Efficacy and Safety of Methoxyflurane for Treatment of Acute Traumatic Pain by EMTs during Alpine Rescue Operations: The "PainDrop" Trial

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Backround

Treatment of acute traumatic pain is a core task for mountain rescue services. Intravenous access, however, is often difficult, and the vast majority of missions are carried out without a physician at the scene. The spectrum of analgesics available for use by non-physician personnel is limited. Inhaled analgesics, such as methoxyflurane, might prove useful, but currently no data exist on their application by non-physicians in the alpine setting.

Methods

Prospective observational alpine field study. Over a period of 15 months, patients suffering traumatic injury and moderate to severe pain (pain score ≥ 5) after downhill bike accidents in the Tyrol mountains (1,362m to 2,666m above sea level) were enrolled. Teams of four mountain rescue service members, one of them a trained EMT, treated the patients with 3ml of methoxyflurane by inhaler. We measured efficacy as reduction in pain from baseline to 15 minutes after treatment on a numerical rating scale. Safety was assessed by change in vital signs or occurrence of side-effects. Sample-size calculations were based on the efficacy-outcome and yielded a need for 20 patients at a power of 0.8.

Abb. 1: Inhalator Device Methoxyfluran (Quelle: Hersteller)

Results

From June 29, 2020 to September 30, 2021, a total of 20 patients (two females, mean age 37 years) were included. The mean age of the patients was 37 years (range 18-51 years). The most common indication for pain therapy was shoulder injury (n = 11, 55%), followed by injury of the forearm (n = 4, 20%), and injury of the chest (n = 3, 15%). The mean time from emergency call to arrival on-scene was 13min (range 1 – 23 min). The mean sea level of the emergency locations was 1,910m (SD 278m), and the mean ambient temperature was 16°C (SD 4°C).

Initial NRS pain scale was 7.2 (SD 1.0) points. Reduction in NRS pain scores within 15mins, the primary efficacy outcome, was significant by 2.9 points (95% CI 2.2 to 3.6; SD 1.4; p<0.001). Age, BMI, sex, region of injury, and initial pain score had no significant influence on this effect. Regarding the primary safety outcome, no relevant deterioration of vital signs, and none of the pre-defined major side effects were observed. Eight patients reported light-headedness, and four reported dizziness, with no cases of respiratory depression, agitation, nausea or vomiting

Before initiation of pain therapy all patients included in the study would have required an emergency physician for treatment of pain, according to local protocol. Fifteen minutes after the start of inhalation, adequate analgesia was achieved in 13 patients (65%), whereas an emergency physician was still needed for extended analgesia in the remaining seven patients (35%). Initial NRS pain scale of those seven patients was slightly higher (7.7 points) compared to patients not needing extended analgesia later on (6.9 points).

Conclusion

This is the first study to demonstrate the efficacy and safety of pain therapy with methoxyflurane by EMTs in alpine rescue operations. EMT-guided analgesia with methoxyflurane in the moderate altitude alpine rescue setting provided appropriate reduction of pain at the same high level of safety as previously described in other settings. This approach could reduce the need for emergency physicians to provide procedural analgesia in hemodynamically stable patients with non-life threatening injuries. In some circumstances, noninvasive analgesia will be the only available option at all.

	N=20
Efficacy	
Reduction of NRS within first 15 min (mean, 95% CI)	2.9 (2.2-3.6) (p<0.001)
NRS at 0 min (mean, SD)	7.2 (1.0)
NRS at 5 min (mean, SD)	5.5 (1.5)
NRS at 10 min (mean, SD)	4.8 (1.6)
NRS at 15 min (mean, SD)	4.4 (1.9)
NRS at 20 min (mean, SD)	4.1 (1.5)
Need for further analgesia by physician (n, %)	7 (35%)
Safety	
Major side-effects (n, %)	
- Relevant change in vital signs*	0 (0%)
- malignant hyperthermia	0 (0%)
- respiratory depression	0 (0%)
- nausea	0 (0%)
- vomiting	0 (0%)
- agitation	0 (0%)
Minor side-effects (n, %)	
- dizziness	8 (40%)
- light-headedness	4 (20%)

Tab 1: Primary and secondary outcomes

References

- Pietsch U, Strapazzon G, Ambühl D, Lischke V, Rauch S, Knapp J. Challenges of helicopter mountain rescue missions by human external cargo: need for physicians onsite and comprehensive training. Scand J Trauma Resusc Emerg Med. 2019;27(1):17.
- Berben SA, Schoonhoven L, Meijs TH, van Vugt AB, van Grunsven PM. Prevalence and relief of pain in trauma patients in emergency medical services. Clin J Pain. 2011;27(7):587-92.
- Ellerton J, Tomazin I, Brugger H, Paal P. Immobilization and splinting in mountain rescue. Official Recommendations of the International Commission for Mountain Emergency Medicine, ICAR MEDCOM, Intended for Mountain Rescue First Responders, Physicians, and Rescue Organizations. High Alt Med Biol. 2009;10(4):337-42.
- Becker J, Runer A, Neunhäuserer D, Frick N, Resch H, Moroder P. A prospective study of downhill mountain biking injuries. Br J Sports Med. 2013;47(7):458-62.
- Rugg C, Woyke S, Voelckel W, Paal P, Ströhle M. Analgesia in adult trauma patients in physician-staffed Austrian helicopter rescue: a 12-year registry analysis. Scand J Trauma Resusc Emerg Med. 2021;29(1):28.
- Bredmose PP, Lockey DJ, Grier G, Watts B, Davies G. Pre-hospital use of ketamine for analgesia and procedural sedation. Emerg Med J. 2009;26(1):62-4.
- Ellerton J, Paal P, Brugger H. Prehospital use of ketamine in mountain rescue. Emerg Med J. 26. England2009. p. 760-1.
- Jennings PA, Cameron P, Bernard S, Walker T, Jolley D, Fitzgerald M, et al. Morphine and ketamine is superior to morphine alone for out-of-hospital trauma analgesia: a randomized controlled trial. Ann Emerg Med. 2012;59(6):497-503.
- Ellerton J, Milani M, Blancher M, Zen-Ruffinen G, Skaiaa SC, Brink B, et al. Managing moderate and severe pain in mountain rescue. High Alt Med Biol. 2014;15(1):8-14.
- Middleton PM, Simpson PM, Sinclair G, Dobbins TA, Math B, Bendall JC. Effectiveness of morphine, fentanyl, and methoxyflurane in the prehospital setting. Prehosp Emerg Care. 2010;14(4):439-47.
- Buntine P, Thom O, Babl F, Bailey M, Bernard S. Prehospital analgesia in adults using inhaled methoxyflurane. Emerg Med Australas. 2007;19(6):509-14.
- Porter KM, Siddiqui MK, Sharma I, Dickerson S, Eberhardt A. Management of trauma pain in the emergency setting: low-dose methoxyflurane or nitrous oxide? A systematic review and indirect treatment comparison. J Pain Res. 2018;11:11-21.
- Windsor J, van der Kaaij J, Ellerton J, Oxer H, Hillebrandt D, Rodway G. Methoxyflurane as an analgesic for prehospital use at high altitude. High Alt Med Biol. 2009;10(2):201-2.
- Jedlicka J, Groene P, Linhart J, Raith E, Mu Stapha DV, Conzen P. [Inhalational anesthetics]. Anaesthesist. 2021;70(4):343-55.Trimmel H, Egger A, Doppler R, Beywinkler C, Voelckel WG, Kreutziger J. [Volatile anesthetics for prehospital analgesia by paramedics-An overview]. Anaesthesist. 2021:1-9.
- Jephcott C, Grummet J, Nguyen N, Spruyt O. A review of the safety and efficacy of inhaled methoxyflurane as an analgesic for outpatient procedures. Br J Anaesth. 120. England: © 2018 British Journal of Anaesthesia; 2018. p. 1040-8.
- Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. Ann Rheum Dis. 1978;37(4):378-81.
- Trimmel H, Egger A, Doppler R, Pimiskern M, Voelckel WG. Usability and effectiveness of inhaled methoxyflurane for prehospital analgesia - a prospective, observational study. BMC Emerg Med. 2022;22(1):8.
- Johnston S, Wilkes GJ, Thompson JA, Ziman M, Brightwell R. Inhaled methoxyflurane and intranasal fentanyl for prehospital management of visceral pain in an Australian ambulance service. Emerg Med J. 2011;28(1):57-63.