Evaluation of therapeutic drug protocol used for control of pain after dental extractions

Avaliação do protocolo terapêutico medicamentoso utilizado para o controle da dor após exodontias

DOI:10.34117/bjdv6n10-082

Recebimento dos originais: 08/09/2020
Aceitação para publicação: 05/10/2020

Ana Cristina Vasconcelos Fialho
Associate Professor, Department of Pathology and Dental Clinic, Federal University of Piauí
Address: Campus Universitário Ministro Petrônio Portella - Ininga, Teresina - PI, 64049-550
E-mail: cristina@ufpi.edu.br

Marina de Deus Moura de Lima
Associate Professor, Department of Pathology and Dental Clinic, Federal University of Piauí
Address: Campus Universitário Ministro Petrônio Portella - Ininga, Teresina - PI, 64049-550
E-mail: mdmlima@gmail.com

Breno Cury-Rad Rodrigues da Silva
DDS, Department of Restorative Dentistry, Federal University of Piauí
Address: Campus Universitário Ministro Petrônio Portella - Ininga, Teresina - PI, 64049-550
E-mail: brenocrr2015@hotmail.com

Francisco Thyales Leite de Oliveira
DDS, Department of Restorative Dentistry, Federal University of Piauí
Address: Campus Universitário Ministro Petrônio Portella - Ininga, Teresina - PI, 64049-550
E-mail: brenocrr2015@hotmail.com

João Victor Frazão Câmara
MSc student, Department of Biological Sciences, Bauru Dental School, University of São Paulo
Address: Alameda Dr. Octávio Pinheiro Brisolla, 9-75 - Jardim Brasil, Bauru - SP, 17012-901
E-mail: jvfrazao92@hotmail.com

Isabel Ferreira Barbosa
PhD, Department of Restorative Dentistry, Piracicaba Dental School, University of Campinas
Address: Av. Limeira, 901 - Areião, Piracicaba - SP, 13414-903
E-mail: barbosa.isabelferreira@gmail.com

Guereth Alexsanderson Oliveira Carvalho
MSc student, Department of Dental Clinic, Federal University of Piauí
Address: Campus Universitário Ministro Petrônio Portella - Ininga, Teresina - PI, 64049-550
E-mail: guerethcarvalho@gmail.com

Josué Junior Araujo Pierote
PhD, Department of Restorative Dentistry, Piracicaba Dental School, University of Campinas
Address: Av. Limeira, 901 - Areião, Piracicaba - SP, 13414-903
E-mail: josuepierote@hotmail.com

Braz. J. of Develop., Curitiba, v. 6, n. 10, p. 75194-75203, oct. 2020. ISSN 2525-8761
ABSTRACT
Pain control after surgery is one of the factors concern of surgical specialties. Aim of this study is to evaluate and compare the efficacy of nimesulide 100 mg and dipyrone monohydrate 500 mg used after extractions performed by a maxillofacial surgery UFPI services in order to support the drug choice appropriately, prioritizing the analgesic effect needed to patients undergoing interventions. Forty patients underwent extractions in the clinic of the UFPI, in the Health Center Poty Velho and Emergency Hospital of Promorar. Patients were divided into groups: undergoing intervention with and without ostectomy. Dipyrone monohydrate 500 mg or nimesulide 100 mg produced by compounding pharmacy, were prescribed for patients randomly, featuring a blind study. The intensity of pain after the extraction was assessed by patients using a visual analogue scale, in a postoperative period of 72 hours at 24 hour intervals. There was no statistical variation between the analgesics studied during the 3 days postoperatively evaluated, considering the presence or absence of ostectomy as a modifier of the search. Analgesia effect of nimesulide was similar to dipyrone according to the present study.

Keywords: Analgesia, Dipyrone, Nimesulide, Postoperative Pain.

1 INTRODUCTION
Acute pain is an unpleasant individual experience associated with actual or potential tissue damage and its occurrence generates a warning signal and protection of the organism, inducing a precautionary behavior and limitation of possible tissue damage.1,2

Control of postoperative pain has been a major challenge among surgical specialties, recent advances in analgesic and analgesic techniques have contributed to this purpose.3

Extraction, with or without ostectomy, is one of the procedures commonly performed by dentists and buccomaxillofacial surgeons. The trauma caused by the surgery performed leads to tissue damage and consequently makes the patients more susceptible to postoperative pain, which
requires an adequate and effective trans and postoperative analgesia.\textsuperscript{4,5} Several pharmacological and non-pharmacological protocols have been instituted to prevent and control post-extraction pain discomfort, but further studies are needed to prove the efficacy of these drugs, which are part of some pharmacological protocols in certain services.

The most common drug therapy for postoperative pain control involves the use of basically three major groups of drugs that will act at different stages of the pain mechanism. These, despite having different indications, have similar results: steroidal anti-inflammatory drugs; non-steroidal anti-inflammatory drugs (NSAIDs) and central and peripheral analgesics.\textsuperscript{4,6} Among these, the option for peripheral action analgesics and NSAIDs is a routine indication for pain control after extraction.

Analgesics act as selective central nervous system depressants, inhibiting prostaglandin synthesis and consequently mild and moderate pain, local vasodilation and increased vascular permeability.\textsuperscript{7} Used for pain relief, raise the patient's threshold to pain without losing consciousness. Peripheral-acting analgesics (non-opioids) act on already installed mild and moderate pain by blocking calcium intake and decreasing cyclic monoaminoperoxidase (cAMP) levels in nociceptors.\textsuperscript{8,9} The standard drug for this group is dipyrone (metamizole). Although its mechanism of action is not well understood, it is one of the most commonly prescribed painkillers in Brazil, but with restricted use in the US and several European countries, due to its side effects they the possibility of depressing the bone marrow causing agranulocytosis and aplastic anemia, in addition to gastrointestinal complications and anaphylaxis.\textsuperscript{10,11}

Peripheral action analgesic (dipyrone monohydrate) and non-steroidal anti-inflammatory drug (nimesulide) were the pharmacological therapeutic classes chosen for this research. The antiinflammatory action of NSAIDs is due to the inactivation of cyclooxygenase enzymes (COX 1 and 2), which will consequently inhibit the production of prostaglandins and other substances released at the time of injury. New NSAIDs, selective COX-2 inhibitors, have been developed and have preferential action on the inflammatory process, avoiding side effects on gastric secretion.\textsuperscript{12}

NSAIDs are effective in low to medium intensity pain and can be administered postoperatively in some surgeries. In addition, they act on the hypothalamus by reducing temperature in febrile processes and inflammation, and are very important in the treatment of musculoskeletal disorders. The most common side effect tends to induce gastric ulceration.\textsuperscript{12}

In order to establish an adequate and accurate analgesic choice after extractions, the purpose of this research was to evaluate the efficacy of dipyrone monohydrate 500 mg and nimesulide 100 mg in pain control. Buco-Maxillo-Facial of UFPI.
2 MATERIALS AND METHODS

Forty patients, who had lower molars with indication for extraction, were randomized and sought care at the Bucco-Maxillo-Facial Surgery and Traumatology Service of the Federal University of Piauí, which met the inclusion criteria of this research. It comprises a randomized, blinded study. Forty patients, who had lower molars with indication for extraction, were randomized and sought care at the Bucco-Maxillo-Facial Surgery and Traumatology Service of the Federal University of Piauí, which met the inclusion criteria of this research. It comprises a randomized, blinded study. Inclusion criteria for patient selection were: patients with indication for extraction, with teeth with appropriate stage of formation and position; patients of both sexes; individuals aged 18 to 30 years; patients considered healthy (ASA - I and II), patients free of active periodontal disease; patients who agreed to participate in the study after reading and signing the informed consent form. Patients with local contraindications to surgery, hyperthermia or limitation of mouth opening at the time of surgery were excluded; patients on contraceptives; patients allergic to any of the drugs used in the research; patients using medications that interact with the drugs used in the present research; patients with chronic systemic alterations; pregnant or nursing patients; patients outside the required age range and patients who did not wish to participate in the research.

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The surgical procedure was performed by the same operator, previously calibrated, ruled and correctly, complying with all the principles of surgical technique. All patients received appropriate postoperative oral and printed instructions regarding hygiene, diet, medication and general care.

The surgeries were performed within a maximum of one hour under local anesthesia, with an average of 2 tubes of 2% Lidocaine anesthetic solution with 1: 100,000 epinephrine (Alphacaine, DFL®) per surgery; Patients who were treated without meeting this profile were excluded from the study. 48 lower molars were extracted, and some patients were treated more than once (split mouth). There were no surgical complications.
Pain intensity was assessed according to the Visual Analog Scale (VAS), which includes the following scores: 0 to 2 (LVE); 3 to 7 (MODERATE) and 8 to 10 (INTENSE), where zero means total absence of pain and ten maximum pain tolerable by the patient. The visual analog scale was provided and verbally explained to the patients by the researcher, who used simple and accessible language so that the patient consciously became familiar with the document.

Postoperative control and pain intensity measurements, widely used in research on drug analgesic efficacy, were performed for 72 hours after extraction. Pain intensity was reported by patients at each previously defined time interval (6 hours) and mean values were obtained in the first 24 initial, final hours, for a total period of 72 hours. For this, an ordinal scale was used in order to obtain the patients' average pain, which required a statistical test for nonparametric data. Thus, for comparison of four populations under study, the Lambda-Wilks test was performed at each time interval (every 6 hours), considering the mean values obtained at 24 hours on the first, second and third postoperative days, totaling 72 hours of evaluation.

3 RESULTS

The present research had as sample 40 patients and 48 surgical interventions and in 04 patients the interventions were of the split mouth type, due to the surgical indication that they had.

According to table 1, demographic characterization, the main reason for complaint was caries (72.9%), followed by pain (25%). The drugs were chosen at random for the treatment of 40 patients, with nimesulide 100 mg (Groups III and IV) most used with 28 donations. The surgeries using bone sectioning (Groups II and IV) totaled 17 interventions corresponding to 35.4% of the total, and the surgical procedure without ostectomy was prevalent, with 31 surgical procedures totaling 64.6% of the cases.

| Variables         | N  | %   |
|-------------------|----|-----|
| **Main complaint**|    |     |
| Pain              | 12 | 25,0|
| 3rd molar         | 6  | 12,5|
| Edema             | 8  | 16,7|
| Caries            | 35 | 72,9|
| Fracture          | 6  | 12,5|
| Orthodontic       | 2  | 4,2 |
| **Drug Type**     |    |     |
| Dipyrone Monohydrate 500 mg | 20 | 41,7|
| Nimesulide 100 mg  | 28 | 58,7|
In figure 1, it is observed that the groups that had osteotomy extractions using dipyrone monohydrate 500 mg, Group II, were higher (40%) than the use of nimesulide 100 mg, Group IV, with 32.1%. In the groups that were performed extractions without osteotomy prevailed the use of nimesulide 100 mg, Group III, in relation to the use of dipyrone monohydrate 500 mg, Group I, in percentages of 60% and 67.9% respectively.

Figure 1: Prevalence relationship (%) between the type of medication and the use or not of ostectomy in the surgical procedure.

According to figure 2, dipyrone monohydrate 500 mg obtained an average pain intensity of 3.10; 2.10 and 1.10, respectively, on the first, second and third day. Nimesulide 100 mg averaged slightly above dipyrone monohydrate 500 mg on the first day, but showed a decrease in mean pain intensity rate greater than dipyrone monohydrate 500 mg, giving a third day final average of 0.79.
Figure 2: Pain intensity on the 1st, 2nd and 3rd day according to the type of medication with the Multivariate Variance Analysis (MANOVA).

4 DISCUSSION

Postoperative pain control is a matter of great interest, as pain interferes with patients' quality of life. Therefore, several authors have researched the analgesic efficacy of some medications and developed protocols aiming at controlling this disorder. The present research evaluates and compares the effect of Dipirone Monoidratada 500 mg and Nimesulide 100 mg (NSAID) on pain control after non-included lower molar extractions.

The trauma resulting from the surgery implies physiological and emotional changes that, if not properly controlled, predispose patients to complications and among the conditions that may affect the recovery of the individual, the pain deserves attention.8,13

When referring to pain, it is important to note that the International Association for Pain Studies (IASP) defines pain as an unpleasant sensory and emotional experience associated with or described in actual or potential tissue damage.14 The incidence and intensity of pain depend on intrinsic characteristics of the individual, as well as the type of operation, the quality of treatment instituted, and the patient's cultural, sociological and personality influences.15

The results obtained in this research show that the main complaint of the patients was caries, which in all cases led to great coronary destruction, reason for the indication of extraction.

Another important factor that could interfere with the results was the type of extraction, although most were without ostectomy, there was a 35.4% percentage with ostectomy which makes the surgical intervention more traumatic, expecting for these cases greater pain intensity. For Chaves
Junior et al. (2006), osteotomy extraction is a technique used when there is no possibility of removal of the tooth or root by the traditional alveolar technique.

According to the statistical analysis, there was no relationship between osteotomy and type of medication (p > 0.05), since 40% of patients in the group receiving dipyridone monohydrate 500 mg required bone sectioning, as well as for nimesulide 100 mg, similar percentage (32.1%). Statistical analysis showed a similar distribution in the use of osteotomy between the two drugs. Pearson's chi-square nonparametric test ($\chi^2$) was used to compare proportions.

These data corroborate findings by Bocanegra et al. (2005) on the efficacy of nimesulide and ibuprofen in pain management after lower third molar extractions included in 86 patients, showing that they had moderate to severe pain after extractions, but the results suggested that both drugs were effective. In the first 24 hours, the analgesic effect of nimesulide started faster than ibuprofen, less than 15 minutes.

The maximum pain peak occurred in the first 24 hours, with gradual reduction of pain intensity in the three consecutive days in both drugs, according to MANOVA (p < 0.05). However, by the effect test between the means there was no significant difference (p > 0.05) between the drugs for the three days under study, although nimesulide 100 mg presented an average slightly above the dipyridone monohydrate 500 mg in the first 24 days. hours and decrease in mean pain intensity rate greater than dipyridone. Results compatible with those of Pouchain et al. (2015) who demonstrated equal efficacy of nimesulide and ketoprofen in pain control in four third molar surgeries of 18 patients.

Regarding metamizole (dipyridone) Stammschuelte et al. (2015) report that there are cases of severe clinical course, mainly related to indiscriminate use, in research developed to analyze cases of agranulocytosis related to metamizole use. In 1986, the risk of agranulocytosis led the German authorities to restrict indications and prescriptions for metamizole use, but the measure did not contain the use of metamizole as cases increased from 10 in 1990 to > 50 in 2012.

5 CONCLUSION

The results of this research lead to the conclusion that the efficacy of nimesulide 100 mg was similar in relation to dipyridone monohydrate 500 mg, in the control of pain after lower molar extractions, thus choosing the drugs at the discretion of the professional.
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