The Use of Inhaled Methoxyflurane in the Prehospital Setting

Report by: Matthew Morin

2nd Party Appraiser: Jen Greene

Clinical Scenario:

A BLS crew is sent to a hockey arena in rural Nova Scotia where they find an anxious 17 year old male sitting on the bench holding his right arm complaining of severe 10/10 pain. Upon further investigation the young athlete informs you that he was body checked into the boards and felt his arm snap. When inspecting the limb, you noticed a bruised and swollen arm with obvious deformity. You suspect a Colles fracture and after a full patient assessment, you go ahead and instruct the patient to self-administer the recommended dose of Methoxyflurane. The injury is splinted and transport is initiated. During transport the patient appears much more comfortable and states that his pain is now a 2/10 on the 10 point pain scale.

PICO (Population-Intervention-Comparison-Outcome) Question:

For patients suffering from an acute pain, would inhaled Methoxyflurane be a safe and effective form of analgesia to be used by primary care paramedics as compared to the standard of care given at present moment as measured by comfort, satisfaction and safety?

Search Strategy:

In PubMed –

(Prehospital OR EMS OR Out-of-hospital OR Ambulance) AND (Penthrox OR Penthane OR Methoxyflurane)

Search outcome: 13 results

In Google Scholar -

“Health effects of prehospital use of Methoxyflurane”

Search outcome: 132 results
### Relevant Papers:

<table>
<thead>
<tr>
<th>Author, Date</th>
<th>Population: Sample Characteristics</th>
<th>Design: Level of Evidence (LOE)</th>
<th>Outcomes</th>
<th>Results</th>
<th>Strengths/Weaknesses</th>
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<tbody>
<tr>
<td>Babl et al.</td>
<td>Children who received methoxyflurane while being transported to a tertiary children’s hospital by ambulance. 105 patients with an age range of 15 months to 17 years.</td>
<td>Prospective observational case series LOE III Green</td>
<td>1. Efficacy of Methoxyflurane in terms of decreases in pain scale and 2. Adverse events in the paediatric population</td>
<td>Patient pain scores dropped from a mean of 7.9 % (95% CI 7.5-8.3) prior to methoxyflurane use to 4.5 (95% CI 3.9-5.0) at 2-5 min and to 3.2 (95% CI 2.8-3.7) at 10 min. No serious adverse events (one-sided 97.5% CL 0-3%). Mild adverse events occurred in 38 patients, 36.2% (95% CI 27.0-46.1%) 5 of 15 (33.3%) patients under 5 years of age were deeply sedated.</td>
<td>S - large variation in pediatric ages  W – Small sample size  W - Pain scale subjectivity  W – Not a large variation in patient presentation</td>
</tr>
<tr>
<td>Buntine et al.</td>
<td>Adults to whom methoxyflurane was administered while traveling by ambulance to a teaching</td>
<td>Observational case series Both quantitative and qualitative study</td>
<td>1. Explored the efficacy in Methoxyflurane in terms of decreasing the verbal numerical rating</td>
<td>A mean reduction in verbal numerical rating scale (VNRS) scores of 2.47 ± 0.24 5 minutes post methoxyflurane with a total</td>
<td>S – large variation in patient age  S – large variation in clinical presentation  W – Small population</td>
</tr>
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</table>

Paramedic Critically Appraised Topic
| Jacobs, G. | Patients managed by the ambulance service in Western Australia from 1990-2000 135 770 patients | Retrospective cohort study using routinely collected administrative data using probabilistic matching LOE III Green | To determine whether the event rates of heart disease, renal disease, hepatic disease, diabetes or cancer in patients who received Methoxyflurane compared with those not receiving Methoxyflurane prehospital | Of the 135 770 patients entered in the study, 17 629 (13%) received Methoxyflurane. Trauma most common indication (9 755, 55.3%) The odds ratio for each of the five disease groups under investigation ranged from 0.87 to 1.06 with the 95% CI for each estimate including | S – large population size S – Many databases used S – Control group W – Study not able to ascertain accuracy/validity of the data for each database used W – Unable to access actual dose of Methoxyflurane used W – Conflict of interest, MDA, the manufacturer |

| hospital 83 patients Paramedics who administered the analgesic | LOE III Green | scale and reduction of 3.21 ± 0.24 at time of arrival at the ED. Both VNRS scores were significantly different from baseline 15 patients (18.1%, 95% CI 9.8-26.4%) reported mild side-effects 68 (81.9%, 95% CI 72.0-89.5%) of the paramedics and 60 (72.3%, 95% CI 61.4-81.6%) of patients interviewed said they felt satisfied with the level of analgesia | size W – not randomized W – not blinded W – VNRS pain score used by multiple clinicians W – no control group yet this is unethical |
**Comments:**

- The most common indication for use of Methoxyflurane was trauma.
- Verbal numerical rating scale is commonly used to assess efficacy of analgesia, some other studies chose to use alternative methods to rate effectiveness such as change in vital signs (i.e. blood pressure, respiration, etc.).
- Many studies in prehospital arena on efficacy and safety of Methoxyflurane. These specific studies chosen to demonstrate safety of use and efficient analgesic properties in all age populations as well as all clinical presentation.
- Specific doses of Methoxyflurane used are not present in all studies, which is important to determine a dose-response relationship.

**Consider: Why would you NOT change practice, based on these articles?**

Based on these articles, changing practice would be premature without further investigation into the dose-response relationship.

**Clinical Bottom Line:**

The use of inhaled Methoxyflurane in the prehospital setting has been shown to be an effective analgesic for a multitude of clinical presentations in all age populations. It has been determined that there is a low adverse events profile when used at recommended dosages for analgesia and no difference in long term health effects as compared to those not treated with Methoxyflurane. Patients and paramedics were satisfied with its analgesic properties and demonstrated a willingness to use Methoxyflurane again in the future. Due to its ease of use, safety, and efficacy profile, Methoxyflurane would be a suitable analgesic for primary care paramedics.

**References:**

Franz E. Babl, MD, MPH, FRACP, FAAP, Consultant in Emergency Medicine; Sarah R Jamison, MB BS, FRACP, Consultant in Emergency Medicine; Maureen Spicer, PhD, Research Coordinator; Stephen Bernard, MB BS, FACEM, FJFICM, Medical Advisor.

Paul Buntine, MB BS, FACEM, Consultant in Emergency Medicine; Ogilvie Thom, MB BS, FACEM,
Consultant in Emergency Medicine; Franz Babl, MD, MPH, FRACP, FAAP, Consultant in Emergency Medicine; Michael Bailey, PhD, MSc(statistics), BSc(hons), Statistical Consultant; Stephen Bernard, MB BS, FACEM, FJFICM, Medical Adviser.

Ian G. Jacobs (2009). Health Effects of Patients Given Methoxyflurane in the Pre-Hospital Setting: A Data Linkage Study. Discipline of Emergency Medicine (M516). University of Western Australia, 35 Stirling Hwy, Crawley 6009, Australia: Bentham Open.