Intrathecal Opioid–Induced Hypothermia Following Subarachnoid Block With Morphine Injection for Elective Cesarean Delivery: A Case Report

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Opioids have been administered intrathecally with subarachnoid block for postoperative pain relief in parturients undergoing elective cesarean deliveries. This case report presents the uncommon occurrence of intrathecal opioid–induced hypothermia in the latent phase of recovery following elective cesarean delivery. There are few case reports on the occurrence of latent-phase postanesthesia care hypothermia in patients receiving subarachnoid block with morphine sulfate injection (Duramorph). Hypothermia can occur postoperatively for many reasons and can be life-threatening. In this case, hypothermia developed and progressed throughout the postoperative period. The causes of hypothermia were evaluated and treated without success initially. Thyroid dysfunction and alternative differential diagnoses were ruled out. Further assessment determined that the morphine injection might have been a contributing factor. Naloxone at 40-μg increments was administered intravenously and corrected the hypothermia. Awareness of hypothermia postoperatively with associated morphine administration through subarachnoid block must be ruled out in cases of progressing hypothermia.

Keywords: Cesarean delivery, hypothermia, morphine injection (Duramorph), postanesthesia care, subarachnoid block.

Intrathecally administered opioids have been used as an adjunct for postoperative pain relief after cesarean delivery. Although many benefits exist, there may be some unwanted side effects of the opioids. Anesthesia providers should be aware of the causes of hypothermia, which may be life-threatening. Prevention and recognition of contributing factors must be identified to help reduce morbidity and mortality in these rare cases. This case report describes the diagnosis and successful treatment of a young woman who experienced mild hypothermia (34.4°C [93.8°F]) in a 4-hour period after cesarean delivery.

Case Summary
A 29-year-old woman, gravida 4, para 1, ASA physical status 2, was scheduled for a primary cesarean delivery because of the diagnosis of breech presentation at gestation of 39 weeks and 1 day. The patient had a history of 2 previous miscarriages and a surgical history for minimal dental work. A previous spontaneous vaginal delivery occurred in 2011 without the aid of any narcotics, epidural analgesia, or pain relief. Preanesthetic evaluation showed no family history of anesthesia complications or any remarkable medical history. Thyroid function screening showed no abnormal values. The patient had no known drug allergies and was taking prenatal vitamins. She was 157.5 cm (5 ft 2 in) tall, weighed 67.5 kg (150 lb), and was neurologically intact. All bloodwork results were within normal limits. Her vital signs included blood pressure (BP) of 119/66 mm Hg, heart rate (HR) of 73/min, respiratory rate of 18/min, oxygen saturation of 97% on room air, and an oral temperature of 36.8°C (98.2°F). The patient gave consent for subarachnoid block with morphine sulfate injection (Duramorph) for pain control.

The patient was brought to the operating room in a sitting position. Preoperative antibiotics, 3 g of ampicillin-sulbactam (Unasyn), were given intravenously. Monitors were placed, and the patient was prepared for subarachnoid block with povidone-iodine solution (Betadine) in the sitting position and was sterilely draped. A skin wheal was created with local injection of 1% lidocaine at level L3-L4. A 25-gauge Whitacre needle was introduced after 1 attempt, and cerebrospinal fluid was obtained, with no paresthesia and no visible blood. A 0.75% concentration of bupivacaine hydrochloride in 8.25% dextrose (1.4 mL) and 200 μg of morphine (Duramorph) was administered, for a total volume of 1.6 mL.

The patient was placed supine with left uterine dis-
placement. An anesthetic level of T4 was achieved. A warming-blanket system (Gaymar, Gaymar Industries Inc) was applied and implemented after a sterile field was created with drapes. The baby was delivered within 5 minutes of the surgical incision, and Apgar scores were 8/9 at 1 and 5 minutes. The patient’s skin temperature was maintained at 36°C throughout the procedure. No adverse outcomes occurred throughout the anesthetic, and the cesarean delivery went as planned without complications. Intravenous medications given throughout the procedure included ephedrine, 60 mg; oxytocin (Pitocin), 40 U; and ondansetron (Zofran), 4 mg. Total warmed intravenous fluids of lactated Ringer’s solution totaled 1,800 mL. Estimated blood loss was less than 500 mL. Urine output was 200 mL. The total operating room time was 1 hour and 6 minutes, which included 40 minutes of surgical time.

The patient was transferred to the postanesthesia care unit (PACU) in stable condition; her vital signs were BP of 109/59 mm Hg, HR of 58/min, oxygen saturation measured by pulse oximetry of 98% on room air, and scanned forehead temperature of 36°C (96.8°F). The patient had an uneventful stay in the PACU, which did not require forced-air warming. Warm blankets were applied as the patient was discharged to the obstetrics unit in satisfactory condition 1 hour postoperatively; her temperature was 36.0°C (96.8°F).

On the obstetrics unit 30 minutes after discharge from the PACU, the patient complained of feeling hot and diaphoretic. Temporal artery scanning of her forehead revealed a 35.0°C (95.0°F) temperature. The patient began vomiting and feeling dizzy; ondansetron, 4 mg, was given intravenously for nausea and vomiting, with unsuccessful results. Warm blankets were applied, and a warming system (Gaymar) was started at 43°C. After 60 minutes, the temperature continued to decrease to 34.9°C (94.8°F). Infusions of warmed intravenous fluids were started. After 90 minutes, there was no therapeutic response from aggressive warming. The obstetrical staff was unable to obtain an oral temperature but recorded a temperature of 34.4°C (93.8°F) rectally. The patient appeared somewhat lethargic and slow to respond, with shivering and decreasing temperatures. Intravenous fluid warming, warm blankets, and warmed forced-air machines (Gaymar) were implemented, with no success in treating the hypothermic reaction.

Secondary causes of hypothermia were reviewed that could account for nonresponsive treatment to warming devices. Intrathecal morphine administration was considered a potential implicating factor. For maintenance of pain control and in an attempt at reversing hypothermia, naloxone was administered at 40-μg increments intravenously. After the first 40 μg of naloxone, the patient started to respond 8 minutes later with an increasing temperature of 34.6°C (94.3°F) rectally. An additional 40 μg of naloxone was administered and the temperature at 15 minutes after administration increased to 35.7°C (96.2°F) rectally. The patient was becoming more responsive, and her nausea was residing.

The patient’s temperature was monitored on the obstetric unit for the next 30 minutes, and then she was transferred to the critical care unit for closer observation. The first temperature there was 36.1°C (97.0°F) by temporal artery scan of the forehead and 36.7°C (98.0°F) rectally. Use of the fluid warmer was discontinued, and the warming blanket was maintained at 38°C. Temperature thereafter each hour was maintained at 36.7°C (98.0°F) temporally and 36.9°C (98.3°F) orally. A magnesium level of 1.6 mmol/L was the only abnormal laboratory value and was treated intravenously. Naloxone was kept at bedside but was not readministered, because the patient maintained normothermia thereafter. The patient was interviewed the next day regarding pain control and responded with a pain score of 2 of 10, showing good relief.

The elapsed time of the hypothermic reaction from the intrathecal administration of morphine was 2 hours. Hypothermia was treated with 80 μg of naloxone, with no other administration from the time the patient had returned to a normothermic state.

**Discussion**

- **Thermoregulation.** The hypothalamus controls thermoregulation, attempting to maintain a core temperature of 37.0°C (98.6°F). Temperature regulation centers are located in the anterior portion of the hypothalamus. Receptors for temperature in the skin and accessory membranes send signals to the anterior portion of the hypothalamus, which interprets information and sends this to the posterior hypothalamus. Internal structures, which include the hypothalamus, send signals to the posterior portion of the hypothalamus to control heat regulation and inhibit certain reactions of the body to conserve heat loss or gain. This thermoregulation center works in conjunction with the autonomic nervous system and different hormones that may change the body’s response to varying temperature gains or losses. The body’s response to these signals may include norepinephrine release from sympathetic fibers constricting skin vessels, brown-fat oxidation, epinephrine release from the adrenal medulla increasing thermogenesis, or release of thyrotropin hormone from the hypothalamus inducing thyroid hormones to increase metabolism and body heat production.

Temperature and body heat in the perioperative setting are most commonly affected by 5 mechanisms: radiation, conduction, convection, evaporation, and respiration. A secondary contributing factor includes dysfunction of the central nervous system in relation to pharmacologic effects. The Table shows the classifications and clinical signs and symptoms that may accompany hypothermia.
reaching specific areas of the brain. Therefore, adverse 
may result in high concentrations of morphine directly 
urinary retention.

depression, sedation, nausea and vomiting, pruritus, and common adverse effects include early and late respiratory 
ways of reversing the hypothermic effects. Sayyid et al7 
This study confirmed the hypothermia but did not show 
fluid that interferes with the thermoregulation center.

is a cephalic spread of morphine in the cerebrospinal 
decrease body temperature. The largest decrease was 
of 150 μg of morphine during spinal anesthesia would 
controlled study that showed intrathecal administration 

a sublingual temperature of 33.6°C developed. All active 
administration. Reviewed case reports of hypothermia de-

reports of hypothermia attributed to intrathecal opioid 

Circulation of the drug throughout the spinal fluid 
may result in high concentrations of morphine directly 
reaching specific areas of the brain. Therefore, adverse 
effects reported may also interfere with thermal regula-
tion based on the activity in the hypothalamus.

• Literature Review. The literature describes few case 
reports of hypothermia attributed to intrathecal opioid 
administration. Reviewed case reports of hypothermia de-
scribe associated symptoms of excessive sweating, nausea 
and vomiting, and pruritus after intrathecal administra-
tion of morphine sulfate. One controlled study evalu-
ated hypothermic effects of intrathecally administered 
morphine and spinal anesthesia for cesarean deliveries. 

Two case reports were found that described treatment of 
intrathecal opioid–induced hypothermia with naloxone.

Hui et al6 performed a randomized double-blind 
controlled study that showed intrathecal administration 
of 150 μg of morphine during spinal anesthesia would 
decrease body temperature. The largest decrease was 
34.3°C. Their results supported the conclusion that there 
is a cephalic spread of morphine in the cerebrospinal 
fluid that interferes with the thermoregulation center. 
This study confirmed the hypothermia but did not show 
ways of reversing the hypothermic effects. Sayyid et al7 
described similar findings in a case report of a spinal 
anesthesia during cesarean delivery with use of 12 mg 
of bupivacaine and 200 μg of morphine (Duramorph). 

Symptoms developed 3 hours after administration, and 
a sublingual temperature of 33.6°C developed. All active 
rewarming devices were unsuccessful, but the adminis-
tration of naloxone, 400 μg intravenously, returned the 
patient to a normothermic state immediately. In another 
case report of cesarean delivery, Harkouk et al8 used 
bupivacaine, 10 mg, with mixed opioids: sufentanil, 50 
μg, and morphine (Duramorph), 50 μg. The patient’s 
temperature had dropped to 34°C, and the patient was 
treated with naloxone 400 μg, creating a partial recovery 
of normothermia. This took an additional 7 hours for full 
recovery with active rewarming devices.

Other case reports identified use of lorazepam as a 
reversal agent so that there would not be any interfer-
ence with pain management postoperatively. Ryan et al9 
reported a patient undergoing total knee replacement 
experiencing hypothermia after morphine (Duramorph) 
administration and used lorazepam, 0.5 mg sublingually, 
to reverse opioid-induced hypothermia. The response 
time was approximately 25 minutes, and the patient 
slowly returned to baseline by the next day. A case study 
presented by Hess et al10 showed that patients treated 
with lorazepam had a cessation of symptoms and increasing 
body temperatures within 90 minutes. The results of 
their study showed improvements from patients who had 
temperatures less than 35.8°C.

The direct mechanism of intrathecal opioid-induced 
hypothermia is still unknown. However, the aforemen-
tioned case reports suggest there may be a correlation 
with the morphine circulating to the hypothalamus 
and exerting an inhibitory pharmacologic effect on the 
control center. Whereas the body would normally receive 
stimuli that it is cold and the thermoregulation center 
would respond appropriately by sending out appropriate 
signals, the morphine interrupted the opioid receptor 
signals, causing the hypothalamus to interpret that the 
body was normothermic. This would inhibit the thermo-
regulation center, causing hypothermia.

It was our attempt to maintain pain control with the 
addition of naloxone at minimal amounts to reverse 
the hypothermic episode that lead to our incremental 
low-dose approach. This proved successful. The patient 
responded with a minimal amount of narcotic antagonist 
and maintained normothermic temperatures throughout 
the course of her stay. The treatment required to reverse 
the narcotic-induced inhibition of the thermoregulation 
center is the administration of a narcotic antagonist.

Conclusion
This case report described a major hypothermic event

<table>
<thead>
<tr>
<th>Classification of hypothermia</th>
<th>Temperature, Celsius (Fahrenheit)</th>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Mild</td>
<td>32.2 - 35.0°C (89.96 - 95.0°F)</td>
<td>Hypertension, shivering, tachycardia, tachypnea, vasoconstriction, apathy, decreased kidney function, and impaired judgment</td>
</tr>
<tr>
<td>Moderate</td>
<td>28.0 - 32.1°C (82.4 - 89.8°F)</td>
<td>Apnea, coma, nonreactive pupils, oliguria, pulmonary edema, ventricular dysrhythmias, and asystole</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 28°C (&lt; 82.4°F)</td>
<td>Life-threatening cardiopulmonary arrest and end-organ failure</td>
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Table. Classification and Clinical Signs and Symptoms of Hypothermia
2 hours following an elective cesarean delivery with the intrathecal injection of morphine sulfate (Duramorph). Attempts with various warming devices were unsuccessful treatment modalities, which lead us to secondary causes of hypothermia. The intrathecal administration of morphine in rare cases has been shown to affect the thermoregulation center of the hypothalamus. Although the direct mechanism is not understood, the treatment of hypothermia related to secondary administration of morphine can be treated with minimal amounts of the narcotic antagonist naloxone. The patient responded in a timely manner with adequate pain control. If hypothermia does not respond to conventional warming devices, one can suspect that morphine injection may be the primary contributing factor. The thermoregulation center of the hypothalamus may be altered by the pharmacologic effects of intrathecally injected morphine and must be evaluated for the treatment of hypothermia.

REFERENCES

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The authors have declared no financial relationships with any commercial interest related to the content of this activity. The authors did not discuss off-label use within the article.

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