal of lower wisdom tooth (15,16) and dipyrone is similar to other analgesics frequently used in the treatment of moderate to severe postoperative pain (17).

Although the drugs under test are safe, it is possible the occurrence of adverse effect. The estimated excess mortality due to community-acquired agranulocytosis, aplastic anemia, anaphylaxis, and serious upper'gastrointestinal complications was 20 per 100 million for paracetamol, 25 per 100 million for dipyrone (18).

Regarding the Paracetamol and Dipyrone large use in Brazil, Spain and other countries as well (17,19), we decided to use them in order to compare the Lysine Clonixinate clinic performance. The adverse effects due to the use of Lysine Clonixinate could be: nausea, vomiting, allergic reactions, vertigo and insomnia (9).

Material and Methods

The sample of 90 individual consisted of all patients under treatment in that semester at the clinic of Oral Surgery and Oral Traumatology from Federal University of Minas Gerais. The following conditions were observed in order to select the cases: (I) individuals with clinical indication for the removal impacted mandibular third molar in Class I or II, positioning A or B according to Pell et al. (20) regardless gender, race or social class; (II) surgeries that would not extend more than 60 minutes; (III) age between 18 and 26 years old; (IV) absence of allergies to the drugs under test; (V) absence of systemic conditions. All surgeries were carried out under local anesthesia-Lidocaine 2% with Felipressine 1:2:500 - Novoco® (SSWhite Artigos Dentais LTDA, Rio de Janeiro, Brazil).

The patients were informed about the purpose of the research project and were asked to give their written consent. The research was approved by the local Ethical Committee.

The drugs tested were bottled in identical opaque white recipient numbered from 1 to 90. Each recipient contained eight tablets of either one of the drugs under test (Dipyrone 500mg; Paracetamol 750mg; Lysine Clonixinate 125 mg). The patients themselves chose the recipient at random and they were unaware of its content.

Each patient was told to take one tablet from the given recipient one hour before the surgery and another tablet was taken after the surgery in 6 hours intervals after first dose during 24 hours. If the pain persisted the patient was given the liberty to take any other drug and the dentist should be informed.

The assessment of pain was performed according to VAS. Pain was measured just after the surgical procedure, and, 1,2,4,6,8,12 and 24 hours after the operation. For each one of the above options they had also to inform the level of pain, according to a decimal scale. The criteria used by the authors to assess patient's pain level were: 0 cm, no pain; 0.1-3 cm, light pain; 3.1-7 cm, moderate pain; 7.1-10 cm, intense pain (9).

The descriptive analyses are presented in percentages with mean, minimum (min), maximum (max) and standard deviation (SD). Kruskal-Wallis and Friedman tests were used and results were considered statistically significant when value of p was less or equal to 0.05 at least 95% of the confidence.

Results

The drop-out in the experiment was of twenty-six cases and therefore the sample was reduced to sixty-four.

The Lysine Clonixinate group was comprised of 20 individuals (8 males and 12 females). The Paracetamol Group was comprised of 23 individuals (9 males and 14 females) and Dipyrone Group was comprised of 21 individuals (6 males and 15 females).

The mean age of the entire sample was 22.3 years (±2.5). The length of the procedures was, in average, 33.9 minutes (±9.8). (Table 1), (Table 2) and (Fig. 1) depict each

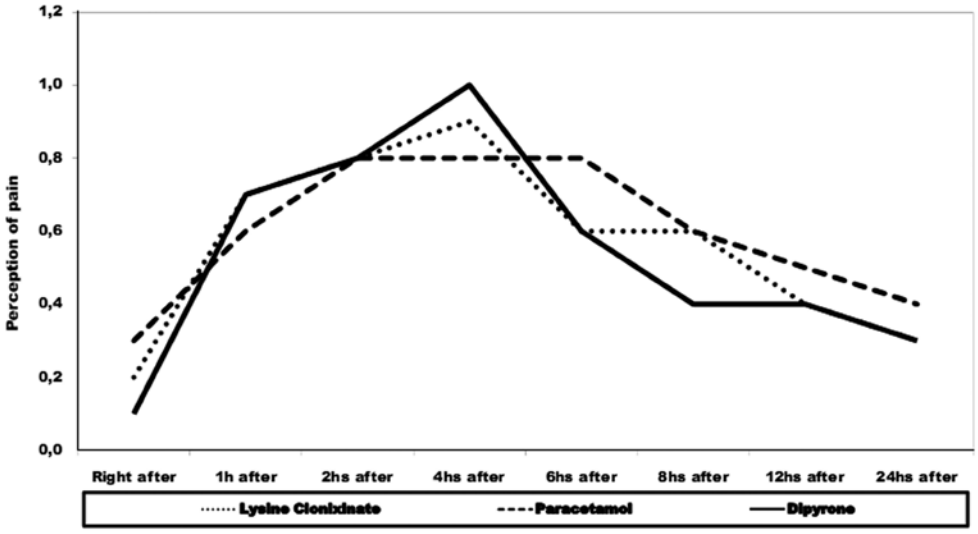

Fig. 1. Distribution of the scale of pain according to the different time interval for each of the drugs tested.

Table 1. Distribution of the variable pain according to VAS in different time period for the tree drugs tested.

Interval	drug	descriptive measurement					P
		min	max	median	mean	SD	
Right after	Lysine clonixinate	0,00	1,00	0,00	0,20	0,40	0,9370
	Paracetamol	0,00	3,00	0,00	0,30	0,70	
	Dipyrone	0,00	1,00	0,00	0,10	0,40	
1 hour after	Lysine clonixinate	0,00	2,00	1,00	0,70	0,60	0,8130
	Paracetamol	0,00	3,00	1,00	0,60	0,70	
	Dipyrone	0,00	2,00	1,00	0,70	0,70	
2 hours after	Lysine clonixinate	0,00	2,00	1,00	0,80	0,70	0,9310
	Paracetamol	0,00	3,00	1,00	0,80	0,90	
	Dipyrone	0,00	3,00	1,00	0,80	0,80	
4 hours after	Lysine clonixinate	0,00	2,00	1,00	0,90	0,70	0,8760
	Paracetamol	0,00	2,00	1,00	0,80	0,70	
	Dipyrone	0,00	3,00	1,00	1,00	1,00	
6 horus after	Lysine clonixinate	0,00	2,00	1,00	0,60	0,60	0,5330
	Paracetamol	0,00	3,00	1,00	0,80	0,90	
	Dipyrone	0,00	3,00	0,00	0,60	0,80	
8 hours after	Lysine clonixinate	0,00	2,00	0,50	0,60	0,60	0,3110
	Paracetamol	0,00	2,00	0,00	0,60	0,80	
	Dipyrone	0,00	3,00	0,00	0,40	0,80	
12 hours after	Lysine clonixinate	0,00	2,00	0,00	0,40	0,60	0,5930
	Paracetamol	0,00	2,00	0,00	0,55	0,70	
	Dipyrone	0,00	3,00	0,00	0,40	0,90	
24 hours after	Lysine clonixinate	0,00	2,00	0,00	0,30	0,60	0,5820
	Paracetamol	0,00	2,00	0,00	0,40	0,70	
	Dipyrone	0,00	3,00	0,00	0,30	0,70	

P refers to Kruskal-Wallis test

Table 2. Distribution of pain perception, in the different time intervals after surgery according to VAS.

Description							
Drug	Interval	min	Max	median	mean	SD	p
Lisyne clonixinate	Right after	0,0	1,0	0,0	0,2	0,4	**< 0,001**
	1 hour after	0,0	2,0	1,0	0,7	0,6	
	2 hours after	0,0	2,0	1,0	0,8	0,7	
	4 hours after	0,0	2,0	1,0	0,9	0,7	
	6 hours after	0,0	2,0	1,0	0,6	0,6	
	8 hours after	0,0	2,0	0,5	0,6	0,6	
	12 hours after	0,0	2,0	0,0	0,4	0,6	
	24 hours after	0,0	2,0	0,0	0,3	0,6	
Paracetamol	Right after	0,0	3,0	0,0	0,3	0,7	**< 0,001**
	1 hour after	0,0	3,0	1,0	0,6	0,7	
	2 hours after	0,0	3,0	1,0	0,8	0,9	
	4 hours after	0,0	2,0	1,0	0,8	0,7	
	6 hours after	0,0	3,0	1,0	0,8	0,9	
	8 hours after	0,0	2,0	0,0	0,6	0,8	
	12 hours after	0,0	2,0	0,0	0,5	0,7	
	24 hours after	0,0	2,0	0,0	0,4	0,7	
Dipyrone	Right after	0,0	1,0	0,0	0,1	0,4	**< 0,001**
	1 hour after	0,0	2,0	1,0	0,7	0,7	
	2 hours after	0,0	3,0	1,0	0,8	0,8	
	4 hours after	0,0	3,0	1,0	1,0	1,0	
	6 hours after	0,0	3,0	0,0	0,6	0,8	
	8 hours after	0,0	3,0	0,0	0,4	0,8	
	12 hours after	0,0	3,0	0,0	0,4	0,9	
	24 hours after	0,0	3,0	0,0	0,3	0,7	

P refers to Friedman test

one of the VAS parameters distributed according to drugs tested.

No adverse effect was observed with the drugs tested.

Discussion

Sixty-four individuals underwent surgical removal of their inferior third molars, among them 23 (35.9%) were male and 41 (64.1%) female. As reported before by Morin et al. (21), the variable gender did not play any important role in the distribution of the variable pain after surgery.

The mean age was 22.3 years (SD±2.5 years) and the sample was quite homogeneous in that aspect, which is an advantage for the categorization of pain related to age. Age can influence the pain control because third molar surgical extraction in older individuals can become troublesome due the cortical bone thickness and bone resilience loss (1). Chiapasco et al. (1) reported a decrease in morbidity and postoperative complication of third molars in young patients. Olmedo-Gaya et al. (14) attributed an increase of pain in older patients due to the more bone density and narrower periodontal ligament.

The patients underwent all the surgical procedures by 2 surgeons with calibration of the techniques avoiding therefore, different approaches. The surgeries length was controlled and therefore did not influence the behavior of pain in this study- 33.9 min (SD±9.8 min). Regarding this, the authors believe there is no bias concerning the time-period of surgery on the results here presented.

The surgery of third molar is a well known procedure. It allows a standardization of case selection reducing, therefore, the number of uncontrolled events that may lead to bias.

Questionnaire and VAS were used to obtain the data. The data bank was categorized by drug and analyzed according to the development of the postoperative condition, as presented in (Table 1).

The results in this study show no statistically significant difference between the drugs under test for controlling postoperative pain. Martí et al. (5) found similar results comparing Paracetamol and Lysine Clonixinate.

The high number of patients without any pain in the postoperative period can be related to the local anesthesia. The number of patients without pain in the postop-

erative period decreases with the passing of time. Four hours after the surgery this percentage was the smallest, and it increases slightly on the 6th and 8th hour after surgery, reaching its peak with 24 hours.

The results presented here are similar to those of Olmedo-Gaya et al. (14), who found out that the postoperative pain reaches its higher intensity during the first 8 hours after the surgery. The moderate postoperative pain is reported when the production of pain mediator increases and also when the effect of local anesthesia is fading away. After the 8th hour and during the subsequently days, the pain decreases progressively.

The results of this study show that the Lysine Clonixinate as well as Dipyrone and Paracetamol are efficient in controlling the postoperative pain in the surgery of inferior impacted third molars. Lysine Clonixinate possesses an analgesic activity similar to that of Dipyrone and Paracetamol and did not show any substantial impact on the control of postoperative pain when compared to those drugs.

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