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Intrathecal Morphine-induced Hypothermia after Caesarean Delivery and Reversal with a Short Acting Benzodiazepine

Reginald Caldecott*

Department of Anaesthesia, Portiuncula University Hospital, Ballinasloe, Ireland
*Corresponding author: Reginaldcaldecott@gmail.com

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Abstract This case report describes a patient with hypothermia induced via spinal morphine and its reversal with Lorazepam, a short acting benzodiazepine. The patient presented with refractory hypothermia following Caesarean section with paradoxical vasodilation and diaphoresis. The successful prompt reversal of the hypothermia with Lorazepam while maintaining pain relief highlights the benefit of its use in cases of morphine-induced hypothermia. However large clinical trials are still needed to verify the benefits of such treatment.

Keywords: *Morphine-induced hypothermia, Benzodiazipine, Lorazepam, spinal anaesthesia, Obstetric anaesthesia , cesarean delivery , medication adverse effect*

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1. Case Presentation

A 30-year-old woman primigravida, American Society of Anesthesiologists (ASA) status 2, underwent a category 1 emergency caesarean section for non-reassuring Cardiotocography (CTG) at 39 weeks gestation. The patient had no previous surgical history. Preoperative evaluation revealed no significant medical history or family history of anaesthetic problems. The patient had no known drug allergies. Examination revealed no significant systemic abnormalities and laboratory investigations where within normal ranges. Prior to theatre blood pressure was 124/71mmHg, heart rate 73bpm, oxygen saturation 99% on room air, respiratory rate of 16/min and oral temperature of 36.7°C. The patient consented to spinal anaesthetic for the procedure.

The patient was brought to theatre and placed in a sitting position while intravenous cannulation was done and monitors placed. The spinal was performed with local infiltration of 1% lignocaine at level L4-L5 and a 25G Whitacre needle was used to perform the spinal anaesthesia. A 2,4mL 0.5% bupivacaine glucose solution (Marcain Heavy) with 150µg morphine and 20µg fentanyl was administered intrathecally. The patient was then moved to a supine position. A T5 anaesthetic block was achieved. The baby was delivered within 2 minutes of incision with good cry at birth. Medication given for the procedure was Ephedrine boluses totalling 9mg, Phenylephrine 100µg, Augmentin 1.2g, Oxytocin 5U followed by 40u in 500ml Ringer's lactate and ondansetron 4mg. Total of 2L ringers lactate and 500mL Gelofusin was given throughout the procedure. Estimated blood loss was around 300mL at the end of the procedure. No maternal or foetal complications were noted.

Within 30 minutes of arrival in recovery there was difficulty in establishing temperatures and finally an axillary temperature of 34,4°C was recorded and forced air warmer applied to patient at 43°C. The patient was complaining of feeling hot and diaphoretic, this was accompanied by dizziness and nausea, another 4mg Ondansetron IVI was given stat. After 15 minutes with temperature unchanged, warmed IVI fluids (Hartman's solution) was initiated. With no change in 10 minutes, secondary causes of hypothermia were reviewed and blood taken for culture, Intrathecal morphine was considered as a cause for the hypothermia and 1mg Lorazepam IVI was given. 15 minutes later the patient was reviewed and she was no longer feeling warm or nauseous. Temperature was reviewed and it was now 35,9°C measured in the axilla. On discharge from the recovery unit her temperature had normalized to 36.5°C and the patient had no further complaints. The following day the patient was reviewed with no new hypothermic episodes noted and good pain relief. Blood cultures and full blood count revealed no signs of infection and patient was discharged from anaesthetic care.

2. Discussion

Morphine is commonly administered epidurally or intrathecally for caesarean section due to its prolonged and

powerful pain relief. There are however some unwanted side effects such as pruritus, nausea and vomiting, urinary retention, hypothermia, hypotension and respiratory depression. [1,2]

Morphine is a known cause of hypothermia in animals it has been theorised by altering the thermoregulatory point [3] and causing peripheral vasodilatation. Hypothermia is common following a caesarean section [4] and there is a need for anaesthetists to be constantly vigilant in detecting life-threatening hypothermia's which require prompt treatment in order to avoid any patient morbidity. We describe the diagnosis and treatment of a patient who experienced hypothermia in the post-operative period.

In this case study we recognized a patient who developed hypothermia post caesarean delivery. Although hypothermia can occur for a multitude of reasons including blunting of sympathetic response by regional anaesthetic agent, sepsis in the post-operative period or due to heat loss from the surgery and theatre environment. It was our belief that the patient symptoms were most likely caused by the intrathecal morphine administration.

The reasoning was that the patient did not have any clear history or signs of sepsis nor exhibit a typical response to hypothermia specifically shivering and vasoconstriction but instead was vasodilated and diaphoretic.

It has been described that regional anaesthesia does not inhibit the shivering response and even decreases the threshold for shivering by approximately 0.5°C [5] while it has been shown that regional anaesthetics increase the threshold for diaphoresis.[5]We would therefore expect the typical shivering response in case of regional anaesthetic sympathetic block. Furthermore, a case study by Su et al [6] found that significant diaphoresis from a spinal anaesthetic was likely to be a central effect of Morphine. While Fentanyl could also cause a similar affect, the short half-life of the drug compared to Morphine removes it from suspicion. The prompt resolution of symptoms and return to normothermia after administration of Lorazepam helps reinforce this hypothesis.

While the direct mechanism of intrathecal opioid-induced hypothermia is unknown the main theory is that the opioids have a thermoregulatory effect on the hypothalamus causing a higher set point causing patients to inappropriately vasodilate and sweat [6,7]. This effect is via opioid receptors found in the central nervous system, however the exact mechanism is unclear. While some investigators suggested μ-receptors others suggested κ-receptors as the primary mechanism [8]. A case report by Mach et el [9] showed promising results with Naloxone (a μ-receptors antagonist) 80μg in two divided doses.

As investigated by Rio-Garcia and Cremades [7] a GABA mechanism was postulated and found that benzodiazepines prevented hypothermia while Flumazenil (a benzodiazepine antagonist) worsened the hypothermia in rats. Hess et al [10] confirmed this with their case study wherein Lorazepam reversed symptomatic hypothermia in 80% of patients. They also noted that Midazolam (1-2mg) also reverses hypothermia but its effects would not last as long.

In an attempt to retain pain control in the postoperative period we opted for the benzodiazepine approach and by using a small dose of 1mg Lorazepam we were able to reverse the hypothermia, treat the symptoms while keeping the patient pain free. A low dose short acting benzodiazepine was advocated to avoid any potentially unwanted side effects in the post-operative period.

3. Conclusion

This case study described a hypothermic episode following an emergency caesarean section with Morphine, Fentanyl and Bupivacaine. While standard warming procedures such as air heating, fluid warming and blankets were unsuccessful we managed to treat the hypothermia with Lorazepam. We contend that in patients who do not respond to conventional therapy with signs of a vasodilation or diaphoresis and progressive hypothermia it is not amiss for the physician to suspect morphine causing thermoregulatory changes in the brain. In such a case in order to treat and prevent life-threatening hypothermia it is not unreasonable for the physician to attempt low dose Lorazepam to correct the hypothermia. To note that no large clinical trials have been conducted on the treatment of spinal morphine-induced hypothermia and certainly further trials should be conducted to verify the therapeutic benefit of benzodiazepines or other drugs in treatment of this.

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Declaration Conflict of Interest

The authors declare no conflict of interest.

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