Int. J. Oral Maxillofac. Surg. 2014; 43: 348–354
http://dx.doi.org/10.1016/j.ijom.2013.08.003, available online at http://www.sciencedirect.com

International Journal of Oral & Maxillofacial Surgery

Clinical Paper
Oral Surgery

Analgesic efficacy of lysine clonixinate plus tramadol versus tramadol in multiple doses following impacted third molar surgery

J. Perez-Urizar[1], R. Martínez-Rider[2], I. Torres-Roque[3], A. Garrocho-Rangel[4], A. Pozos-Guillen[5]

[1]Department of Pharmacology, Faculty of Chemistry, Universidad Autónoma de San Luis Potosí, Mexico; [2]Department of Oral and Maxillofacial Surgery, Faculty of Stomatology, Universidad Autónoma de San Luis Potosí, Mexico; [3]Dixpertia Investigación Biofarmacéutica y Farmacológica SC, San Luis Potosí, Mexico; [4]Institutional Program in Engineering and Materials Sciences, Universidad Autónoma de San Luis Potosí, Mexico; [5]Basic Sciences Laboratory, Faculty of Stomatology, Universidad Autónoma de San Luis Potosí, Mexico

J. Perez-Urizar, R. Martínez-Rider, I. Torres-Roque, A. Garrocho-Rangel, A. Pozos-Guillen: Analgesic efficacy of lysine clonixinate plus tramadol versus tramadol in multiple doses following impacted third molar surgery. Int. J. Oral Maxillofac. Surg. 2014; 43: 348–354. Crown Copyright © 2013 Published by Elsevier Ltd on behalf of International Association of Oral and Maxillofacial Surgeons. All rights reserved.

Abstract. This study compared the analgesic and anti-inflammatory efficacy, trismus control, and tolerability of the combination of lysine clonixinate and tramadol (LCT) versus tramadol (T) alone after surgical removal of impacted mandibular third molars. This study was a double-blind, randomized clinical trial, including two study groups of 20 patients each, who exhibited acute pain subsequent to surgical extraction of two mandibular third molars. Pain intensity was quantified over a 96-h period using a visual analogue scale and a 5-point verbal rating scale. Secondary indicators of analgesic and anti-inflammatory efficacy, trismus control, and tolerability were determined. Patients administered LCT exhibited better therapeutic effects that those administered T. Fifty percent of patients in the LCT group rated this therapy as 'excellent analgesia' compared with only 10% in the T group. The onset of the analgesic effect of LCT was significantly faster, without any therapeutic failures. There were no significant differences between the groups with regard to anti-inflammatory effect or trismus. The results of this study suggest that the postsurgical analgesic efficacy of LCT in combination (LC 125 mg + T 25 mg) is superior to that obtained with T alone, administered at the standard dose of 50 mg, for up to 96 h after the extraction of both impacted mandibular third molars.

Keywords: Lysine clonixinate; Tramadol; Balanced analgesia; Third molar surgery.

Accepted for publication 9 August 2013
Available online 14 September 2013

The surgical extraction of third molars under local anaesthesia is a standardized, very common clinical procedure for controlling problems produced by their impaction. This procedure is usually followed by postoperative pain, swelling, and trismus, caused mainly by tissue damage.[1] The pain resulting from the surgical removal of one or more impacted third molars reaches its greatest intensity 6–8 h after the procedure; therefore, this pain profile has been adopted as a validated and reliable pain model that is commonly used to test the efficacy, safety, and tolerability of analgesic drugs for acute dental pain.[2]

There are different strategies for postoperative pain management, including the

0901-5027/030348 + 07 $36.00/0 .Crown Copyright © 2013 Published by Elsevier Ltd on behalf of International Association of Oral and Maxillofacial Surgeons. All rights reserved.

use of local anaesthesia or the administration of diverse types of analgesics, mainly non-steroidal anti-inflammatory drugs (NSAIDs) and opioids.[3–6]

The combination of different analgesics, or 'balanced analgesia', can increase the safety and duration of pharmacological analgesia. The rationale for balanced analgesia is to provide sufficient pain relief through additive or synergistic effects using different analgesics, with a concomitant reduction of side effects due to the resulting lower doses of individual drugs. Analgesic combinations that target both central and peripheral pain pathways have different onset times and durations of action, as well as different sites of action, and they can enhance the individual drugs' capacities to minimize pain.[7–9] Over the past decade, preclinical and clinical studies have supported the concept of balanced analgesia, with improved pain relief after surgery. In this regard, the use of an opioid combined with an NSAID can be useful in oral surgical procedures.[10]

Tramadol hydrochloride is a centrally acting opioid analgesic that is clinically effective in treating moderate to severe pain and that has a low potential for addiction. It is used for many types of acute pain, including pain of postoperative, obstetric, terminal cancer, and coronary origins. Tramadol acts on opioid receptors and seems to modify the transmission of pain impulses by inhibiting the reuptake of monoamines. It is administered as a racemic mixture of two enantiomers: (+)-tramadol, which has a moderate affinity for the opioid μ receptors and inhibits serotonin reuptake, and (−)-tramadol, which is a norepinephrine reuptake inhibitor. Both enantiomers are metabolized by the liver. O-desmethyl tramadol (M1) is the only active metabolite with a high affinity for the μ receptors.[11] The mean elimination half-life is about 6 h. Tramadol has been evaluated in oral surgery, specifically in the surgical removal of impacted third molars as a pre-emptive analgesic[6,12] and via a combination of routes.[13]

Lysine clonixinate (LC) is an NSAID without narcotic effects that belongs to the family of non-salicylates and to the subgroup of anthranilic derivatives, resembling the chemical structure of flufenamic acid. Its structural formula (2-(3-chloro-*o*-toluidine)pyridino-3-carboxylate) allows for fast absorption. It inhibits prostaglandin synthesis through the effects of inhibiting the enzyme cyclooxygenase, and it is indicated to relieve moderate to severe episodes of dental pain, postoperative pain, dysmenorrhea, and migraine. LC is 96–98% protein-bound, and its hepatic metabolism results in four different inactive metabolites. LC has shown a mean elimination half-life of 4 h.[14,15] The analgesic efficacy of LC has also been tested in third molar extractions without showing any substantial impact on postoperative pain control compared with paracetamol and dipyrone.[4]

Despite their well-known side effects, opioid analgesics remain the main therapies for moderate to severe pain after surgery. However, NSAIDs have been used adjunctively with opioids in the management of pain after a variety of surgical procedures, including oral surgery.[10]

Studies on the efficacy and safety of analgesics for the control of postoperative pain have been performed using single doses. However, patients must take analgesics for several days after surgical procedures; accordingly, the use of multiple-dose designs has been proposed.[16,17] In addition, there has not been a study on the clinical analgesic efficacy of the combination of LC and tramadol using the third molar surgical extraction model previously mentioned. Therefore, the aim of the present study was to compare the analgesic efficacy, anti-inflammatory efficacy, trismus control, and tolerability of the combination of lysine clonixinate and tramadol (LCT) versus tramadol alone (T) after the surgical removal of two impacted mandibular third molars.

Patients and methods

Patients and study design

This study was designed as a double-blind, randomized, controlled, parallel-group, multiple-dose trial. It was conducted in accordance with the declaration of Helsinki, and the study design was approved by the local ethics committee. All of the subjects were informed of the possible risks of oral surgery and experimental treatments, and they signed institutionally approved consent forms.

A total of 40 volunteer patients were recruited into the study from the clinic of maxillofacial surgery. Inclusion criteria were as follows: age 19–26 years, either gender, systemically healthy, and clinical and radiographic diagnoses of two partial or full bony impacted mandibular third molars, asymptomatic preoperatively. The exclusion criteria were: pregnancy, lactation, a history of seizure disorders, and the consumption of analgesic, sedative, or contraceptive drugs or alcohol 48 h prior to the surgical procedure. In addition, every patient was required to avoid solid foods and liquids after midnight on the night before surgery.

The patients were assigned sequential numbers in the order of their enrollment and received their allocated treatment according to a previously designed randomization schedule. The study groups were balanced using permuted blocks of 10 numbers. Even numbers corresponded to treatment A, or the experimental group (LCT): patients were given lysine clonixinate 125 mg + tramadol 25 mg. Odd numbers corresponded to treatment B, or the control group (T): patients received tramadol 50 mg. Both regimens were administered orally every 8 h. Both medications, in solid formulations, were placed in sealed, opaque, and labelled containers, each with an amount corresponding to one dose of each medication, which was taken every 8 h for 4 days. Thus, the patients and data collectors were blinded to the treatment assignment.

Interventions

All of the surgeries were performed by the same surgeon using a standard oral surgical procedure under local anaesthesia by nerve block of the inferior alveolar and buccal nerves, using 4% articaine containing 1:100,000 epinephrine (Medicaine, Septodont, France). A mucoperiosteal flap was prepared by making an incision distal to the lower second molar, along the anterior edge of the ascending ramus of the mandible; the flap was also used to close the surgical wound using 4–0 silk sutures. The difficulty of the removal procedure was evaluated as follows: grade I, extractions with forceps only; grade II, extraction by osteotomy; grade III, extraction by osteotomy and coronal section; and grade IV, complex extraction. In all of the cases, the duration of each surgical procedure, from incision until the placement of the last suture, was recorded. Both impacted third molars were extracted at the same visit, first one and then the other.

Assessments

When postoperative pain reached a moderate or severe intensity, or at the end of the anaesthetic effect, patients received the first single dose of the corresponding study medication, which was given orally with water. Then, patients remained at the clinic for 6 h after the end of surgery to evaluate pain intensity and pain relief. A 10-cm visual analogue scale (VAS) was used to assess pain intensity over a 96-h period. Before starting the treatment, an investigator explained the VAS to patients; this scale consisted of an interval scale, ranging from 0, representing no pain or discomfort, to 10, representing maximum pain or discomfort. The VAS score

Download English Version:

https://daneshyari.com/en/article/3132344

Download Persian Version:

https://daneshyari.com/article/3132344

Daneshyari.com