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HOT OFF THE PRESS

Hot off the press: the RAMPED trial—methoxyflurane for analgesia in the emergency department

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BACKGROUND

Pain is one of the primary reasons that patients present to the emergency department (ED).[1-6] Oligoanalgesia is a significant problem and effective pain management is an important indicator of the quality of patient care.[7-12] Multiple factors have been thought to contribute to oligoanalgesia including overcrowding, language barriers, age, sex, ethnicity, and insurance status.[13-16] Delays in providing adequate analgesia lead to poorer patient outcomes, prolonged ED length of stay, and reduced patient satisfaction.[17,18] Previous research in Australian EDs has shown that the median time to analgesia administration can be between 40 and 70 minutes, while one study in the United States reported a mean of 116 minutes.[19-21] To minimize delays, various strategies have been implemented to address the problem, including the use of novel analgesic agents that do not require intravenous access.[22]

Recently, there has been increased interest in using methoxyflurane (Penthrox), an inhaled nonopioid volatile anesthetic, to provide rapid short-term analgesia.[23,24] In Australia, methoxyflurane has been widely used at subanesthetic doses for analgesia in the prehospital setting since 1975. It has been used more widely recently and at low doses and has a very reassuring safety profile, with no reports of addiction or abuse related to its use.[25-28] The majority of studies of methoxyflurane for pain focus on traumatic pain; this study aimed to assess its effectiveness in treatment of both traumatic and nontraumatic pain.

ARTICLE SUMMARY

This is a randomized controlled trial of adult ED patients with severe pain, defined by an initial numeric rating scale (NRS) pain score of greater than or equal to 8 on an 11-point scale. Treatment arm participants were given inhaled methoxyflurane at ED triage and the comparison group received standard analgesic care, which could include acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), tramadol, oral oxycodone, or intravenous morphine. The primary outcome was the proportion of patients who had at least a 50% reduction in pain score at 30 minutes. Secondary outcomes included median pain score at 15, 30, 60, and 90 minutes; the proportion of patients that achieved a >2-point drop in their NRS pain score, and data pertaining to adverse effects.

QUALITY ASSESSMENT

The most notable limitation of this study is the open-label design. There is substantial difficulty in blinding study participants to the use of an inhaled medication (methoxyflurane) that has a particular smell and taste, but the lack of allocation concealment likely biases the results toward the intervention group. Other limitations include

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Associated podcast: https://www.thesgem.com/2021/02/sgem320-the-ramped-trial-its-a-gas-gas-gas/

the selection bias of nonconsecutive patient recruitment and the exclusion criteria which removed many patients with abnormal vital signs. These abnormal vital signs could have simply been due to severe pain and thus would be an excellent group of patients to study. Finally, only 4% of patients arrived by ambulance in this study, which may not be representative of many hospitals.

KEY RESULTS

Overall, 121 patients were randomized into the RAMPED study and there was no statistical difference in the primary outcome between methoxyflurane and standard analgesic care. In the methoxyflurane arm five (10%) patients had a reduction of pain score by >50% at 30 minutes compared with three (5%) in the standard care arm (p = 0.49). The administration of methoxyflurane was associated with a significant reduction in pain score at all time points and a notable secondary outcome was that the median time to rescue analgesia was longer in the methoxyflurane arm, 66 minutes compared with 46 minutes in the standard care arm (p = 0.024). There were no adverse effects attributed to the methoxyflurane.

AUTHOR'S COMMENTS

In this study of methoxyflurane versus standard analgesic therapy in the ED, there was no difference in pain reduction at 30 minutes. However, methoxyflurane does appear to be a safe and effective additional option for analgesic at ED triage.

TOP SOCIAL MEDIA COMMENTARY

Brent Driscoll: Great rapid analgesic for procedural and visceral pain even better when used in conjunction with opiates. Great synergistic effect. Fell out of favour for a while the excitement of intranasal fentanyl took hold but back in vogue as quick effective relief in trauma while IV access and opiates are readied. The ability of the patient to concentrate and titrate their dosage ("if it hurts, keep sucking") and that it is self-regulating- if they have too much, they drop the inhaler and nod off is a great quality control. An Australian EMS staple for decades.

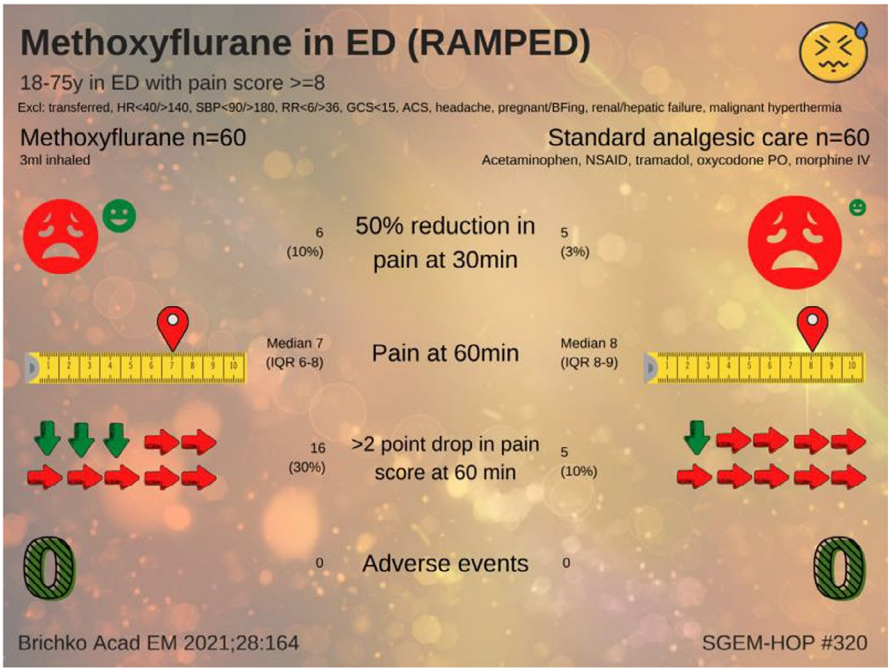
Minh Le Cong @ketaminh: It's a great piece of kit imo. I have one in my car kit for roadside attendances. Easy to use and effective in kids and adults. There is environmental contamination of exhaled gas to be aware of. It's like a portable mini nitrous oxide kit.

Julie Rankin @JulieRa00539796: Regular analgesia use for msk injuries in Northern Ireland - great quick easy effective analgesia.

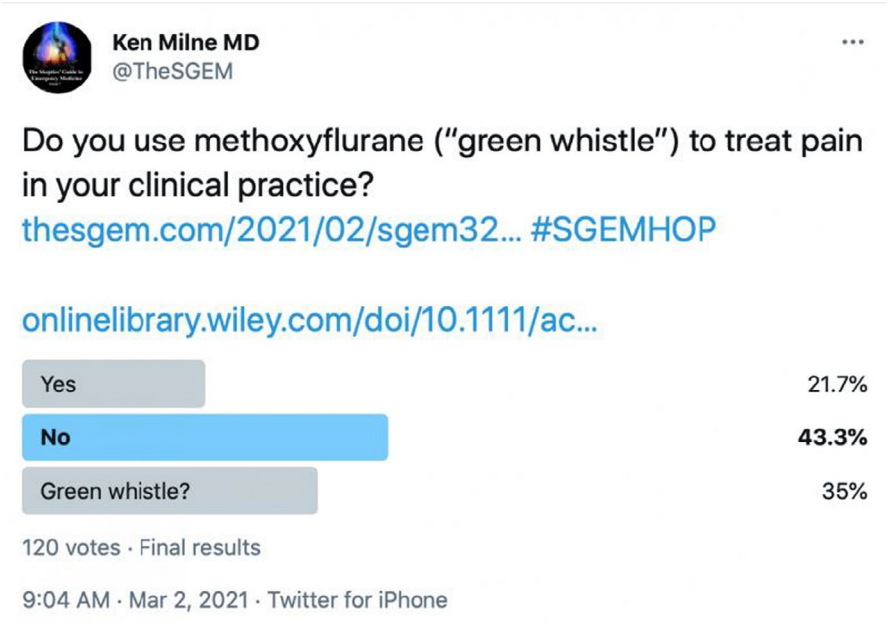
Prof Tim Hardcastle @vemadoc: They use it for burn dressing changes here. Works well in kids.

Evan Schwarz @TheSchwarziee: This seems to be very popular in countries outside the US. It's nice as no IV required and can be another component of multimodal pain medication whether an opioid is necessary or not.

PAPER IN A PIC BY DR. KIRSTY CHALLEN



TWITTER POLL BY KEN MILNE



TAKE-TO-WORK POINTS

In this randomized controlled trial, methoxyflurane was an effective analgesic agent for severe pain but was no more effective than standard analgesic care at 30 minutes. If available it remains an alternative analgesic strategy to usual therapies.

CONFLICT OF INTEREST

The authors have no potential conflicts to disclose.

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