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ORIGINAL ARTICLE

Efficacy and safety of intraoperative intravenous methadone during general anaesthesia for caesarean delivery: a retrospective case-control study

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ABSTRACT
Background: Most patients undergoing caesarean delivery with general anaesthesia require systemic opioid administration. Due to its rapid onset and long duration of action, intravenous methadone may make it suitable for analgesia after caesarean delivery. Intraoperative methadone combined with postoperative intravenous patient-controlled analgesia with fentanyl or morphine has recently been introduced in our unit.
Methods: A retrospective case-control study of 25 patients who had received methadone was performed. Fifty control patients undergoing elective or emergency caesarean delivery were matched for the use of postoperative intravenous patient-controlled analgesia, transversus abdominis plane (TAP) block and regular non-steroidal anti-inflammatory drugs. Exclusion criteria included preoperative neuraxial analgesia or pre-delivery opioid consumption greater than 10 mg of intravenous morphine equivalents.
Results: Patients in the methadone group had lower pain scores and were less likely to require intravenous opioid supplementation in the post-anaesthetic care unit ($P < 0.001$). Opioid consumption over 48 h was significantly lower in the methadone group. Delayed discharge from the post-anaesthesia care unit was due to sedation in one patient in the methadone group compared to three control patients in whom it was due to sedation and inadequate analgesia.
Conclusion: A single intraoperative bolus of intravenous methadone appeared to provide effective analgesia with an acceptable side-effect profile.

Keywords: Caesarean delivery; General anaesthesia; Methadone; Patient-controlled analgesia

Introduction

Most caesarean deliveries at our institution are performed using neuraxial techniques with intrathecal or epidural opioids given for postoperative analgesia. When general anaesthesia is required, the multimodal analgesic regimen includes intravenous opioids after delivery of the baby. Methadone is a mu-opioid receptor agonist with mixed antinociceptive activity, including non-competitive N-methyl D-aspartate antagonism, and prevention of 5-hydroxytryptamine and noradrenaline reuptake. Methadone is often used orally in opioid dependency and chronic pain, but infrequently in the perioperative setting.[1,2] The latter may be due to issues that include a stigma associated with its use for opioid dependence, misperceptions about the speed of onset, and concern about side effects, especially prolonged sedation or respiratory depression. However, potential benefits of a single dose of intravenous methadone include improved early postoperative analgesia; prolonged efficacy, which may eliminate the need for patient-controlled intravenous analgesia (PCIA); efficacy against neuropathic pain, and possible prevention of chronic wound pain; and low cost.[1] There is renewed interest in intraoperative methadone administration,[1,3–5] but publications in the obstetric literature are limited to the use of oral methadone administration in opioid dependence.[6]

The use of intraoperative, post-delivery, intravenous methadone during general anaesthesia for caesarean delivery has recently gained popularity in our institution. The primary aim of this study was to examine

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the effect of intraoperative methadone on opioid consumption in the first 48 h. Secondary aims looked at opioid consumption in the post-anaesthesia care unit (PACU) and the first 24 h, and assessed complications and side effects. Since most patients receive general anaesthesia for emergency delivery, making a randomised-controlled trial difficult, a retrospective case-control study was used. A chart review explored the efficacy and side effects from a single intraoperative intravenous dose of methadone and these patients were compared with matched controls who received intravenous fentanyl and/or morphine.

Methods

The study received approval from the regional ethics committee. A retrospective case-control study of patients who had undergone caesarean delivery under general anaesthesia between 1st August 2010 and 15th March 2012 was performed. Patients who had received intraoperative methadone (methadone group) and those who had not (control group) were identified from the department database. Each patient who received methadone and postoperative PCIA was matched to two controls for factors that might alter postoperative analgesic requirements. The controls were the next two chronological patients in the same setting (elective or emergency surgery), who had received the same anaesthetic technique, including use of transversus abdominis plane (TAP) blocks and regular postoperative non-steroidal anti-inflammatory drugs (NSAIDs). Patients were excluded if they had received preoperative neuraxial analgesia, a pre-delivery opioid dose >10 mg of intravenous morphine equivalents, were non-English speaking, or in whom a Pfannenstiel incision had not been used. Only patients with postoperative PCIA were matched and included in the case-control study. To explore the safety profile of methadone further, data were collected on patients who received methadone and were managed without PCIA.

Patients received opioids immediately after delivery and cord clamping. Most patients received postoperative analgesia and antiemetic therapy according to departmental guidelines: regular paracetamol and/or NSAIDs (ibuprofen 400 mg 8-hourly, celecoxib 200 mg 12-hourly); as required tramadol orally or intravenous (50–100 mg 1-hourly) or oral oxycodone (5–15 mg 1–2 hourly) in addition to PCIA. Intravenous naloxone (50 μg 1-hourly) was prescribed to treat severe pruritus. The PCIA regimen used either fentanyl (20 μg) or morphine (2 mg) boluses with a 5-min lockout and no basal infusion. Standardised order sheets prescribed antiemetics in a stepwise approach using ondansetron (4 mg 6-hourly), metoclopramide (20 mg 4-hourly), droperidol (0.5 mg 6-hourly) and promethazine (25 mg 6-hourly). Patients were reviewed daily by the Acute Pain Service. Verbal numerical pain scores (VNPS) (0 = no pain, 10 = worst pain imaginable) were recorded 2-hourly by nursing staff.

Data were extracted retrospectively from the Acute Pain Service database, anaesthesia medical records, PACU and inpatient observation charts. Outcomes were examined across three time periods: the PACU stay; after PACU discharge and up to 24 h postoperatively; and 24–48 h after surgery. Analgesic outcomes included the worst VNPS (0–10) and opioid consumption. Opioid doses were converted to intravenous morphine equivalents. Intravenous morphine 10 mg was considered equivalent to either intravenous fentanyl 0.1 mg, intravenous methadone 10 mg, oral oxycodone 20 mg, intravenous tramadol 120 mg or oral tramadol 150 mg.[7,8] If administered, pre-intubation, single bolus doses of either remifentanil or alfentanil were not included. Complication outcomes were over-sedation (sedation score of 3 – difficult to rouse), respiratory depression (respiratory rate <9 breaths/min, need for reversal with naloxone or respiratory arrest), hypotension (systolic blood pressure <90 mmHg or treatment with a vasopressor drug), desaturation (<90%, or extra oxygen requirement), altered mental state (confusion and/or hallucinations) or delayed recovery (>45 min to discharge from PACU due to patient factors). Treatment of side effects such as pruritus, nausea or vomiting and the duration of extra oxygen requirement were noted.

Statistical analyses

Categorical data are presented as percentage or number and were analysed using the Fisher's exact test. Continuous data are presented as mean (SD) or median (IQR [range]) as appropriate and were analysed by Mann Whitney tests for non-parametric data and Student's t tests for parametric data. Statistical analysis was performed using Prism 5.0a (GraphPad Software, Inc., La Jolla, CA, USA). A P value of <0.05 was considered statistically significant.

Results

During the study period a total of 3151 caesarean deliveries were performed, 252 (8%) conducted under general anaesthesia. The indications for general anaesthesia were fetal compromise (46%), failed neuraxial anaesthesia (21%), patient request (20%), contraindication to neuraxial anaesthesia (5%) and other (8%). Forty-four patients received intraoperative methadone; 25 of these received PCIA, and 19 received oral opioids. Those who received PCIA were matched to 50 controls for emergency caesarean delivery (76%), intra-operative TAP blocks (24%) and NSAIDs (76%).

Demographic and obstetric characteristics were similar for age, body weight and height, body mass index,