

Will the Body Temperature be Affected by Lowering Intrathecal Morphine Dose from 100 to 50 Micrograms?

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Abstract

Hypothermia has been reported in parturient undergoing caesarean section during spinal anesthesia. Hypothermia has been reported when a large dose of morphine was used in spinal anesthesia as well as in smaller doses of morphine; however it is not studied yet whether a very small dose of morphine (50 µg) would affect the body temperature without changing the analgesia effect. Our study was performed to determine if the body temperature will be affected significantly by lowering the intrathecal dose of morphine from 100 to 50 micrograms. We performed a prospective randomized double blinded study on parturients scheduled for elective caesarean sections under spinal anesthesia. Body temperatures data was processed using t-test with p-value >0.05. There was no statistical significance in the average body temperatures between patients getting intrathecally 50 versus 100 µg of morphine. Our study demonstrated that the body temperature is not affected by decreasing the intrathecal dose of morphine with no change in parturient's pain scale.

Keywords: Hypothermia; Intrathecal Morphine; Spinal anesthesia

Introduction

Intrathecal morphine is an analgesic medication commonly used in spinal anesthesia for a variety of surgical procedures, including caesarean sections. Large doses of morphine are rarely used in current obstetric anesthetic practice due to significant side-effects such as nausea, vomiting, shivering, pruritus, urinary retention and delayed respiratory depression [1,2]. Therefore, smaller doses of morphine are used instead for caesarean section [3,4]. Hypothermia has been reported in parturients undergoing caesarean section during spinal anesthesia [5]. Morphine prolongs the duration of per- and post-operative analgesia when added to bupivacaine and local anesthetics [6]. Hypothermia has been reported when a large dose of morphine was used in spinal anesthesia as well as in smaller doses of morphine however it is not studied yet whether a very small dose of morphine (50 µg) would affect the body temperature without changing the analgesia effect [7-9]. Our randomized double-blind study was performed to determine if the body temperature will be affected significantly by lowering the intrathecal dose of morphine from 100 to 50 micrograms in parturients during elective caesarean section under spinal anesthesia.

Methods and Materials

We performed a prospective double blinded randomized study over a period of four months between February 1st and May 30th, 2013. We included parturients undergoing caesarean sections performed under spinal anesthesia. This research work was done in the service of Anesthesiology and Gynecology at the Holy Spirit University Hospital-Our Lady of Help in Jbeil, Lebanon. Our study was approved by the institutional reviewing board of the University Hospital.

A power analysis was done to determine the sample size necessary to detect a temperature difference of 0.5°C with a value of 0.05. The estimated sample size for each group of parturients was 20. We included 48 parturients divided equally in two groups. Each parturient was assigned either to Group A or Group B following a computerized double blinded randomized approach. Group A consisted of 24 parturients receiving 10 mg of Marcaine (bupivacaine 0.5%) and 50 µg of morphine in single intrathecal injection. Group B consisted of 24 parturients receiving 10 mg of Marcaine (bupivacaine 0.5%) and 100 µg of morphine in single intrathecal injection. The data were processed

by the SPSS system and Student's *t*-test was utilized to compare the two groups. A p-value less than 0.05 were considered statistically significant.

Inclusion and exclusion criteria were implemented as the following:

Parturients' Inclusion Criteria

- Having a scheduled caesarean section under spinal anesthesia
- Taller than 1.55 meter (5.08 ft)
- Classified as ASA I or II

Parturients' exclusion criteria

- Less than 18 years old
- Patients taking medications interfering with thermoregulation (vasodilator, antipsychotic)
- Contraindication to spinal anesthesia (bleeding disorder)
- Contraindication to bupivacaine and morphine
- Contraindication to paracetamol: allergy, hypersensitivity to paracetamol, hepatic failure, hepatic porphyria, G6PD deficiency
- Contraindication to ketoprofen
- Having a twin pregnancy
- Severe hepatocellular insufficiency (with encephalopathy)
- Uncontrolled epilepsy

Intravenous fluids given to all parturients were prewarmed to 37°C and the room temperature was kept constant at 24°C. Body temperatures were recorded from the same ear with an infrared

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tympanic thermometer (Welch Allyn[®], Skaneateles Fall, NY, USA). A basic temperature was obtained and labeled as T_{basic} (Table 2). Patients were monitored continuously during the first six hours, then regularly over 24 postoperative hours. This monitoring included Heart Rate (HR), Blood Pressure (BP), Body Temperature, and pain assessment using the Simple Verbal Scale (SVS).

A 22-Gauge spinal needle was introduced into the subarachnoid space at the L3-L4 or L4-L5 interspace in the sitting position. Body temperature was recorded immediately after spinal anesthesia as T₀, and then at different time intervals over 24 hours as labeled in Table 2.

Results

The basic characteristics of the two groups are shown in Table 1. Eight patients (33%) in group A and 7 (29%) in group B had previous C-sections. Both groups were classified as ASA I or II. There was no statistical significance in the average body temperatures between parturients getting intrathecally 50 versus 100µg of morphine (Table 2). The time to nadir temperature was not significantly longer (79 vs 82 minutes; $p=0.67$) between the two groups (Chart 1).

The maximum decrease in temperature from a 37°C baseline was 34.9°C recorded after 4 hours of spinal injection, then after a body temperature was recorded at T₆ in the order of 35.2°C, 36.5°C at T₁₂ and T₂₄. This was not statistically significant when comparing the corresponding means between the two groups.

The first requested dose of analgesic was after 7 hours on average in parturients who have received a dose of 50 µg and after 9 hours for

Parturients' Characteristics:	Groupe A (50 µg)	Groupe B (100 µg)
Average age (years)	29.85 ± 2.57	30 ± 3.19
Average height (cm)	161.8 ± 2.87	162.6 ± 2.53
Average weight (kg)	76.29 ± 5.97	78.25 ± 6.96
Average operating time (min)	44.40	43.30

Table 1: The mean age, height, weight and duration of operation between the two groups of parturients during elective caesarean section under spinal anesthesia.

T°C	Group A (50 µg)	Group B (100 µg)	p-value	SVS/A	SVS/B
T basic	36.83 ± 0.19	36.87 ± 0.13	0.31		
T ₀	36.67 ± 0.42	36.34 ± 0.16	0.29	2	2
T ₃	36.22 ± 0.34	36.39 ± 0.12	0.59	2	3
T ₄	36.51 ± 0.22	36.88 ± 0.14	0.33	3	2
T ₆	36.66 ± 0.35	36.68 ± 0.19	0.28	2	3
T ₁₂	36.59 ± 0.17	36.87 ± 0.22	0.76	3	3
T ₂₄	36.77 ± 0.11	36.71 ± 0.12	0.33	3	3

Table 2: Average body temperatures in °C and pain scores at different times after intrathecal administration of morphine 50 µg (group A) and 100 micrograms (group B) in parturients during elective caesarean section under spinal anesthesia.

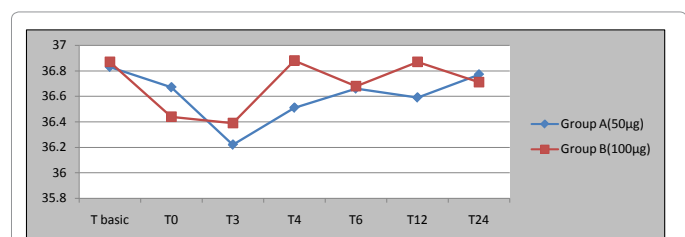


Chart 1: The body temperatures are plotted at different time intervals after intrathecal administration of morphine 50 µg (group A) and 100 micrograms (group B) in parturients during elective caesarean section under spinal anesthesia.

the other group. In both groups, the simple verbal scale of pain was between 2 and 3. Group A (50 µg) did not have any significant side-effects such as nausea, vomiting, shivering, pruritus, urinary retention nor delayed respiratory depression. Four patients of Group A (100 µg) had nausea, that responded well to intravenous Dimenhydrinate 25 mg.

Discussion

Several mechanisms for hypothermia associated with spinal anesthesia have been reported. The hypothalamus, the main thermoregulatory center, maintains core temperature close to 37°C. Morphine may play a role in hypothermia by altering the temperature set point in the hypothalamus. The compensatory responses to hypothermia such as shivering and vasoconstriction can be blunted in spinal anesthesia [10].

Hypothermia is the result of many factors taking place through two mechanisms. The three factors are the patient's exposure to a cold environment, inhibition of thermoregulation by anesthetic agents and a negative energy balance. Both mechanisms are internal redistribution and thermal losses [11]. The mechanism of hypothermia is the same as that under general anesthesia and spinal anesthesia, and it is divided into three phases: The initial drop in core temperature is mainly due to a phenomenon of internal redistribution of heat. It will cause a fall of 0.5 to 1.5°C in core temperature during the first hour of anesthesia. The slower decline in the second period, for 2 to 3 hours, is the result of a negative caloric balance, when heat loss is exceeding production. The second phase is followed by a heat plateau in which the core temperature does not fall, while the heat content in the periphery continues to decrease. This corresponds to the involvement of cutaneous vasoconstriction that is effective enough to maintain core temperature [12].

Studies on animals have shown that the effect of morphine on thermoregulation is dose-dependent, with low doses causing hyperthermia and larger doses causing hypothermia [13]. In a randomized controlled study of 60 parturients undergoing Cesarean delivery, Hui et al. compared the temperatures of those undergoing spinal anesthesia using bupivacaine 10-12 mg with intrathecal morphine 150 µg with those undergoing spinal anesthesia using bupivacaine 10-12 mg without morphine but an equivalent volume of intrathecal 0.9% saline [14]. There were decrease in tympanic temperatures in both groups, but the morphine group experienced a larger decrease than the placebo group. The lowest tympanic temperatures were 34.3°C and 35.2°C in the morphine and placebo groups, respectively [12]. Kavee et al. observed that the addition of intrathecal morphine in patients who underwent elective caesarean section had average body temperature decrease of 1.4°C lasting up to 24 hours [7].

The major hypothermia after intrathecal injection of morphine has been reported in several clinical cases including dozens of obstetric and non-obstetric patients, where the lowest temperature was 33.2°C and the duration of hypothermia ranged from 2 to 22 hours as demonstrated in Table 3 [8,15-18].

Fentanyl and subfentanyl medications were used in addition to the anesthetic and morphine in all studies listed in Table 3, except Sayyid's study. This may provide an explanation for the difference in the lowest body temperatures in the order of 36°C as seen in our series, when compared to the range of 33-34°C in above cited studies.

All recent clinical studies agree on the adverse effects of intra-operative hypothermia: the increase in bleeding, infection and cardiovascular risk. During spinal anesthesia, hypothermia may also occur and can be as severe as in general anesthesia [19]. Palmer et al.

Studies:	Products	Lowest Temperature (°C)
Wishaw ¹⁶	Bupivacaine: 11mg Fentanyl: 10 µg Morphine: 250 µg	33.6
Peillon et al. ¹⁷	Bupivacaine: 10mg Sufentanil: 2.5 µg Morphine: 100 µg	33.6 34.6
Sayyid et al. ⁸	Bupivacaine: 12mg Morphine: 200 µg	33.6
Kosai et al. ¹⁸	Tetracaine 0.5%: 14 mg Phenylephrine: 3.5 mg Morphine: 140 µg	34.0
Hess et al. ¹⁹	Bupivacaine: 11.25 mg Fentanyl: 25 µg Morphine: 250 µg	34.9
Fisher et al. ¹⁵	Bupivacaine: 10 mg Morphine: 100 µg	33.2

Table 3: Publications of hypothermia post spinal anesthesia for cesarean.

showed that there is no increase in analgesic effect between 100 and 400 µg of intrathecal morphine, but with a dose of 400 µg, pruritus is observed [20]. Uchiyama et al. have shown that there are more side effects with 200 µg intrathecal morphine and a dose of intrathecal morphine <100 µg produced less nausea and vomiting than what was observed with 100 µg [21]. Similarly Yang et al. found no difference between the 100 and 250 µg of morphine, but there was an increase in the occurrence of nausea and pruritus with 250 µg of intrathecal morphine [22]. In our study, there were no significant side-effects such as nausea, vomiting, shivering, pruritus, urinary retention or delayed respiratory depression seen in the group A, who has received intrathecally the very small dose (50 µg) of morphine.

In addition, the first requested dose of analgesic was after 7 hours on average in patients who received the dose of 50 µg and after 9 hours after the injection of 100 micrograms. In both groups, the pain scale was tolerable with a score between 2 and 3. Our study limitation was the small sample size when compared to other research topics. However, most peer studies included less than 30 patients in terms of sample size [23]. A study performed by Wong included a larger sample, but it was retrospectively performed [24]. Our study was prospectively performed with a powerful and adequate sample size. Another limitation consisted in including only parturients taller than 1.55 meters (5.08 ft), however this was set to be compatible with most peer studies.

Conclusion

There was no difference in body temperatures between patients getting intrathecally 50 versus 100 µg of morphine. Our study demonstrated that the body temperature is not affected by decreasing the intrathecal dose of morphine. We have also demonstrated that the analgesia effect of intrathecal morphine did not change significantly between 50 and 100 µg.

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