Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/vg8tyn39

COMPARATIVE EFFICACY OF CODEINE AND ARTICAINE IN REDUCING PROPOFOL-INDUCED PAIN: A RANDOMIZED, DOUBLE-BLIND STUDY

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ABSTRACT

Background: Patient satisfaction with perioperative care is a mandatory point, and one of the most frequent issues is the pain related to the usage of propofol injection, which occurs in 40-86 percent of patients. Promptly to treat this pain, articaine (LID) pre-treatment is regularly utilized, though it has been reported to cause the destabilization of the propofol emulsion, as well as the possible dangers of developing pulmonary fat embolism. In this study, the efficacy of an opioid with agonist-antagonist properties Codeine (DEZ) was examined against LID and placebo (normal saline) in the pain reduction of propofol injection. Methods: It was a placebo-controlled, double-blind and randomized study of 98 patients age: 16-65years whose procedure is: elective surgery under general anesthesia. Three random groups were created which comprised a Control (normal saline) and which was offered in Articaine (40 mg) and Codeine (2 mg). The extent of pain during the administration of propofol was determined using the assistance of the Verbal Rating Scale (VRS), and the pain was assigned a number of 0 (no pain), 1 (mild pain), 2 (moderate pain) or 3 (severe pain). Chi-square and analysis of variance were performed to perform statistical analysis on statistical data of the <lov_ climbing volume and effects of the <elle_ climbing volume and effects of the Results: The percentage occurrence as well as the magnitude of propofol-caused pain was highly minimized in LID and in DEZ groups when compared to the Control group. No pain was registered by 18.18 percent of the patients in the Control group, 60.61 percent and 71.88 percent of patients in the LID and DEZ groups respectively. The administration of DEZ demonstrated the most and significant reduction of pain, as none of the patients experienced severe pain, which is in contrast to 6.06% of the LID group. Conclusions: The pre-treatment with 2 mg Codeine has the same effect as 40 mg Articaine in lowering the cases and level of pain of propofol injection. It is possible that the analgesic action of DEZ is a centrally mediated partial agonist of μ-opioid receptor. DEZ seems to be a potential solution to replacement of Articaine in the treatment of pain associated with propofol, but there should be additional research with different dosages of DEZ and power analysis to determine the optimum dose, and define whether it is effective enough to be used clinically.

Keywords: Propofol, Codeine, Articaine, Pain Management, Anesthesia

INTRODUCTION

The satisfaction of the patients relating to perioperative care has received attraction over the past several years. Propofol is a general intravenous anesthetic that is commonly related to injection pain among 40-86% of patients packed with 20-50% cases experiencing pain after injection.[1]To reduce such discomfort, it would be typical to use articaine (LID) pre-treatment.[2-4] This intervention, however, places question marks on the propofol emulsion emulsion formulation stability in combination with LID that supposedly predisposes to a threat of pulmonary fat embolism.[5]Another method is pre-treatment of opioids and this can reduce the pain with the propofol injection both centrally and peripherally.[3, 6-10] Codeine (DEZ) is an agonist, antagonist opioid that acts on certain receptors in several regions of the central nerves system (CNS), influences both the pain perception and the emotional reaction to pain. This trial was done to determine the effectiveness of 2 mg DEZ against placebo (normal saline) and Articaine (LID).

MATERIALS & METHODS

It was a double-blind placebo-controlled and a randomized study. All participants voluntarily agreed to be involved; the consent was established in writing, and the ethical approval of the study was issued. There were 98 patients both sexes aged 16-65 years of age and with an American society of anesthesiologists (ASA) grades I and II which were offered elective surgery under general anesthesia. Patients were excluded based on history of renal or hepatic insufficiency, allergies or adverse reactions to the investigational drugs, neurological or cardiovascular side effects, obesity, difficult airways, pregnancy and pain-modifying medication. The participants were randomly assigned to groups with the aid of the computers generated random numbers.

The patients were grouped into three different groups; Group CON (n = 33) [which was injected with 2 ml of normal saline], Group LID (n = 33) [which was injected with 2 ml of 40 mg articaine], and Group DEZ (n = 32) [which was injected with 2 ml of 2 mg codeine]. All the three drugs (normal saline, articaine and codeine) produces identical appearance when all their solutions were found. All the patients recommended were informed of the verbal rating scale (VRS) to be applied in measuring her pain when injected with the propofol.

Through intramuscular application, patients were prescribed 0.1 g of phenobarbital prior to induction of anesthesia in a half an hour. On reaching the operation room, an 18G IV cannula was placed into the largest dorsal of the hand vein and commencement of lactated Ringer solution. The drug under study was given and at 1 minute interval, 50 mg propofol was introduced inside a span of 20 seconds. During the administration of propofol, the evaluator used the VRS to determine the pain, an anesthesiologist who was not aware of the used treatment. Patients were to testify on the pain or discomfort they feel using a four point scale; 0 (no pain), 1 (mild pain), 2 (moderate pain), and 3 (severe pain). The rest of the dose of propofol (2mg/kg) was then instilled and the patient placed under anesthesia. The statistical value p was < 0.05. SPSS software (version 10.0) utilization in data analysis on the basis of SPSS.

RESULTS

The trial involved a total of 98 patients whose mics were found to be 33 patients (Control), 33 patients (Articaine) and 32 patients (Codeine). The gender, age, weight, height, and ASA grade of the patients were substantially similar in all the three groups (Table 1).

When it came to gender distribution, the Control group consisted of 16 males and 17 females, the Articaine group had 17 males and 16 females whereas in the Codeine group there were 15 male and 17 female members. The averages of the ages of patients in the Control group, Articaine group and Codeine group were in 50+/-12, 47+/-13 and 47+/-13 years items, respectively. Mean patient weight in the Control group was 62 10 kg, Articaine group was 63 8 kg and in Codeine group was 68 25 kg. The comparison was of the mean height of the Control group, Articaine group and Codeine group as 164 2560 cm, 163 2560 cm and 160 2560 cm, respectively.

The ASA (I/II) classification was also close to each other in each of the groups as 14/19 patients in the Control group, 16/17 in the Articaine group, and 15/17 in the Codeine group. The groups did not present significant differences in these demographic variables, indicating that these factors were well balanced to be analyzed on a similar basis.

Table 1: The characteristics of the patient in the group of CON, LID and DEZ

Group	Gender (M:F)	Age (year) (mean±SD)	Weight (kg) (mean±SD)	Height (cm) (mean±SD)	ASA (I/II)
Control (n=33)	16:17	50±12	62±10	164±8	14/19
Articaine (n=33)	17:16	47±13	63±8	163±9	16/17
Codeine (n=32)	15:17	47±13	68±25	160±18	15/17

Incidences of propofol- induced pain were determined among the three groups of participants that included Control, Articaine, and Codeine. The Control group had the most number of patients who experienced moderate to severe pain as indicated in Table 2. Namely, 18.18%, 33.33%, 30.30% and 18.18% of patients in the Control group experienced no pain (Pain Score 0), mild pain (Pain Score 1), moderate pain (Pain Score 2), severe pain (Pain Score 3), respectively.

On the contrary, a considerable drop in pain rates was observed in the Articaine group. Sixty point six one percent of the patients said that they did not have any pain (Pain Score 0), 21.21 percent city reported mild pain (Pain Score 1), 12.12 percent city reported moderate pain (Pain Score 2), and only 6.06 percent said that they have severe pain (Pain Score 3).

The group Codeine demonstrated the best outcomes since 71.88 per cent of patients did not report any pain (Pain Score 0). 21.88 percent of them had mild pain (Pain Score 1), 6.25 percent had moderate pain (Pain Score 2) and none in Codeine group had severe pain (Pain Score 3).

These findings indicate that Articaine, as well as, Codeine in many ways alleviated the occurrence of propofol-induced pain when compared to the Control group, with the latter proving to be the most effective in the prevention of the pain.

Table 2: Epidemiology of propofol triggered pain: a comparison involving CON, LID and DEZ groups

Group	N	Pain Score 0 (%)	Pain Score 1 (%)	Pain Score 2 (%)	Pain Score 3 (%)
Control	33	6 (18.18)	11 (33.33)	10 (30.30)	6 (18.18)
Articaine	33	20 (60.61)	7 (21.21)	4 (12.12)	2 (6.06)
Codeine	32	23 (71.88)	7 (21.88)	2 (6.25)	0 (0)

DISCUSSION

Our research findings reveal that propofol injection paint was highly reduced by pre-treatment of 2 mg Codeine (DEZ) or 40 mg Articaine (LID), which tremendously decreased the occurrence and the magnitude of pain.

Propofol has been shown to cause irritation of the skin, the mucosal membrane, and the intima of the veins and most of the pain of the contraction is relayed by polymodalociceptors that are found in peripheral veins.[11]The pain experienced with administration of propofol can be dependent on the formulation of the drug.[12][13] Larsen et al. [12] discovered that a new formulation of propofol (10 % fat emulsion long- and medium-chain triglycerides) resulted in improvement in the level of pain experienced at the time of administration, compared to those with conventional formulation. However, microemulsions of propofol are more likely to cause frequent and severe pain during injection as compared to lipid emulsions of propofol.[12]

Fentanyl, remifentanil and alfentanil are examples of the opioid based pain relievers used in the alleviation of the pain induced by the intravenous use of propofol.[3][6][7][8][9][10] Pre-treatment with these opioids not only alleviates the injection pain, but also enables the minimization of the post-operative pain which includes nausea and vomiting and the subsequent requirement to administer additional post-operative opioids.[14][15] It is believed that theAlso central opioid receptors have been considered as helpful in alleviating the pain caused by propofol injection. Being the partial agonist of the open receptor 2, DEZ, gets to work with stereospecific receptors in all parts of the central nervous system (CNS). It influences the personal awareness of pain and the emotional response of the person in those areas of the central nervous system. It has been proposed that opioid receptors of the 19 types, 2 receptors 2, and 3, are involved in producing the analgesic effects. The following hypothesis is proposed by us: The suggested effect of DEZ on relieving pain is mainly of central character since the experiment was not conducted with use of the tourniquet method. Past reports have demonstrated that the use of an intravenous opioid held with a tourniquet before injection of propofol, had no effect in alleviating pain.[8]

This study has a limitation in that, we did not carry out a power analysis of our results so we could understand the statistical strength of our results. Moreover, the research did not investigate different proportions of DEZ and the minimal quantity that will actively avoid the discomfort of pain in the administration of propofol cannot be defined.

CONCLUSION

In our study, we `ve seen that administering 2 mg Codeine (DEZ) prior to use is as much effective as 40 mg Articaine (LID) in reducing the number and the intensity of pain that are causes of propofol injection. Both of the above (DEZ and LID) relieve the pain of propofol considerably, yet DEZ has even stronger analgesic effect. Analgesia in DEZ was found to be primarily central and is caused by the partial agonist effect of this drug on the μ-opioid receptor, which mediates pain perception and emotional reaction of the subject to pain. This paper offers that it is possible to treat the injection pain of propofol using DEZ as an alternative to articaine. The adequate dosage, power analysis and additional studies of the use of DEZ at different doses in relation to propofol-induced pain should be carried out with the aim to prove further effectiveness of DEZ as a standard pre-treatment agent to this type of pain.

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