



Service Evaluation of Methoxyflurane Versus Standard Care for Overall Management of Patients with Pain Due to Injury

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Received: January 17, 2020 / Published online: March 30, 2020
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ABSTRACT

Introduction: Inhaled methoxyflurane is an analgesic used for the emergency relief of moderate to severe pain in conscious adult patients with trauma and associated pain that is increasingly being used in hospital emergency departments to provide rapid analgesia. It is widely accepted that effective pain relief can facilitate patient care and flow through the emergency department (ED). The main aim of this evaluation was to assess the impact of inhaled methoxyflurane on patient length of stay (LOS) in the ED compared with standard care.

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Methods: Adult patients with moderate to severe trauma pain and Glasgow coma score of 15 were included in the evaluation. Evaluation forms were completed for 79 patients who received methoxyflurane and were matched with 80 patients who received standard care.

Results: Overall the mean time spent in the ED was reduced by 71 min in those patients who were administered methoxyflurane compared with patients who received standard care. Furthermore, analysis of LOS by injury type demonstrated a reduction in ED LOS by 183 min for patients with shoulder dislocation who were treated with methoxyflurane compared with patients who received standard care. There was no reduction in ED LOS for patients with lower limb, hip or pelvic injuries between the two treatment groups.

Conclusion: Use of methoxyflurane in adult patients with trauma pain significantly reduced the ED LOS and may potentially improve patient flow through the ED.

Keywords: Acute pain; Analgesic; Emergency Department; Inhaled analgesic; Methoxyflurane; Pain; Pentrox; Trauma

Key Summary Points

Why carry out this study?

The service evaluation was completed because there has been limited reviews of the impact of methoxyflurane in the emergency department (ED).

This was a prospective, observational, cohort-defined service evaluation, with data collected over 6 months, which was compared with retrospective data from the same period the previous year.

What was learned from the study?

Length of stay (LOS) in the emergency department varied according to injury type and the treatment administered.

A sub-group analysis based on injury type demonstrated a significant reduction in ED LOS for patients with shoulder dislocation administered methoxyflurane.

Patients administered methoxyflurane for other upper limb injuries also demonstrated a reduction in ED LOS.

Patients attending the ED with lower limb, hip and pelvic injuries did not see a statistically significant reduction in ED LOS vs. standard care.

There were no reported significant adverse events associated with methoxyflurane treatment, and it was generally well tolerated.

facilitate patient care and flow through the ED [5].

The impact of pain management practices on patient flow in the ED is an under-investigated area. One large retrospective study, which included > 2000 patients, found that while administration of adequate analgesia to patients did not reduce the ED length of stay (LOS) overall compared with patients not receiving adequate analgesia, the multivariate analysis did show a significant reduction in ED LOS of 2 h when the time to analgesia was shortened [6]. This study suggests that it is not just adequacy of analgesia, but also time to adequate analgesia that impacts patient LOS in the ED. Many analgesics demonstrate a similar rate to onset of action from the time of administration, but that time to administration can be impacted by many factors, including staff-to-patient ratios, access to controlled drugs and time to prepare drugs and gain intravenous (IV) access, if required [5].

A recent study on the use of inhaled methoxyflurane vs. procedural sedation for reduction of anterior shoulder dislocation demonstrated a significant reduction in ED LOS of approximately 50% for patients in the inhaled methoxyflurane arm, leading the authors to suggest that use of methoxyflurane analgesia may improve ED efficiency [7].

Methoxyflurane has been used extensively, primarily in Australia but more recently in Europe, as a self-administered, rapidly acting inhaled analgesic agent [8]. It has been shown in multiple studies to rapidly provide effective analgesia [6, 9, 10] and potentially reduce patient length of stay [6].

Our aim is to evaluate the impact of introducing inhaled methoxyflurane to the ED on LOS for adult patients with pain from trauma.

INTRODUCTION

Pain management and choice of analgesia are often guided by the World Health Organization's analgesic ladder [1]; however, it is evident that assessment and treatment of pain in the pre-hospital phase and in the emergency department (ED) are often inadequate [2–4]. It is widely accepted that effective pain relief can

METHODS

The service evaluation was conducted in the Emergency Department of St. Mary's Hospital London. St Mary's is a Major Trauma Centre and sees > 3000 trauma patients per year. Methoxyflurane was introduced to the department in December 2017, with the service

evaluation beginning in May 2018. This was to allow for staff training on administering methoxyflurane and to ensure adequate numbers of completed evaluation forms.

This was a prospective observational, cohort-defined service evaluation, completed over 6 months. The data collected prospectively were compared with a matched cohort of patients who did not receive methoxyflurane.

The aim of the evaluation was to assess the efficacy, overall analgesia provision costs, impact on pain scores and service impact of inhaled methoxyflurane compared with standard care.

ED clinical staff and research nurses from the local research team completed evaluation forms for patients aged ≥ 18 years, Glasgow coma scale (GCS) 15, who received methoxyflurane for their pain from injuries. Data were collected on adult patients presenting with moderate to severe pain [i.e., verbal numerical pain scores (VNPS) 4 to 10 out of 10]. Data were also obtained from routinely collected data in the electronic patient records. Some baseline pain scores were obtained, where relevant, from ambulance patient report forms.

Patients in both the methoxyflurane and standard care cohorts were matched for analytical purposes based on patient characteristics, including age group, gender, injury type and previous medical history, to limit any potential for bias.

The cohort of matched patients were sought by using the local Database team to extract certain fields of data; these were (1) patient's aged ≥ 18 years, (2) GCS 15 on arrival and (3) triaged as limb injury or trauma and/or patients referred to orthopaedics.

Available data were presented by paired groups to compare 'cases' (methoxyflurane) and 'controls'. Mean and medians were calculated for each group. *P* values were calculated for statistical significance of differences between groups using Student's *t*-test.

Ethical approval was not required as this was a service evaluation, with all interventions being routine and all data recorded as standard.

RESULTS

During the period of May to November 2018, 50 evaluation forms were completed for patients who were administered methoxyflurane. After patients were excluded from analysis because of incomplete data recording, 30 patients were included. The initial data analysis demonstrated a significant reduction in ED LOS for patients, particularly those with upper limb and shoulder injuries; however, patient numbers were too low to draw conclusions for some injury types. The evaluation was re-opened in May 2019 to collect data on an additional 50 patients. The ED staff were now more familiar with inhaled methoxyflurane and evaluation forms; consequently, the data on the additional patients were gathered in a significantly shorter time

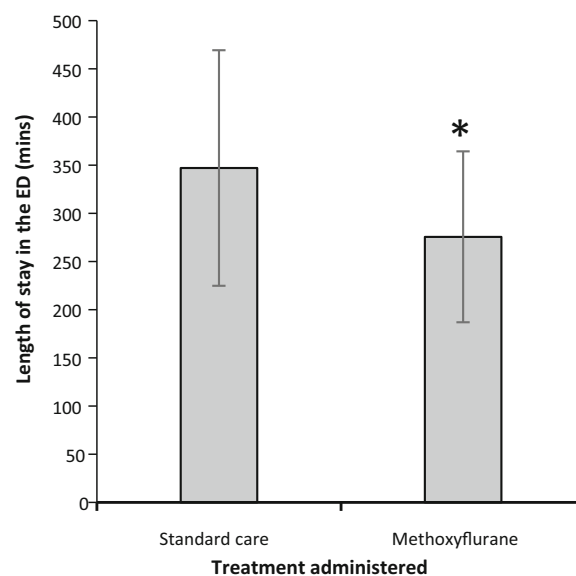
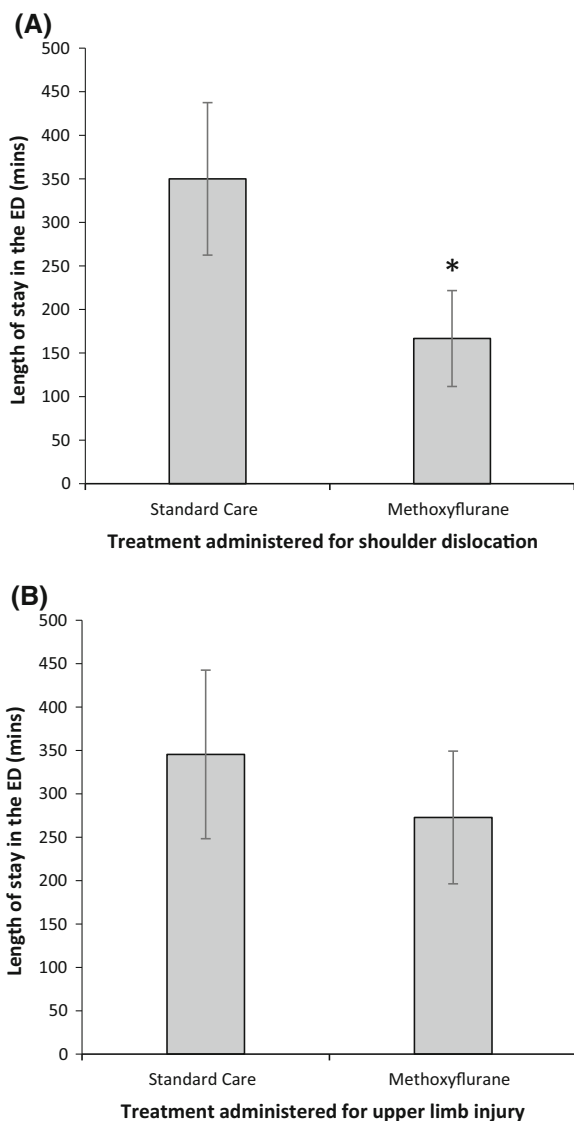


Fig. 1 Methoxyflurane treatment reduced patient length of stay in the emergency department (ED). Bar graph comparing length of stay in the ED, from arrival to discharge or admission, for patients treated with methoxyflurane compared with patients who received standard care. The mean length of stay in the ED for patients who received standard care was 347 min (range 94–1382). The mean length of stay in the ED for patients who received methoxyflurane was 276 min (range 30–967 min). Data presented are the mean time in minutes \pm standard deviation. Statistically significant differences were determined by a Student's *t*-test; **p* = 0.038



◀**Fig. 2** Length of stay in the emergency department (ED) according to injury type and treatment administered. **a** Bar graph illustrating length of stay in the ED for patients with shoulder dislocation who received methoxyflurane compared with those who received standard care. The mean length of stay in the ED for patients who received standard care was 350 min. The mean length of stay in the ED for patients who received methoxyflurane was 167 min. **b** Bar graph illustrating length of stay in the ED for patients with upper limb injuries who received methoxyflurane compared with those who received standard care. The mean length of stay in the ED for patients who received standard care was 345 min. The mean length of stay in the ED for patients who received methoxyflurane was 273 min. Data presented are the mean time in minutes ± standard deviation. Statistically significant differences were determined by a Student’s *t*-test; **p* = 0.009

period than the initial part of the evaluation and completed July 2019.

In total, 79 patients were included in the methoxyflurane group and 80 patients in the matched standard care group. The mean overall time spent in the ED for patients with injuries was reduced by 71 min for patients administered methoxyflurane vs. standard care, 276 min (range 30–967 min) vs. 347 min (range 94–1382 min) (*p* = 0.038), respectively (Fig. 1).

A sub-group analysis based on injury type demonstrated a significant reduction in ED LOS for patients with shoulder dislocation administered methoxyflurane of 183 min (*p* = 0.009) vs.

standard care (Fig. 2a). Patients administered methoxyflurane for other upper limb injuries also demonstrated a reduction in ED LOS of 72 min; however, the difference was not significant (Fig. 2b). Patients attending the ED with lower limb, hip and pelvic injuries did not see a statistically significant reduction in ED LOS vs. standard care (366 min vs. 343 min, *p* ≤ 0.6) (Fig. 3).

There were no reported significant adverse events associated with methoxyflurane treatment and it was generally well tolerated. In the majority of cases, standard care was composed of IV opioids or procedural sedation. Details of other treatments administered for relief of pain in addition to methoxyflurane for pain following injury in patients presenting to St. Mary’s emergency department are provided in Table 1.

DISCUSSION

Despite a recent focus on early analgesia, many departments are failing to reach the goal set out by the Royal College of Emergency Medicine for provision of analgesia within 20 min of arrival [13]. Many factors have been shown to impact the provision of adequate analgesia in ED, such as ED waiting times for triage, overcrowding, suboptimal staff numbers and time to access

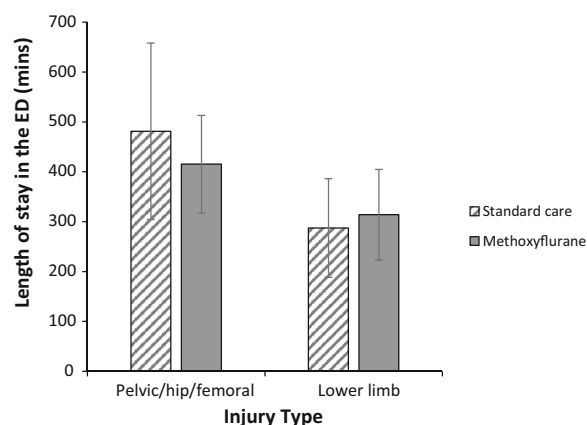


Fig. 3 Length of stay in the emergency department (ED) for patients attending with pelvic, hip, femoral and lower limb injuries. Bar graph illustrating length of stay in the ED for patients with pelvic/hip/femoral or lower limb injuries who received methoxyflurane compared with those who received standard care. The mean length of stay in the ED for patients with pelvic/hip/femoral injuries who received standard care or methoxyflurane was 481 and 415 min, respectively. The mean length of stay in the ED for patients with lower limb injuries who received standard care or methoxyflurane was 287 and 314 min, respectively. Data presented are the mean time in minutes \pm standard deviation

and prepare opioids for IV administration as well as availability of beds in the resuscitation areas. Long waiting times, slow discharge times and overcrowding are affecting almost every ED in the UK, and the situation does not show any signs of significant improvement at present. Provision of adequate analgesia and the overall impact of this on the ED are an area of patient management that is not well studied. In this service evaluation, we aimed to assess whether the introduction of an effective, fast-acting, non-parenterally administered analgesic, namely methoxyflurane, would have an impact on patient length of stay, potentially reducing the numbers of staff involved in individual patient care and the burden on the vital resuscitation area beds.

This evaluation showed that the availability of methoxyflurane significantly reduced ED patient length of stay vs. standard care. There was a reduction of approximately 3 h in patient length of stay for those presenting with

Table 1 Number of patients who received additional analgesia within 30 min of methoxyflurane being administered in the ED

Medications administered in the ED	Pentrox group (<i>n</i> = 79)
Local anaesthetic regional block* (lidocaine/bupivacaine/ levobupivacaine)	5
Intravenous opioids* (fentanyl/morphine)	12
Intravenous ketamine* (\pm administered with midazolam/ opioid)	5
Intravenous propofol	1
Inhaled nitrous oxide only	0
Intravenous midazolam only	1
Oral opioids	2
Paracetamol	3
Methoxyflurane only	50

*Patients were administered combinations of the above-listed medications

shoulder injuries, which was higher than expected. For other upper limb injuries, while the difference was not statistically significant, there was a mean reduction of 72 min. The finding that methoxyflurane use is associated with a significant reduction in patient length of stay is consistent with recent findings in other hospitals [6, 7, 14]. It appears to be primarily due to a reduction in the use of intravenous procedural sedation, which, prior to the introduction of methoxyflurane, was frequently used for relocation of shoulders and manipulation of fractures. Intravenous procedural sedation requires a resuscitation area bed, which is not always immediately available, and requires three or more members of staff to carry out the procedure. Many of the patients administered procedural sedation also exceed the 4-h target for discharge. In comparison, for many patients receiving methoxyflurane, this analgesic alone was sufficient for the patients to be

comfortable during assessment and treatment, negating the need for intravenous procedural sedation. Methoxyflurane use also enabled us to treat patients in a regular bay and usually required only two members of staff. However, there were 11 patients where methoxyflurane alone provided insufficient analgesia for the procedure to be completed, and these patients had to be converted to procedural sedation.

The length of stay for patients with hip and other lower limb injuries was not reduced with methoxyflurane, which was not an unexpected outcome. In many cases, patients with pelvic or lower limb fractures will require hospital admission and further treatment. Their time in the department is therefore likely to reflect the wait for an inpatient bed. This evaluation was not designed to determine if there were benefits to this patient group; however, it is reasonable to suggest that the timely provision of analgesia would benefit patients even with no improvement in ED length of stay.

It is difficult to ascertain accurate costing for the provision of analgesia for patient assessment and treatment, as the cost involves not only the drug cost, but also the associated consumables and staff costs. The NICE Guideline [15] on management of non-complex fractures (NG38) contains detailed costings sourced primarily from the NHS supply chain. This guideline calculated that the overall cost of procedural sedation is £155.47. Utilizing the costings listed, we have calculated that the overall cost of methoxyflurane use is £73.39, which is comprised of staff costs and the cost of methoxyflurane (Penthrox) itself. Therefore, for each patient administered methoxyflurane for upper limb/shoulder injuries, there is a potential saving to the trust of £82.08.

IMPLICATIONS/CHALLENGES

During the evaluation, there were challenges in identifying patients who had been prescribed methoxyflurane. This was possibly due to a change in prescribing, from administering Entonox immediately to prescribing methoxyflurane. This led to the slow collection of evaluation forms initially. Following training

and highlighting this with the emergency medical team, prescriptions improved and allowed for the research staff to identify the patients earlier, when in the department.

Another challenge was the recording of data points to determine how many health care professionals attended to the individual for the provision of analgesia or procedural sedation, along with collecting data on all consumables used for costing purposes. It was also noted that pain scores were not always documented or, if they were, a subsequent pain score was not recorded following analgesic provision. Therefore, the full costing and impact on pain scores could not be analysed from this data set. However recent clinical trial data have demonstrated the superiority of methoxyflurane over standard analgesic treatments, including IV morphine, IV paracetamol, IV ketoprofen and NSAIDs, with patients administered methoxyflurane reporting both greater pain relief and a shorter time to onset of pain relief compared with standard analgesic treatments [12, 16]. These data combined with the service evaluation data where 29 patients in the methoxyflurane group required additional analgesia suggest that for many patients pain relief with methoxyflurane is comparable to that of standard treatments.

CONCLUSION

Managing patients' pain continues to be a challenge within the ED. This evaluation demonstrated that the early use of methoxyflurane can positively impact length of stay within the ED and provide effective pain relief for patients.

The cost implications of methoxyflurane being introduced to the ED warrant further investigation, as the evaluation suggests that methoxyflurane use and the associated reduction in intravenous procedural sedation use may have financial benefits. Overall, the staff in our ED reported that the introduction of methoxyflurane has had a positive impact on our department and for our patients.

ACKNOWLEDGEMENTS

We are grateful to Ltnt Cln Chris Wright for helping introduce methoxyflurane to St Mary's Emergency Department, thank the NET Research team and St Mary's Emergency Department clinical staff for their help with completing the service evaluation forms and give special thanks to clinical research nurse Andrea D'Mello for help collecting and collating the data.

Funding. Funding for the research nurse time was provided by Galen Ltd. The journal's Rapid Service and Open Access Fees were also funded by Galen Ltd. No other funding was provided.

Medical Writing Assistance. Medical writing assistance has been provided by Dr. Sarah Dolan at Galen Ltd.; however, the authors were in full control of the final publication. Dr. Sarah Dolan is an employee of Galen Ltd.

Authorship. All named authors meet the ICMJE criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

Disclosures. Louise Young, George Bailey and Jayne McKinlay have nothing to disclose. Jayne McKinlay changed affiliation after the initial service evaluation completed in 2018.

Compliance with Ethics Guidelines. Ethical approval was not required as this was an observational service evaluation, which was registered with the local NHS Trust as per local policy and guidelines. All interventions were routine and all data were recorded as standard.

Data Availability. The datasets generated during and/or analysed during the current study are not publicly available as the data was generated for a service evaluation from routine clinical care, but are available from the corresponding author on reasonable request.

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