ONDANSETRON FOR THE PREVENTION OF EPIDURAL FENTANYL INDUCED PRURITUS - A CASE REPORT

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SUMMARY
Ondansetron is known to prevent and relieve established pruritus following intravenous fentanyl. A case report is presented in which two epidurals were done in the same patient with an interval of three months between each. On the first occasion, pruritus occurred following epidural fentanyl and this was relieved by giving intravenous ondansetron. On the second occasion ondansetron was given prophylactically and on this occasion only mild pruritus occurred. Ondansetron may have a role in the prevention of epidural fentanyl induced pruritus and this has not been reported previously.

Keywords: Epidural opioid, epidural fentanyl, ondansetron, prophylaxis, pruritus.

INTRODUCTION
Infusion of a mixture of fentanyl and bupivacaine through an epidural catheter by a patient controlled analgesia machine is an effective technique of providing postoperative analgesia after major abdominal surgery. Pruritus is a known side effect of epidural fentanyl administration with a reported incidence 5-75%1-12. The current management strategies for opioid-induced pruritus are unsatisfactory13 but several agents like antihistamines14,15 droperidol16,17, nalbuphine18,21 nalaxone20,24, tenoxicam25 and propofol26-28 have been used with varying success. Ondansetron is commonly used for postoperative nausea and vomiting and has been successfully used in the treatment of pruritus induced by most commonly used epidural opioid29-35. It has also been suggested that prophylactic administration of ondansetron may have a role in the prevention of intravenous opioid induced pruritus34. This case report describes the use of ondansetron for the prevention of epidural fentanyl induced pruritus.

CASE REPORT
A 66-year-old 65 kg female, with a diagnosis of subacute intestinal obstruction was scheduled for laparotomy under general anaesthesia. She had suffered from myocardial infarction 12 months ago. She had undergone cardiac artery bypass graft surgery after 3 months but she continued to suffer from angina. Medications included atenolol (50mg) daily, aspirin (100mg) daily and sublingual glycerine trinitrate (5mg) when required. Her ECG was suggestive of an old myocardial infarction. Her urea, electrolytes and clotting profile were within normal limits. Lung functions were normal. There was no other systemic disease.

The patient received preoperative sedation with oral temazepam (20mg) and transdermal nitroglycerine patch (5mg). Routine patient monitoring was instituted with pulse oximetry, ECG and non-invasive blood pressure. An intravenous line was secured and the patient received one litre of 0.9% normal saline before the epidural was sited. Epidural catheter was inserted awake at T10-11 interspace under aseptic conditions. Proper placement of the epidural catheter was confirmed after a test dose of 3mls of 0.5% bupivacaine followed by 6mls of 0.5% bupivacaine. Pre-oxygenation was given before the induction of anaesthesia. General anaesthesia was induced with fentanyl (100mcg), propofol (140mg) and suxamethonium (100mg). Cricoid pressure was applied and the trachea was intubated. Anaesthesia was maintained with 33% oxygen, 66% nitrous oxide and 1% isoflurane. A triple lumen central line was secured into the right internal jugular vein. Intraoperative relaxation was maintained with atracurium and supplementary analgesia was provided with fentanyl (100mcg). Further monitoring included an oesophageal temperature probe and a nerve stimulator. A urinary catheter was in place. She had a large rectal tumour and a definitive surgery was not possible hence Hartman's resection surgery was performed. There were no other intraoperative complications related to surgery or anaesthesia. At the end of surgery the muscle relaxant was reversed with glycopyrrolate (600mcg) and neostigmine (2500mcg).

In the post anaesthesia recovery room an epidural infusion containing 0.1% bupivacaine and fentanyl 4mcg/ml was started at the rate of 6ml/hour with a bolus of 2ml and a lockout interval of 15 minutes through a patient controlled analgesia machine (APM II, Abbott Laboratories Inc, Illinois, USA). The upper level of the sensory block extended to T6 (sensation to cold spray) and the pain control was satisfactory (visual analogue pain scale). The patient was transferred to the high dependency unit for further postoperative care. On the same postoperative day the patient suffered from vomiting and dis-
tressing pruritus limited to the trunk. Diphenhydramine 50mg intravenously was administered to treat pruritus but was unsuccessful. One-hour later ondansetron 4mg was administered intravenously to treat the postoperative vomiting. There was no further episode of vomiting and it was also noted that there was a dramatic relief from pruritus. The epidural regimen was continued for 3 days without further episodes of vomiting and pruritus. On the 4th day an intravenous morphine patient controlled analgesia was substituted for the epidural. The patient received metronidazole (500mg) and cefoxorome (750mg), which were started on the first day of surgery and continued for four further days. The patient did not require blood transfusion during the postoperative period. Further postoperative period was uneventful and she was discharged home after 10 days.

She was rescheduled for anterior resection surgery after 3 months. There were no further changes in her medical conditions. On this occasion premedication included temazepam (10mg) and transdermal nitroglycerine patch (5mg). She was very keen to receive epidural analgesia for pain relief. Routine patient monitoring was instituted with pulse oximetry, ECG and non-invasive arterial pressure. Epidural catheter was again inserted awake at T11-T12 interspace under aseptic condition. Proper placement of the epidural catheter was confirmed after a test dose of 3mls of 0.5% bupivacaine followed by 6mls of 0.5% solution. On this occasion, ondansetron 4mg was administered intravenously before the induction of anaesthesia. Similar general anaesthetic technique was employed. Anterior resection of rectum was performed as planned uneventfully and there were no intraoperative surgical or anaesthetic problems. She was transferred to the high dependency unit for further management. Postoperative pain relief included patient controlled epidural analgesia utilising same volume and machine settings as during previous surgery. Postoperatively there was only mild itching limited to the trunk, which required no intervention. She continued to receive epidural analgesia for 3 days without any further itching and postoperative period was uneventful. The patient received similar antibiotics regimen and no blood transfusion was required during the postoperative period. She was discharged home after 2 weeks.

DISCUSSION

Pruritus or itch is a subjective, unpleasant and irritating sensation arising from the superficial layers of skin that provokes an urge to scratch.13 It is a common often distressing side effect associated with spinal opioid administration and incidence of opioid-induced pruritus varies widely.14-15 It is often elicited on direct questioning and there is associated high incidence of nausea and vomiting5 and depends on the opioid used and its mode of administration5.

The exact etiology of epidural opioid induced pruritus is not very well understood13,36,37. A variety of stimuli and substances such as histamine, substanceP, neuropeptides, calcitonin gene related peptide, neuropeptide Y, a vasoactive intestinal peptide, tryptase, chymotrypsin, kallikrein, papain, prostaglandins (E1 and E2) and serotonin have been implicated13.

Several agents have been reported to combat pruritus including antihistamines14,15, droperidol16,17, nalbuphine,18,21 naloxone,20-24, tenoxicam25 and propofol26-28. These agents have not been completely effective in the prevention or treating pruritus and all have additional side effects associated with their use30.

Published reports suggest that pruritus may be mediated by serotonergic pathway and this theory has lead researchers to use 5HT3 antagonist ondansetron in the treatment of opioid induced pruritus.29-33 As nausea and vomiting with pruritus are common features after epidural opioid administration, the use of ondansetron is very attractive.

This patient developed severe pruritus after epidural fentanyl infusion during first surgery and the relief from pruritus was observed following the administration of ondansetron. Other causes of pruritus in this patient such as blood transfusion, antibiotics etc were carefully considered and epidural fentanyl administration appeared to be the most probable cause. As ondansetron was effective in the treatment of pruritus during the first surgery, hence prophylactic administration of ondansetron was considered at the induction of anaesthesia during the subsequent surgery. Indeed the patient only suffered minor pruritus on this occasion. Although it is very difficult to prove that this patient would have definitely suffered severe pruritus but as there were minor itching sensations which suggest that it was very likely that she would have suffered from severe pruritus and ondansetron administration at the induction of anaesthesia had a role in the prevention of severe pruritus. Following this case ondansetron 4mg intravenously has been used in a further 48 patients without any report of severe pruritus.

In conclusion, this case report suggests that ondansetron 4mg given intravenously at the induction of anaesthesia may have a role in the prevention of epidural fentanyl induced pruritus.