Low dose methoxyflurane analgesia in the emergency department: a subgroup analysis of inhaler use in patients with severe acute trauma pain from the STOP! study

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BACKGROUND AND GOAL OF STUDY

- **Acute pain is a frequent complaint in the Emergency Department (ED)[1] but remains widely undertreated[2].**
- **STOP! was a randomised, double-blind, placebo-controlled study that investigated the efficacy and safety of low-dose methoxyflurane analgesia administered via a handheld inhaler (Penthrox®, 3 mL dose) for the treatment of acute pain in patients aged ≥12 years presenting to the ED with non-life-threatening trauma.**
- **Reduction in pain intensity in the first 20 minutes of treatment has previously been reported for the overall study population[3] and adult subgroup[4].**
- **The STOP! study included patients with moderate to severe pain (score of 4–7 on the 11-point Numeric Rating Scale [NRS]). We present a post hoc subgroup analysis of number of inhalations to first pain relief and inhaler use in adult and adolescent patients with severe pain (NRS=7) at baseline.**

MATERIALS AND METHODS

- A total of 300 patients were randomised at triage to receive methoxyflurane (up to 2 x 3 mL) or placebo (normal saline), both inhaled as needed from a Penthrox® inhaler. Rescue medication (paracetamol/opioids) was available immediately upon request of the patient at any time. The number of inhalations to first pain relief was recorded.
- Patients could cover the diluter hole in the mouthpiece to inhale a higher concentration of study medication if required. Whether the patient covered the diluter hole during inhalation was recorded (yes/no).
- A second inhaler was provided if requested by the patient. Whether the patient requested a second inhaler and the time between dispensing the first and second inhalers was recorded.
- To maintain the blind, a drop of methoxyflurane was placed on the outside of the primed inhalers so that the smell between active and placebo treatments was indistinguishable.
- The number of inhalations to first pain relief and patterns of inhaler use were summarised for the severe pain subgroup.

RESULTS AND DISCUSSION

Patient Characteristics

- The severe pain subgroup included:
  - 62 methoxyflurane-treated patients; 65% male:35% female; mean age 29 years
  - 71 placebo-treated patients; 52% male:48% female; mean age 30 years
- A summary of injury type and site is presented in *Table 1*. Most patients had injuries involving the limbs and categorised as “other” (predominantly sprains, soft tissue injury and muscular pain).

Table 1. *Injury Details (Severe Pain Subgroup)*

NUMBER (%) OF PATIENTS		METHOXYFLURANE (N=62)	PLACEBO (N=71)	TOTAL (N=133)
Injury site	Back	2 (3.2)	3 (4.2)	5 (3.8)
	Chest	3 (4.8)	0	3 (2.3)
	Face	1 (1.6)	0	1 (0.8)
	Left lower limb	12 (19.4)	19 (26.8)	31 (23.3)
	Left upper limb	9 (14.5)	8 (11.3)	17 (12.8)
	Other	6 (9.7)	1 (1.4)	7 (5.3)
	Right lower limb	15 (24.2)	25 (35.2)	40 (30.1)
	Right upper limb	14 (22.6)	15 (21.1)	29 (21.8)
Injury type*	Burn	0	3 (4.2)	3 (2.3)
	Contusion	16 (25.8)	15 (21.1)	31 (23.3)
	Dislocation	0	2 (2.8)	2 (1.5)
	Fracture	15 (24.2)	10 (14.1)	25 (18.8)
	Injury due to foreign body	2 (3.2)	0	2 (1.5)
	Laceration	2 (3.2)	3 (4.2)	5 (3.8)
	Other†	27 (43.5)	38 (53.5)	65 (48.9)

Seven patients had more than one injury. Second injuries included contusions (3 Placebo patients, 1 Methoxyflurane patient) and “other” (2 Placebo patients, 1 Methoxyflurane patient). Third injuries included contusion (1 Placebo patient) and “other” (1 Methoxyflurane patient).

Pain Relief

- Pain relief was experienced within 1-5 inhalations for 32/62 patients (51.6%) in the methoxyflurane group and 15/71 patients (21.1%) in the placebo group *(Figure 1)*.

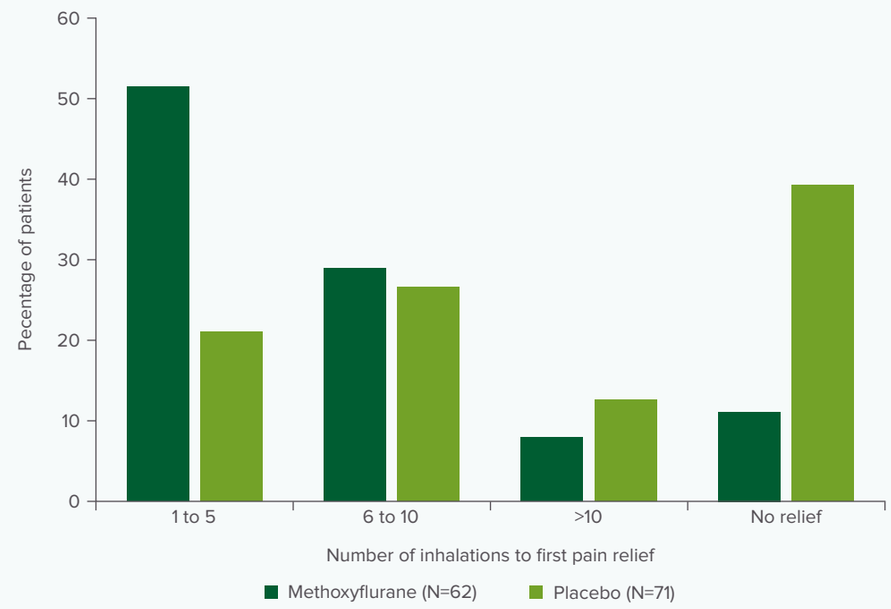

Figure 1. *Number of Inhalations to First Pain Relief (Severe Pain Subgroup)*

- Pain relief was experienced within 1-10 inhalations for 50/62 patients (80.6%) in the methoxyflurane group and 34/71 patients (47.9%) in the placebo group.
- Seven patients (11.3%) in the methoxyflurane group and 28 patients (39.4%) in the placebo group did not experience any pain relief without rescue medication.

Inhaler Use

- Sixteen patients (25.8%) in the methoxyflurane group and 12 patients (16.9%) in the placebo group requested a second inhaler *(Figure 2)*.

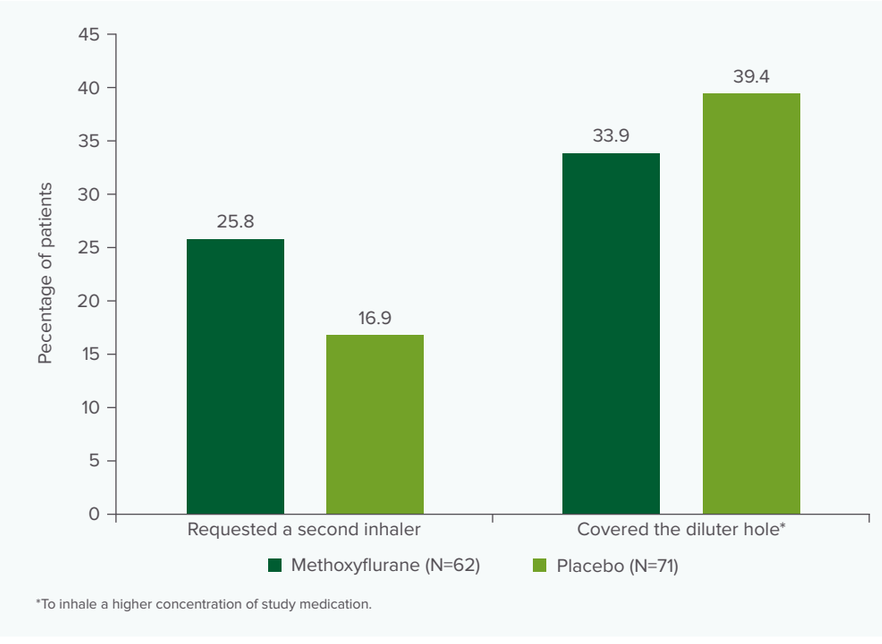

Figure 2. *Inhaler Use (Severe Pain Subgroup)*

- Median time between dispensing of the first and second inhalers was 55.0 minutes (range: 35 to 120 minutes) for methoxyflurane and 37.5 minutes (range: 10 to 63 minutes) for placebo.
- Twenty-one patients (33.9%) in the methoxyflurane group and 28 patients (39.4%) in the placebo group covered the diluter hole to inhale a higher concentration of study medication *(Figure 2)*.

CONCLUSION

- Low-dose methoxyflurane was shown to provide rapid-acting analgesia within 1–10 inhalations in the majority (80.6%) of patients with severe trauma pain.

REFERENCES

1. Cordell WH, Keene KK, Giles BK, et al. The high prevalence of pain in emergency care. Am J Emerg Med 2002;20:165–169.
2. Pierik JG, IJzerman MJ, Gaakeer MI, et al. Pain management in the emergency chain: the use and effectiveness of pain management in patients with acute musculoskeletal pain. Pain Med 2015;16:970–84.
3. Coffey F, Wright J, Hartshorn S et al. STOP!: a randomised, double-blind, placebo controlled study of the efficacy and safety of methoxyflurane for the treatment of acute pain. Emerg Med J 2014;31:613–8.
4. Coffey F, Dissman P, Mirza K et al. Methoxyflurane analgesia in adult patients in the emergency department: a subgroup analysis of a randomized, double-blind, placebo-controlled study (STOP!). Adv Ther 2016;33:2012–31.

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