



The Efficacy of Inhaled Methoxyflurane Versus Intravenous Sedation for the Reduction of Acute Shoulder Dislocation

Chavalit Iemsaengchairat, MD

Department of Orthopedics, Nakhonpathom Hospital, Nakhonpathom, Thailand

Purpose: Anterior shoulder dislocation is one of the most common emergency orthopedic conditions. In general practice, intravenous sedation is the standard treatment to relax patients during shoulder reduction procedures. Sedatives and analgesics are drugs that have side effects after administration, especially when administered intravenously. They can depress neurological function and cause respiratory and cardiovascular system side effects. Self-inhaled methoxyflurane relieves moderate to severe pain. Hospitals may benefit from minimized respiratory and cardiovascular side effects.

Methods: This randomized controlled trial included 50 patients who were randomly assigned to two groups: the inhaled methoxyflurane group (Inh Group) and the intravenous sedation group (IV Group). All patients were assessed for efficacy, procedure duration, pain score during reduction, patient satisfaction, and adverse effects.

Results: Fifty patients satisfied the inclusion requirement: 25 each in the Inh and IV Groups. Reduction was successfully achieved in 92% and 88% of the patients in the Inh and IV Group, respectively. The mean procedural time was 6.4 min and 15.4 min the Inh and IV Group, respectively. Moreover, the mean recovery time was 22.5 min in the Inh Group and 32.4 min in the IV Group.

Conclusions: Inhaled methoxyflurane has better efficacy in reducing acute shoulder dislocation than intravenous sedation alone. Procedural and recovery times were shorter in the Inh Group. Adverse events (hemodynamic instability, desaturation, nausea, vomiting, drowsiness, and dizziness) were more frequent in the IV Group than in the Inh Group.

Keywords: inhaled methoxyflurane, intravenous sedation, acute shoulder dislocation, shoulder reduction

Anterior shoulder dislocation is one of the most common orthopedic emergency conditions caused by sports injuries or road traffic accidents.

Article history:

Received: January 6, 2024 Revised: June 8, 2024

Accepted: July 15, 2024

Correspondence to: Chavalit Iemsaengchairat, MD

Department of Orthopedics, Nakhonpathom Hospital,
Nakhonpathom, Thailand

E-mail: st_bank@hotmail.com

Patients with traumatic shoulder dislocation present with a gross deformity, limited movement, and severe pain. Physical examination of the shoulder shows abduction and external rotation, flattening of the deltoid muscle contours, and a limited range of motion. Patients are unable to touch the opposite shoulder by crossing an arm in front of the body. This pathognomonic sign is referred to as the Dugar method. Associated injuries include axillary nerve palsy. In suspected cases, shoulder radiography is required to confirm diagnosis.

In general practice, intravenous sedation is the standard treatment to relax patients during shoulder reduction procedures⁽¹⁾. Healthcare professionals must perform intravenous cannulation before administering sedatives. Moderate to deep safety protocols require close monitoring by medical staff. Sedatives and analgesics are drugs that have side effects after administration, particularly when administered intravenously. They can depress neurological function and cause respiratory and cardiovascular system side effects.

With the introduction of methoxyflurane, the treatment method has completely changed from intravenous cannulation to self-inhaled administration. This method has been widely used in Singapore and Australia for procedures such as endoscopic gastroscopy and in prehospital settings⁽²⁾. Self-inhaled methoxyflurane relieves moderate to severe pain. Hospitals may benefit from the associated minimized respiratory and cardiovascular side effects. Moreover, the workload can be reduced by changing the procedure to provide more patient-controlled analgesia. With this technique, patients recover faster than with intravenous sedation. Although inhaled methoxyflurane can cause central nervous system depression, sedation, hypopnea, and desaturation, the effects last no longer than 25-30 min⁽³⁾. Notably, inhaled methoxyflurane has already been approved by the Food and Drug Administration of Thailand; however, its research and usage are still relatively limited. One bottle contains 3 mL methoxyflurane for vaporization. The maximum recommended dosage is 6 mL of methoxyflurane per day and 15 mL per week.

This study primarily aimed to assess the efficacy of inhaled methoxyflurane compared with intravenous sedation in reducing acute shoulder dislocation. Secondary objectives were the duration of the procedure, pain score during reduction, patient satisfaction, and side effects.

METHODS

Study Design: A Randomized Controlled Trial

Design Flow Description

This randomized controlled trial included patients with acute shoulder dislocation admitted

to the emergency room of our hospital between November 2021 and December 2023. The inclusion criteria were as follows: (1) traumatic anterior shoulder dislocation; (2) age 18-60 years; and (3) communication in Thai. The exclusion criteria were as follows: (1) recurrent shoulder dislocation; (2) history of methoxyflurane, Morphine, or Midazolam allergy; (3) history of contraindications for methoxyflurane; and (4) multiple organ trauma.

The study design was modified to actively exclude and control confounding variables, including randomization and restrictions. Randomization was performed using a block of four created by the principal investigator. Patient age and exclusion criteria (recurrent shoulder dislocation and multiple organ trauma) were used to restrict the confounding variables. In addition, patient characteristics were analyzed to identify differences. The data were analyzed using a regression model if there were differences.

This study was approved by the local research ethics committee (number 032-2021). All the enrolled participants provided written informed consent.

A total of 145 patients presented to the emergency department with an acute shoulder dislocation. Ninety-five patients with recurrent shoulder dislocations or an associated fracture were excluded from the study. Finally, 50 patients were included in this study, and they were randomly assigned into two groups, as shown in Fig 1: the inhaled methoxyflurane group (Inh Group) and the intravenous sedation group (IV Group). Randomization was performed using a block of four created by the principal investigator.

Patients in the Inh Group were treated with inhaled 3 mL of inhaled methoxyflurane (patients were instructed to inhale intermittently for approximately 6-10 inhalations to achieve adequate analgesia). Patients in the IV Group received midazolam 0.05 mg/kg and morphine 0.05 mg/kg. After patients have received inhaled methoxyflurane or intravenous sedation, the dislocated shoulder was reduced using traction and counter-traction techniques by an orthopedic physician. In both Inh and IV Groups, success was confirmed using shoulder radiography. Simultaneously, we

recorded the duration of the procedure, pain score during the reduction, patient satisfaction score (measured using patient satisfaction surveys that enabled patients to rate how happy they were with the investigator on a 1-10 rating scale), and the side effects on the nurse. Vital signs of patients with hypotension were monitored until hemodynamic stabilization was achieved. Patients with oxygen desaturation received oxygen cannula support until they were able to tape off. Medications were

not administered for nausea, vomiting, drowsiness, or dizziness, since they are short-term side effects. A patient was diagnosed as having failed shoulder reduction if the patient was unable to succeed within 30 min after infusion of Inh methoxyflurane or IV sedation or if the patient was unable to tolerate pain during shoulder reduction. Patients with unsuccessful reduction underwent closed reduction under general anesthesia.

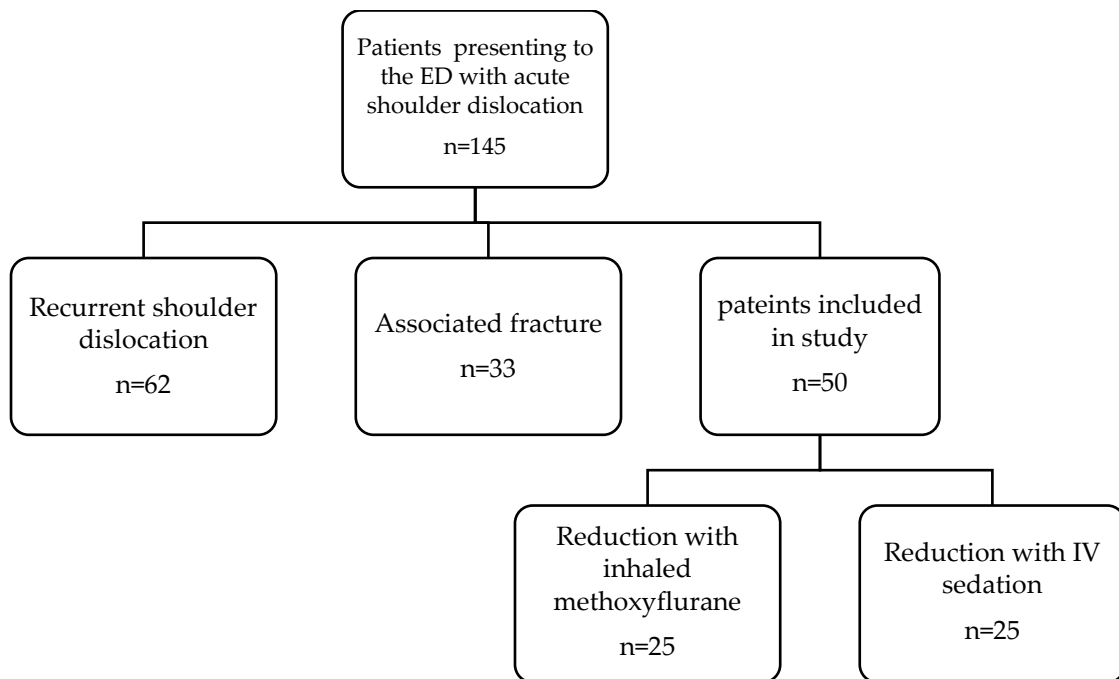


Fig. 1 Flow diagram.

Statistical Analysis

The required sample size was calculated by a binary outcome non-inferiority trial to be 22 in each group when $\alpha = 0.05$ and $\beta = 0.3$, for a ratio of effectiveness of 0.846 in Inh Group and 0.865 in IV Group with a non-inferiority limit (d) of 25%. Assuming a complication rate of 90%, the sample size was determined to be 25 in each group^(6,13). Intention-to-treat and pre-protocol analyses were also performed. Shoulder reduction success was compared between the groups using the chi-square test. Other outcomes were calculated with the t-tests. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 50 patients satisfied the inclusion requirement: 25 in the Inh Group and 25 in the IV Group. Participants' mean age was 42.4 and 37.9 years in the Inh and IV Groups, respectively. Table 1 shows patient characteristics and associated variables for both groups.

Inh Group

Successful reduction was achieved in 92% of the patients who received inhaled methoxyflurane. The mean procedural and recovery times were 6.4 min (SD: 3.17) and 22.5 min (SD: 6.28),

respectively. The most common adverse events were dizziness (8.7%) and drowsiness (13.0%).

IV Group

Successful reduction was achieved in 88% of patients who were administered intravenous sedation. The mean procedural and recovery times were 15.4 min (SD: 1.37) and 32.4 minutes (SD 8.27), respectively. Adverse events included dizziness (50%) and drowsiness (54.5%).

The procedural and recovery times were significantly reduced in the Inh Group. Adverse events (hemodynamic instability, desaturation, nausea, vomiting, drowsiness, and dizziness) were significantly more frequent in the IV Group than in the Inh Group. Patient satisfaction was better in the Inh Group (9.65) than in the IV Group (9.31); however, the difference was not statistically significant.

Table 1 Patient characteristics.

Patient characteristics	Inhaled methoxyflurane group	Intravenous sedation group	P-value
Patient (N)	25	25	
Sex (male/female)	17/8	14/11	0.22
Side (right/left)	16/9	15/10	0.68
Dominant side	68%	64%	0.67

Table 2 Study outcome.

Results	Inhaled methoxyflurane group	Intravenous sedation group	P-value
Success rate	23/25 (92%)	22/25 (88%)	0.54
Procedural time	6.4 (3.17)	15.4 (1.37)	<0.01
Recovery time	22.5 (6.28)	32.4 (8.27)	<0.01
VAS score			
Pre-med	9.92 (0.4)	9.76 (0.66)	0.30
At 3 min	2.92 (0.91)	2.8 (0.91)	0.64
At 5 min	2.36 (0.64)	2.48 (0.77)	0.55
Post reduction	1.21 (0.67)	1.27 (0.63)	0.78
Pre discharge	1.13 (0.69)	1 (0.69)	0.53
Patient satisfaction scores	9.65 (0.71)	9.31 (0.94)	0.19
Side effects			
Hemodynamic unstable	0	6/22 (27.27)	<0.01
Desaturation	0	6/22 (27.27)	<0.01
Nausea	0	6/22 (27.27)	<0.01
Vomiting	0	6/22 (27.27)	<0.01
Drowsiness	3/23 (13%)	12/22 (54.54)	<0.01
Coughing	0	0	NA
Dizziness	2/23 (8.7%)	11/22 (50)	<0.01
Amnesia	0	0	NA
Fever	0	0	NA

DISCUSSION

Although statistically significant, our randomized controlled trial showed a better efficacy for inhaled methoxyflurane than intravenous sedation in reducing acute shoulder dislocation. Regarding secondary outcomes, the procedure duration and recovery time were better in the Inh Group. Adverse events (hemodynamic instability, desaturation, nausea, vomiting, drowsiness, and dizziness) were more frequent in the IV Group than in the Inh Group. However, the study did not include blinding, which may have biased the results.

When compared with previous reports that were retrospective reviews and case series, we found the same results as those reported by the Young L study: methoxyflurane can be used to reduce acute anterior shoulder dislocation with the same efficacy as the gold standard technique. Adverse events (hemodynamic instability, desaturation, nausea, vomiting, drowsiness, and dizziness) were more frequent in the IV Group than in the Inh Group, similar to the results of the Mir-Kohler study. However, the current cost of inhaled methoxyflurane is more than five times higher than that of intravenous sedation.

Although, inhaled methoxyflurane is approximately five times more expensive than traditional intravenous sedation, it requires fewer health care providers because it does not require nurses or nursing assistants for intravenous drug administration or drug preparations like traditional intravenous sedation.

This study has some limitations. First, the study population had a first-time shoulder dislocation; however, in a real situation in the emergency department, we found that half of the patients had recurrent dislocations. Second, patients with associated fractures were excluded; however, in real-life situations, shoulder fracture-dislocation requires reduction. Another limitation of this study is the mean recovery time, which was superior in the Inh Group, approximately 9.9 min when compared with the IV Group. This difference may have been due to adverse events; therefore, the patient was not discharged.

Our study showed statistically significant adverse events in the IV Group compared to the Inh

Group. Since the adverse events of analgesic and sedative drugs were dose-related, we administered the medications to patients in the IV Group as a single dose. Therefore, adverse events may decrease if the dosage of IV sedation is separated into sedative and visual analog scale scores.

For future research, the inclusion criteria should be expanded to include all directions of shoulder dislocation, fracture-dislocation of the shoulder that needs to be reduced, and young and older age patient groups. Future studies may require two doctors to conduct blinding studies to minimize bias, with the first doctor selecting a group and administering medication and another doctor performing the shoulder reduction. Cost-benefit analysis is a good project that provides a clearer picture of economic implications. Future research also needs to repeat intravenous sedation until the maximum dosage is reached to assess the patient's hemodynamic stability and sedation score. Finally, patients should be monitored for a long time for factors that may occur, such as the rate of recurrent shoulder dislocation or long-term side effects of medications.

CONCLUSIONS

The efficacy of self-inhaled methoxyflurane in reducing acute shoulder dislocation was better than that of intravenous sedation; however, the difference was not statistically significant. The procedure duration and recovery time were shorter in the Inh Group. Fewer adverse events (hemodynamic instability, desaturation, nausea, vomiting, drowsiness, and dizziness) were observed in the Inh Group.

REFERENCES

1. Azar FM, Canale ST and Beaty JH (eds). *Campbell's Operative Orthopaedics*. 14th ed. Philadelphia: Elsevier; 2020.
2. Nguyen NQ, Toscano L, Lawrence M, et al. Portable inhaled methoxyflurane is feasible and safe for colonoscopy in subjects with morbid obesity and/or obstructive sleep apnea. *Endosc Int Open* 2015;3:E487-93.

3. Umana E, Kelliher JH, Blom CJ, et al. Inhaled methoxyflurane for the reduction of acute anterior shoulder dislocation in the emergency department. *CJEM* 2019;21:468-72.
4. Young L, Bailey GP, McKinlay JAC. Service evaluation of methoxyflurane versus standard care for overall management of patients with pain due to injury. *Adv Ther* 2020;37:2520-7.
5. Mir-Kohler, C. Lojo Rial, S. Suresh, R. Ferguson; L. Hunter. Impact of Methoxyflurane in shoulder dislocations on patient care and crowding – Can the green whistle improve our care and our flow?. EUSEM presentation 2019 [abstract].
6. Ho SF, Ganti S, Omar E, et al. Comparison of inhaled methoxyflurane versus procedural sedation for manipulation and reduction of acute shoulder and elbow dislocation in the emergency department. *Proc Singap Healthc* 2022;31:1-6.
7. Campbell S, Wiemer H, Fitzpatrick R, et al. A pilot study of inhaled low-dose methoxyflurane to support cunningham reduction of anterior shoulder dislocation. *Eurasian J Emerg Med* 2022;21:242-5.
8. Ferguson R, Faulkner J, Hunter L. Methoxyflurane is effective and time-saving in the management of shoulder dislocation in the Emergency Department. *GSTT A&E Shoulder Dislocation Audit*. Proceeding for the Scottish Emergency Medicine Clinical Conference; 2019 May 14; Glasgow, Scotland.
9. Forrest M, Porter K, Velde JVD. Methoxyflurane (Penthrox®)—a case series of use in the prehospital setting. *J Paramed Pract* 2019;11;54-60.
10. Adewusi M, Richards O, Hickey B, et al. 900 an audit of effectiveness of inhaled methoxyflurane (Penthrox) use for reduction of shoulder dislocation. *Br J Surg* 2021:108.
11. Fabbri A, Ruggiano G, Collado SG, et al. Role of inhaled methoxyflurane in the management of acute trauma pain. *J Pain Res* 2020;13:1547-55.
12. Hasebroock AW, Brinkman J, Foster L, et al. Management of primary anterior shoulder dislocations: a narrative review. *Sports Med Open* 2019;5:31.
13. Blackwelder WC. "Proving the null hypothesis" in clinical trials. *Control Clin Trials* 1982;3:345-53.