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Implementation of Inhaled Methoxyflurane for the Reduction of Distal Radius Fractures in a Third-Level Hospital: A Descriptive Cohort Study

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Abstract: Orthopedic emergencies due to fractures are one of the main reasons for surgical intervention. The distal radius is a structure prone to fractures, particularly in young people. The main objective of this study was to evaluate the success rate of methoxyflurane in the reduction in distal radius fractures that required conservative treatment. The medical records of all the patients with Frykman type I and type II distal radius fractures who underwent fracture reduction with methoxyflurane or propofol from December 2021 to January 2023 were reviewed. The success rate of distal radius fracture reduction with methoxyflurane was analyzed, and the secondary outcomes, such as the recovery time and length of stay in the orthopedic emergency department, were assessed and compared with propofol. A total of 145 patients with distal radius fractures presented to the emergency department during the study period. Seventy-five patients met our inclusion criteria. Fifty patients had a fracture reduction with methoxyflurane, while twenty patients received propofol. The median recovery time and reduction duration were 30 min and 65.5 min, respectively, resulting in a shorter period for the methoxyflurane group. Methoxyflurane was successfully used in 48 of the 82 patients undergoing Frykman type I and type II distal radius fracture reduction while improving the recovery time due to its easy self-delivery and rapid effectiveness in the patient, as well as being able to estimate the level of pain so that the amount of anesthetic needed can be estimated and adverse effects avoided. Methoxyflurane represents a great candidate for surgical interventions like the reduction in distal radius fractures.

Keywords: anesthetic; methoxyflurane; fracture; distal radius; orthopedic emergencies

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1. Introduction

The forearm is a complex anatomical structure that plays a critical role in the function of the upper extremity as the dexterity of the upper extremity depends on the combination of the hand, wrist, and forearm to perform rotation (pronosupination) [1,2].

The distal radius is one of the largest bones that make up the forearm, and it is the structure that most frequently presents fractures, affecting young patients who experience high-velocity trauma, as well as older adults subject to lower-energy injuries because of

the physiological and pathophysiological mechanisms related to age [2]. Additionally, sex, Caucasian race, obesity, diagnosis of osteoporosis, and frequent falls represent the compensatory factors [3].

Orthopedic emergencies most of the time require outpatient surgical interventions, and in these cases anesthetics that have limitations are used [1].

Methoxyflurane is an anesthetic introduced in 1960 by Abbott Laboratories. This anesthetic is mainly used for the management of pain associated with trauma for medical procedures in children and adults. Its easy administration (inhaled) makes it a great alternative to treat this type of emergency, being an anesthetic used in much of the world [4–9].

Particularly, methoxyflurane in surgical procedures and obstetrics is indicated for minor pain relief. Among its benefits, cardiac stability and analgesia over time stand out, which is extended in the postoperative period with subanesthetic doses. Its effect is produced by the addition of methyl alcohol to fluoroethylene, which is why it was described as the first "modern" halogenated ether. It is known that the adverse events reported with the use of methoxyflurane are usually brief and self-limited, without clinically significant effects [1].

In Mexico, the Federal Commission for the Protection from Sanitary Risks (COFEPRIS) authorizes its use in patients over 12 years of age for the treatment of acute or moderate pain secondary to trauma, for conscious sedation in brief surgical procedures, dressing changes, and the treatment of dislocations and fractures [10]. As this medication is administered to conscious people, the patients can self-assess their pain level, controlling the necessary amount administered [3].

The study aimed to evaluate the success rate of methoxyflurane in distal radius fracture reductions against propofol in the orthopedic emergency department.

2. Materials and Methods

2.1. Study Population

A retrospective and observational study was conducted from December 2021 to January 2023 in the orthopedic emergency department of Hospital Regional de Alta Especialidad de Ixtapaluca, Mexico.

2.2. Inclusion Criteria

- Patients over 18 years;
- Patients diagnosed with Frykman type I and type II distal radius fractures;
- Patients requiring closed reduction, using inhaled methoxyflurane versus propofol.

2.3. Exclusion Criteria

- Patients with Frykman types III, IV, V, VI, VII, and VIII fractures;
- Open fractures, polytraumatized patients, and patients with previous sedation or using advanced airways.

2.4. Evaluation of Propofol

All patients admitted to the orthopedic emergency department were kept under observation by an orthopedic attending physician and under the supervision of the nursing staff in charge. Patients who underwent propofol sedation had placed nasal cannulas at a rate of 3 L per minute and were monitored.

2.5. Evaluation of Methoxyflurane

Patients using methoxyflurane were kept at the orthopedic emergency department under the surveillance of resident doctors and attending physicians. Two fracture reduction attempts were granted, and each treating physician on duty performed the reduction technique with which they were most comfortable. The application of the anesthetic was carried out through two inhalations. If the result was unsatisfactory in patients treated

with propofol, more doses were administered than initially requested. Finally, patients were admitted to the hospital for surgical treatment in case of a negative result.

2.6. Functionality Evaluation

To evaluate the patient's evolution, the Visual Analog Scale (VAS) for pain was used. This tool allows us to measure the intensity of the pain described by the patient by means of a 10 cm horizontal line, which at its ends are the extreme expressions of a symptom.

The patient is asked to mark on the line the point that indicates the intensity of the pain, and it is measured with a millimeter tool (ruler), expressing the intensity in centimeters or millimeters.

The valuation is obtained from the following:

Mild pain if the patient rates the pain as less than 3;

Moderate pain if the rating is between 4 and 7;

Severe pain if the rating is equal to or greater than 8.

2.7. Statistical Analysis

Information such as age, gender, date of injury, and other characteristics such as mechanism of injury, classification of injury, and analgesia/sedation used were collected. Additionally, the secondary results of the two groups of patients, to whom propofol or methoxyflurane was administered, were collected and contingency tables were created, which were analyzed to determine if there was a difference in fracture reduction in terms of pain. Statistical significance was considered $p < 0.05$ with a 95% confidence level.

3. Results

3.1. Study Population

A total of 145 patients with distal radius fractures were treated by the orthopedic emergency service. Regarding sex, 72.2% were women (n = 39) and the rest were men (n = 15/27.8%). According to the analyzed data, the age range presented in the patients included in the study had a mean of 47.11 years, with a maximum of 58 years and a minimum of 23 years.

Of the total study population, it was identified that the most common diagnosis was Frykman type II left distal radius fracture at 47%, followed by Frykman type II right distal radius fracture at 23% and right distal radius fracture at 20%. Figure 1 shows the diagnoses expressed in percentages.

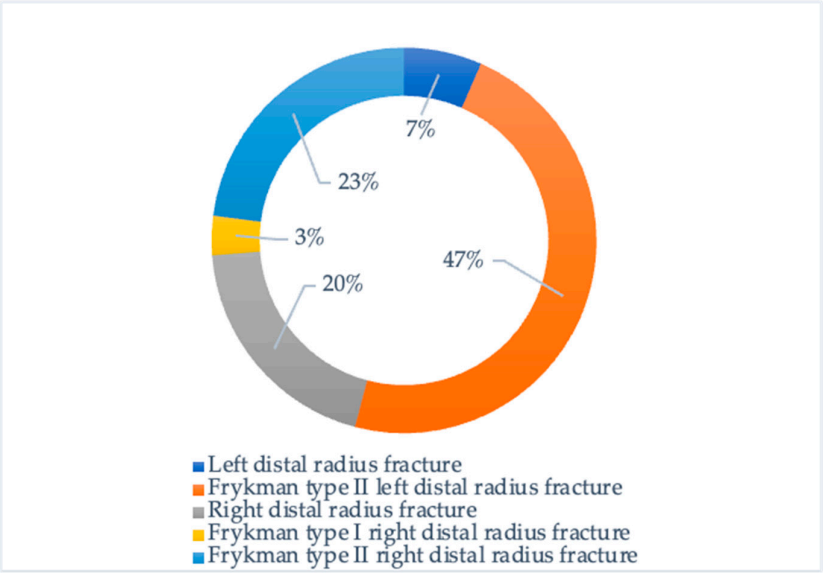

Figure 1. Diagnoses presented in patients with distal radius fractures in the orthopedic emergency department.

The patients who comprised the group that was administered methoxyflurane had the following characteristics: half of the population was composed of patients between 46 and 58 years old, followed by those 36–45 years old and 23–35 years old. In this population, more than half was composed of women (70%). Frykman II fractures (72%) were those with the highest incidence compared to Frykman I. Finally, fracture reduction occurred in 76% (Table 1).

Table 1. Characteristics of patients sedated with methoxyflurane.

Variable		Percentage
Age	23–35 years	6%
	36–45 years	44%
	46–58 years	50%
Sex	Man	30%
	Women	70%
Fracture classification	Frykman I	28%
	Frykman II	72%
Fracture reduction	Si	76%
	No	24%

3.2. Evaluation of Methoxyflurane vs. Propofol

Of the 145 patients who were admitted to the emergency department for a distal radius fracture, 50 demonstrated a reduction in said fracture by methoxyflurane, while 20 patients received propofol. Of these, the group that received propofol presented a greater reduction in fractures without pain compared to a smaller number of patients who did present pain. On the other hand, the group of patients that received methoxyflurane reduced the fractures without pain more than two times compared to the group that received propofol without pain (Figure 2).

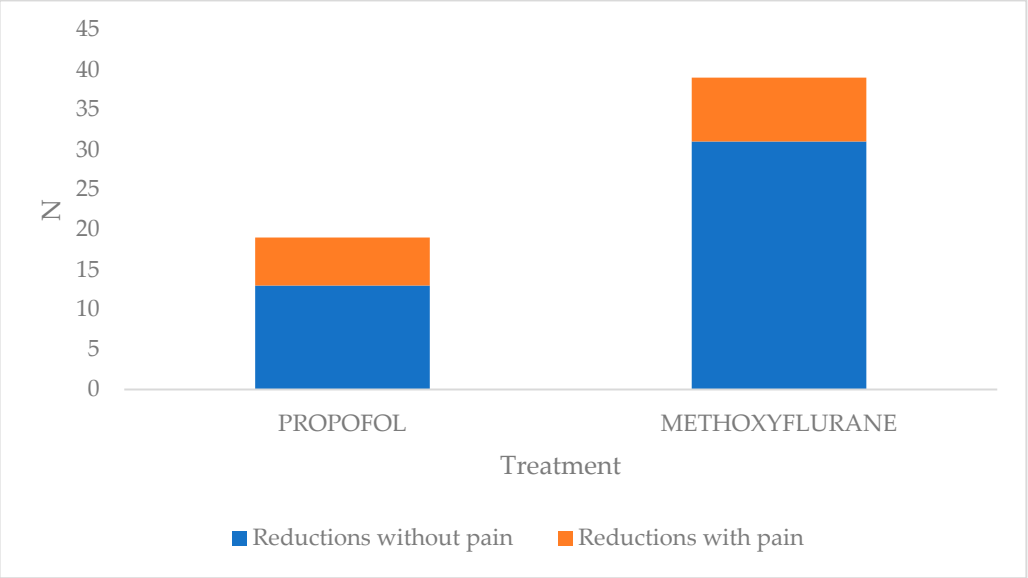

Figure 2. Percentage of patients treated with anesthetic drugs for pain control in distal fracture reductions.

Contingency analyses were performed to determine if there was a difference in the fracture reduction in terms of pain, and both drugs demonstrated adequate pain control, with a Chi2 of $p = 0.355$ (Figure 3). Regarding the type of fracture, the statistical analysis revealed a difference between the type of fracture and the reduction, with a Chi2 of $p < 0.001$. In this respect, it was found that, in some patients with Frykman type II right and left distal

fractures, the reduction was not favorable and pain presented. However, 80% of the cases were successful in both anesthetics.

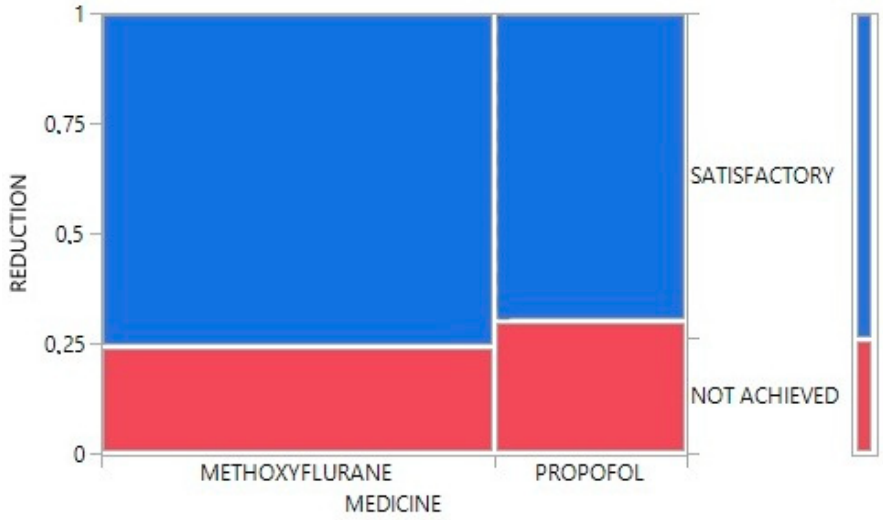

Figure 3. Contingency table of the anesthetic used and the pain reduction in the study groups.

3.3. Functionality Evaluation

Based on the results obtained through the VAS scale, the total population to which methoxyflurane was administered presented a VAS value of 2–3; that is, the patients in this group reported mild pain. Meanwhile, the group that underwent surgery for distal radius reduction using propofol as an analgesic reported mild pain (0).

3.4. Adverse Events

In the present work, the success rate of methoxyflurane in reducing distal radius fractures was analyzed in comparison with propofol. Indeed, 100% of the patients who received propofol had CNS depression as an adverse effect, drowsiness, while 36% of the group that was administered methoxyflurane presented nausea (14%), headache (10%), vertigo (8%), and drowsiness (4%) as adverse effects.

4. Discussion

In the present work, a population of patients who presented distal radius fractures was selected according to the study selection criteria. The success rate of methoxyflurane in reducing distal radius fractures was identified with respect to propofol. Two groups were formed; one group was administered methoxyflurane via inhalation and the other group was administered propofol intravenously. The population was evaluated using the VAS scale to determine the presented reduction in terms of pain. When evaluating the results, both anesthetics presented good results; however, methoxyflurane reduced the distal radius fractures to a greater degree. Therefore, methoxyflurane represented an alternative anesthetic for this type of intervention since the method of administration made it possible to evaluate the pain experienced by the patient, as well as to calculate the necessary dose and avoid complications due to major adverse effects.

Of the two anesthetics used, methoxyflurane was administered inhalationally. It is known that the pharmacological action of inhalational anesthetics depends on their physical and chemical properties, which is mainly due to their liposolubility in such a way that there will be variations in patients with obesity since they will retain the drug for a longer time. In the case of methoxyflurane, 30% is covalently absorbed into the tissue, 29% is found in uresis, and 15% is deposited in bone matter [2,11]. In the present work, a percentage of the population had diabetes, so the success rate of methoxyflurane could be influenced.

In a randomized controlled trial of patients over 12 years of age with acute traumatic pain, it was concluded that methoxyflurane resulted in a significantly greater reduction in

pain than a placebo. These results agree with the obtained results since methoxyflurane significantly reduced the distal radius fractures compared to propofol. It was also observed that about 80% of the patients obtained pain relief with ten inhalations over the course of 4 min, while the placebo took 10 min [10]. In another study by [1], the authors reported that methoxyflurane provided a clinically important benefit, with an improvement in the mean difference in change from the baseline in pain intensity (from −0.44 to −1.23 cm, $p < 0.001$). This result was achieved within the first 20 min compared to the control. Furthermore, this anesthetic decreased the onset time of the pain relief. Those results are like the ones obtained in the present study, where a success rate of 80% was obtained in the studied population, significantly reducing the pain by an average of two inhalations per hour of fracture reduction and thus achieving a favorable conservative treatment.

Regarding the evaluation of functionality, in the present study, the VAS scale was implemented. In the group that was administered methoxyflurane, they had an index of less than 3, which is interpreted as an average pain scale. According to a study in which inhaled methoxyflurane and intranasal fentanyl for prehospital management were compared by [12], methoxyflurane produced the greatest reduction regarding the initial pain scale with a 95% confidence interval.

After methoxyflurane administration, adverse results are rare. However, the most common adverse event reported is mild central nervous system depression, which usually presents as drowsiness, headache, vertigo, nausea, and vomiting. Therefore, the drug is contraindicated in patients with altered states of consciousness, traumatic brain injury, patients with a history of drug addiction, cardiovascular instability, clinically evident respiratory depression, renal failure, and liver damage [11]. In the present work, the group that was administered methoxyflurane presented adverse events including vertigo, nausea, and headache, which are typical for this anesthetic [10,12]. However, as in other studies, the benefits of almost all the secondary outcomes with pain did not represent clinical significance.

Unfortunately, the toxic effects of the anesthetics used could not be estimated. However, to date, no evidence of hepatotoxicity or nephrotoxicity with methoxyflurane for analgesia has emerged from the clinical trial data. However, the duration of followup is limited, and the number of hepatic and renal events reported in routine pharmacovigilance is too small to draw reliable conclusions. However, a retrospective comparative observational study with a followup of up to 14 years did not show an increased risk of liver or kidney disease in patients who received methoxyflurane as a low-dose analgesic [13,14]. The low concentrations at which it is administered usually keep the patients conscious and rarely require airway manipulation, unlike deep intravenous sedation [13–15]. These are the doses administered to the group whose fractures were reduced with this anesthetic without the presence of pain.

It is worth mentioning that oxalic acid crystals in renal biopsy samples and increased urinary excretion of oxalic acid have been observed after using methoxyflurane in several patients with postoperative renal failure. This evidence shows that the renal toxicity is possibly due to the metabolism of methoxyflurane and the release of the fluoride ions produced by the O-demethylation of methoxyflurane [10,16,17].

Regarding the drug action, methoxyflurane presents advantages in this application. The aerosolized form used to administer the drug for inhalation is especially beneficial in terms of the pharmacokinetic profile. Propofol also has a favorable pharmacokinetic profile and efficacy in producing anesthesia and sedation [18,19]. However, its use requires careful titration and monitoring to minimize the risk of adverse effects. The most reported adverse effects include respiratory depression, hypotension, pain at the injection site, nausea and vomiting, headache, allergic reactions, confounding by indication, and propofol-related infusion syndrome (PRIS), which in rare cases at high doses can trigger metabolic acidosis, rhabdomyolysis, heart failure, and other life-threatening symptoms [20,21].

Among the limitations of our study is the small number of patients included, so the detailed analysis of the characteristics of the study groups may be affected. In this

sense, the small number of patients may cause bias when methoxyflurane is used in an insufficiently diverse population. However, the promising results highlight the efficacy of methoxyflurane as an excellent alternative for reducing distal radius fractures in orthopedic emergencies. It is also essential to conduct studies with a longer followup time, which will allow us to identify other adverse reactions and evaluate other opportunities for using methoxyflurane.

From what was obtained, we can highlight that, as a practical implication, methoxyflurane can be implemented to reduce distal radius fractures successfully and without pain in patients over 18 years of age. Therefore, we suggest the integration of this anesthetic into treatments in an orthopedic emergency context.

5. Conclusions

In the present study, the success rate of methoxyflurane against propofol in reducing distal radius fractures was evaluated. Methoxyflurane reduced these fractures superiorly compared to propofol, particularly in the group with Frykman I type distal radius fractures.

From the contingency analysis, methoxyflurane achieved a reduction in the distal radius fractures in terms of pain. Meanwhile, through the evaluation by the VAS scale, it was determined that, in the group that was administered methoxyflurane, there was a reduction in pain.

Finally, among the adverse events identified were nausea, headache, vertigo, and dizziness, without clinical significance, for the group. The anesthetic was methoxyflurane.

Due to its easy self-delivery and rapid effectiveness in the patient, methoxyflurane represents a great candidate for surgical interventions of this type. In addition, it offers the ability to assess pain, enabling an adequate supply of the medication and thus avoiding side effects in the patient. The adverse effects identified were mild, such as dizziness and headache, and were successfully resolved.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Data are contained within the article.

Conflicts of Interest: The authors declare no conflicts of interest.

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