Preemptive analgesia of dexamethasone as compared to ketorolac tromethamine in simple tooth extractions*

Analgesia preemptiva da dexametasona em relação ao cetorolaco de trometamol em extrações dentárias simples

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INTRODUCTION

Pain is a biological phenomenon important for body defense, but uncomfortable for affected individuals. It is inherent to some dental procedures, especially surgical procedures, being its intensity often related to surgery extension1. According to Kissin3, postoperative pain control in dentistry, by means of preemptive analgesia, is an antinociceptive treatment to prevent the altered processing of an afferent input, which would amplify postoperative pain. Preemptive analgesia has four major objectives: decrease acute pain induced by surgical trauma, both in the intraop-
operative and postoperative periods; prevent the establishment of neural plasticity mechanisms of the central system responsible for referred and chronic pain (“memory of pain”); inhibition of persistent postoperative pain; and development of chronic pain.

There are basically three major groups of drugs used to control postoperative pain: steroid anti-inflammatory drugs, non-steroid anti-inflammatory drugs (NSAIDs) and central and peripheral action analgesics. These drugs promote similar pharmacological results; however, each one has different indications and acts in a different pain mechanism stage.

Steroids may be defined as synthetic hormones mimicking actions of endogenous cortisol secreted by the adrenal gland. Their therapeutic effects are in general attributed to the suppression of multiple mechanisms involved in the inflammatory response, leading to a decrease in pro-inflammatory chemical mediators levels at injury site.

According to the National Agency of Sanitary Surveillance (ANVISA), ketorolac tromethamine is a potent analgesic agent of the NSAIDs class, also with anti-inflammatory and antipyretic effects. Its action mechanism is through the inhibition of the cyclooxygenase enzymatic system and, as a consequence, of prostaglandins synthesis. It may be considered an analgesic with peripheral activity. The drug has no sedative or anxiolytic properties.

Authors have evaluated the efficacy of ketorolac tromethamine preemptive analgesia after third molar extraction. Intravenous ketorolac tromethamine (30 mg) was administered immediately before surgery in one group and immediately after surgery in the other. The conclusion was that ketorolac administered before surgery has induced postoperative analgesia of up to 8-9 h after surgery, when patients needed rescue analgesics for postoperative pain. For the other group, the mean was 6-9 h to begin consuming rescue analgesics. Preemptive ketorolac was better as compared to its administration after surgery.

Understanding that pain is the most important postoperative problem and given the need to establish a therapeutic protocol to control post-tooth extraction pain, in addition to few studies in the literature with ketorolac tromethamine, is that our study is justified.

This study aimed at evaluating and comparing the preemptive analgesic effect of dexamethasone and ketorolac tromethamine, both administered in bolus.

METHODS

This is an experimental study as from a clinical trial with human beings. It is a double-blind, crossover and randomized study.

Participated in the study 51 patients seen by the Ambulatory of Oral Surgery, Department of Dentistry, Federal University of Sergipe (DOD/UFS), from September 2011 to September 2012, who needed alveolar extractions in different hemiarcsades.

Each patient was individually addressed and the importance of the research was explained. Those who agreed to participate have signed the Free and Informed Consent Term (FICT).

After signing the FICT, patients were individually referred to a waiting room where the first researcher delivered one of the studied drugs, dexamethasone (4 mg) or ketorolac tromethamine (10 mg), which were manipulated in pharmacy so that patients and remaining researchers could not identify them. Only the first researcher had such information.

For research purposes, it was established that dexamethasone (4 mg) would be drug A and ketorolac tromethamine (10 mg) would be drug B. So, the clinical record was filled as follows: first procedure drug A and second procedure drug B, or vice-versa. Patient was referred to the surgeon, who performed the extractions according to Marzola and Toledo-Filho protocol.

All patients were anesthetized with 2% lidocaine hydrochloride, with 1:100.000 epinephrine, not exceeding two tubetes, according to Reed, Malamed and Fonner protocol. After extraction, patients were fully informed about postoperative care and were asked to return 24 h after. After 24 h, the third researcher has evaluated the analgesic efficacy of the drug through the 10-cm visual analog scale (VAS), where zero means no pain and 10 unbearable pain. Patients have recorded in the scale their level of sensitivity and whether there has been the need to have the rescue analgesic paracetamol (750 mg).

Patients were then asked to return 48 h after the second postoperative day for new evaluation of pain intensity with VAS and to check whether there had been the need for rescue drug. Eight days after the first procedure, patients returned to remove stitches and to be submitted to new extraction with the other drug to be tested (A or B, as the case might be). All procedures were recorded in clinical cards duly developed for the research.

After collection, data were tabulated and submitted to the following statistical tests: Friedman test with p<0.05 and Fisher Exact test with p<0.05.

This study was approved by the Ethics and Research Committee, Federal University of Sergipe (UFS), protocol CEP 257/2011 and N° CAAE – 0223.0.107.000-2011.

RESULTS

The research was carried out with 51 patients, being 29 females and 22 males with mean age of 29.57 years.

Figure 1 shows VAS values obtained as a function of drugs. There have been no statistically significant differences (Friedman, p>0.05) between periods or drugs. So, there have been no differences between ketorolac and dexamethasone.

Table 1 shows the use of paracetamol as a function of the drug and usage period.

There have been no statistically significant differences (Fisher Exact test, p>0.05) between drugs (considering the same period) or between periods (considering the same drug).
A study states that steroids, such as dexamethasone and strategies to pharmacologically treat pain.

Preemptive analgesia is becoming one of the most promising periods. In this sense, there are three therapeutic lines: one advocating the use of preoperative drugs, one using drugs in the postoperative period only, and one that uses them in the pre, intra and postoperative periods.

Preemptive analgesia is becoming one of the most promising strategies to pharmacologically treat pain.

A study states that steroids, such as dexamethasone and betamethasone, are drugs which prevent nociceptors sensitization by phospholipase A2 inhibition. In addition, these drugs are of choice for dentistry and have some advantages as compared to cyclooxygenase inhibitors, among them: do not have significant adverse effects, do not interfere with hemostasis and inhibit leukotriens synthesis. Their dosage is single preoperative dose and their cost-benefit ratio is better, because in a single dose they do not delay healing.

As to dexamethasone, clinical trials have shown that a single preoperative dose may effectively decrease inflammatory responses after oral surgeries. This was the reason why this drug was chosen as comparison standard for this research.

As to analgesic efficacy, ketorolac tromethamine has shown to be more potent among different NSAIDs under similar experimental conditions. Ketorolac has also been used in association with opioids, as adjuvant, to decrease their consumption and common adverse effects, such as respiratory depression, itching, urinary retention, sedation and nausea. So, supported by the literature, this research has adopted this drug to be tested and compared to dexamethasone.

In the postoperative period of oral surgeries, single and multiple 10 and 20mg ketorolac tromethamine doses were administered and both doses were equally effective, but were better than acetaminophen (600mg) with codeine. Such data confirm our study results where ketorolac tromethamine (10mg) in single dose was effective to relieve pain in 92.15% of patients in the first 24h and in 94.11% in 48h, with no need for rescue analgesics.

Dionne et al. have compared dexamethasone and placebo and dexamethasone and ketorolac. Authors have concluded that dexamethasone has decreased inflammation elements in the surgical area (prostaglandins and thromboxanes) without any effect on postoperative pain. However, ketorolac tromethamine has significantly decreased pain, and also prostaglandin and thromboxanes levels at surgery site. However, in our study, dexamethasone (4mg) as compared to ketorolac (10mg) has promoted similar analgesia. Our results confirm the study by Dionne et al. where ketorolac and dexamethasone have induced similar analgesia. In the first 24 and 48h, analgesia was approximately 94.11% for dexamethasone and for ketorolac tromethamine approximately 92.5% in the first 24h and 94.11% in 48h with no need for paracetamol.

### DISCUSSION

Postoperative pain control is a concern for dentists and the search for pharmacological protocols to decrease the problems caused by more invasive interventions has been constant. However, there is major controversy about which drug to use and how to administer it. In this sense, there are three therapeutic lines: one advocating the use of preoperative drugs, one using drugs in the postoperative period only, and one that uses them in the pre, intra and postoperative periods.

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### REFERENCES


