Penthrox® (methoxyflurane) in the Emergency Department (ED) - is it worth the hype?

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Disclosures

• Galen has had no editorial input to this presentation but have reviewed to ensure ABPI code compliance only
• I have been asked to give my experience of Penthrox at Bedford General Hospital
• I am remunerated by Galen for this talk
Bedford Hospital NHS Trust ED

- 90,000 footfalls/year
- 250 patients/day
- Tertiary level DGH
88 year old lady, ASA Grade III, 5 day old Colles’ fracture

82 year old male, frail, given IV morphine after fall, with suspected fracture neck of femur

22 year old male with a moderate pneumothorax after trauma, requiring intercostal drain insertion

30 year old male with recurrent dislocation of shoulder
How could we improve patient throughput?
Penthrox®
(methoxyflurane)
in the ED

• Methoxyflurane has been used in Australia for the relief of trauma-associated pain in the ED via a handheld device since the 1970s

• Currently indicated in the UK for the emergency relief of moderate-to-severe pain in conscious adult patients with trauma and associated pain

• Patient-controlled analgesia, under supervision of a person trained in its administration

• Halogenated ether

• Provides high-quality, well-tolerated analgesia which may negate the need for procedural sedation

• In my experience, Penthrox has shown significant advantages including rapid recovery, early return to normal activities and cost savings
Checklist for administration of Penthrox®

- **C** cardiovascular instability
- **H** hypersensitivity to methoxyflurane or any fluorinated anaesthetics
- **E** elevated temperature from an anesthetic (malignant hyperthermia)
- **C** consciousness reduced (including alcohol)
- **K** kidney impairment
- **A** age below 18 years
- **L** lung/respiratory impairment
- **L** liver impairment
- **L** last administration of methoxyflurane

- **Drugs- CYP 450 inducers**
  - alcohol, isoniazid, phenobarbital, rifampicin

- **Nephrotoxic antibiotics**
  - tetracycline, gentamicin, colistin, polymyxin B, amphotericin B
Penthrox® audit

Methods

- Use of proforma to collect retrospective and prospective data
- 30 patients’ data collected between December 2017 to April 2018
- Compared with RCEM procedural sedation audit data (2015-16)
- Penthrox was used as a first-line drug for trauma analgesia and as primary analgesia for reduction of fractures and dislocations
- Our focus was:
  - Efficacy
  - Adverse effects
  - Time to discharge
  - Cost effectiveness
Efficacy - pain scores fell five VAS points within first minute

- Pain scores out of 10 - prior to administration, 1 minute post administration and 15 minute post administration were recorded
- Patient-controlled analgesia - with supervision by trained personnel
- 4 cases required the use of further IV procedural sedation (in the form of propofol/fentanyl)
  - Three involved anterior shoulder dislocations and one a bi-malleolar ankle fracture

**Figure 1: Pain Scores Pre- & Post-Penthrox Administration**

- Prior
- 1 Minute
- 15 Minutes
Average time to discharge: 39 minutes

- For patients not requiring additional sedation (4 patients) or admission (9 patients)
- Post IV procedural sedation would require a 60 min observation time as per Trust guidelines
- Return to baseline vitals, GCS, pain score, no respiratory compromise would be required as per RCEM Safe Sedation guideline
A small number of adverse events were recorded in some cases.

A few Penthrox audit patients reported noticing a mild/transient taste/smell of the drug and/or feeling ‘drunk’.

By contrast, in the RCEM procedural sedation audit (2015-16) an adverse event rate of 4.7% was recorded for procedural sedation.

None of the patients withdrew from the audit.

There were no observed effects on cardiovascular or respiratory parameters.
Costs

- **Procedural sedation for reduction of fractures/dislocations requires:**
  - a second doctor and suitably qualified nurse
  - continuous monitoring
  - IV access
  - IV drugs/fluids
  - oxygen
  - suction
  - resuscitation room
  - capnography
  - etc

- **Penthox requires:**
  - two trained personnel
  - a trolley in the ED
  - one inhaler costing £17.89
Limitations

Limitations of audit
- Small single-center study
- Lack of comparative data
- Uniformity of assessment, operator confidence/experience

Limitations of Penthrox
- Contraindicated in patients with known renal failure for which active treatment is being given or highly likely to significant renal impairment
- Should be followed up with oral analgesia or regional blocks for effective and ethical pain management
Conclusions – A CLEAR BENEFIT!

- Effective analgesia for trauma and first-line approach to where possible, negate the need for procedural sedation, especially in the elderly or high ASA grades
- Can be used as an alternative to Entonox, as it is portable and can be used in trauma where there is encapsulated air in the body
- Fewer potential adverse effects
- Rapid recovery
- Decreased time to discharge
- Excellent cost effectiveness
Trauma pain management
(a better day at the office)

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Ongoing work

- Incorporated into Trust guidelines standard operating procedure as primary analgesia for trauma, in conscious patients.
- In the process of formulating a opioid free fracture NOF pathway using Penthrox® as bridging analgesia.
- Further data being analysed for publication.
My Take-Home Message:

Use Penthrox® in your ED

Consider Penthrox as a 1st choice analgesic as it can negate the need for procedural sedation in the ED (for high-risk patients – especially elderly, obese, poor lung capacity)

Easy administration, high compliance, well-tolerated and effective

Early return to normal activities, early discharge and lower burden on the available resources

Cost effective
Penthrox Additional Learnings/Evidence

• Randomised, double-blind, placebo-controlled study of the efficacy and safety of methoxyflurane for the treatment of acute pain
  • Coffey F et al. Emerg Med J 2014;31:613-618

• Health effects of patients given methoxyflurane in the pre-hospital setting: A data linkage study
  • Ian G. Jacobs The Open Emergency Journal 2010, 3, 7-13

• Pre-hospital analgesia in adults using inhaled methoxyflurane
References


• Royal College of Emergency medicine. Procedural sedation in adults clinical audit 2015-16 national report.

Administration on consecutive days is not recommended and the impairment:

To reduce occupational exposure to methoxyflurane, the following administration schedule is recommended: no more than 6 ml in a frequency at which PENTHROX can be safely used is not established. The rapid and occurs after 6-10 inhalations. Patients are able to titrate the amount of months.

one Activated Carbon (AC) chamber.

pack consists of one bottle of 3 ml PENTHROX, one PENTHROX Inhaler and moderate to severe pain in conscious adult patients with trauma and associated pain. Dosage and administration: PENTHROX should be self-administered under supervision of a person trained in its administration, using the hand held PENTHROX Inhaler. It is inhaled through the custom-built PENTHROX inhaler.

Adults: One bottle of 3 ml PENTHROX as a single dose, administered using the device provided. A second bottle should only be used where needed. The frequency at which PENTHROX can be safely used is not established. The following administration schedule is recommended: no more than 6 ml in a single day, administration on consecutive days is not recommended and the total of 18 ml in a week should not be exceeded.

PENTHROX Inhaler should always be used with the AC Chamber which cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and respiratory depression.

Relief of trauma related pain in closely repeated episodes for the same patient. Relief of break-through pain/exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient.

PENTHROX contains the excipient, butylated hydroxytoluene (E321) which may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and respiratory depression.

Relief of trauma related pain in closely repeated episodes for the same patient. Relief of break-through pain/exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient.

PENTHROX should be used with care in patients with underlying hepatic conditions or for risks for hepatic dysfunction. Previous exposure to halogenated hydrocarbon anaesthetics (including methoxyflurane when used as an anaesthetic agent), especially if the interval is less than 3 months, may increase the potential for hepatic injury. Potential effects on blood pressure and heart rate are known class-effects of high-dose methoxyflurane used in anaesthesia, and may be amplified in patients with underlying hepatic disease due to possible reduction in blood pressure. Potential CNS effects such as sedation, euphoria, amnesia, ability to concentrate, altered sensorimotor co-ordination and change in mood are known class-effects. The possibility of CNS effects may be seen as a risk factor for potential abuse, however reports are very rare in post-marketing use. PENTHROX is not appropriate for providing relief of break-through pain/exacerbations in chronic pain conditions or for the relief of trauma related pain in closely repeated episodes for the same patient.

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