The Analgesic and Adverse Effects of Intrathecal Opioids for Cesarean Section: 11 Years’ Experience in 10,061 Cases

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Authors’ contributions

This work was carried out in collaboration between all authors. Author MSN designed the study, wrote the protocol, performed the statistical analysis, managed the literature searches and wrote the first draft of the manuscript. Author RQY collected the data from the records. All authors read and approved the final manuscript.

ABSTRACT

Purposes: To evaluate analgesic effect and adverse effects of intrathecal morphine and fentanyl in parturients undergoing cesarean section.

Methods: This is a retrospective, descriptive study from anesthetic and recovery room records from January 2001 to August 2011.

Results: From this 11-year retrospective, descriptive analysis in 10,061 patients undergoing cesarean section who received intrathecal opioids, it had been found that their pain scores both at rest and with movement were mild and moderate, respectively. Nausea / vomiting and pruritus were common complications but no patient experienced respiratory depression.

Conclusions: Intrathecal morphine is effective for controlling postcesarean pain with minor adverse effects.

Keywords: Analgesic effects; adverse effects; intrathecal morphine; parturients; cesarean section.
1. INTRODUCTION

Cesarean section is a very common operative procedure on a daily basis. Spinal anesthesia is an anesthetic of choice for parturients scheduled for this operation. In general, the patients have pain following the operation which leads to unwanted consequences including immobilization which prevent them from nursing their babies. One of the methods to provide postoperative pain relief is an intrathecal opioid given while spinal anesthesia is performed.

Morphine and fentanyl are frequently utilized for intrathecal analgesia. In our institute, we usually use intrathecal morphine 0.2 mg in parturients undergoing cesarean section and we started to use it about 10 years ago. We retrospectively analyzed data in 10,061 patients regarding analgesic effect and adverse effects of intrathecal morphine with a small number of patients receiving intrathecal fentanyl.

2. MATERIALS AND METHODS

This retrospective, descriptive study was approved by the Ethics Committee of our institute. Data for evaluation were included from January 2001 to August 2011 from the anesthetic and recovery room records.

We included all patients who underwent cesarean section under spinal anesthesia using 2-2.2 ml of hyperbaric bupivacaine and received an intrathecal opioid (either morphine or fentanyl). Data from the anesthetic records for analysis included age, body weight, height, BMI, ASA physical status, techniques performed and intraoperative complications. Data from the recovery room records for analysis included complications. Data of postoperative events occurring within 24 hours after intrathecal injection included maximum pain intensity at rest and while moving (rated with numerical rating score 0-10 when 0 = no pain and 10 = worst pain imaginable) and complications.

Data are presented as mean ± SD or percentage.

3. RESULTS

This retrospective, descriptive study involved 10,061 parturients undergoing cesarean section. The demographic data are shown in Table 1. All of them received either intrathecal morphine (10,051 patients, 99.9%) or fentanyl (10 patients, 0.01%). The dose of intrathecal morphine used was 0.2 mg.

Within 24 hours after intrathecal injection, the average pain intensities at rest (n = 5,575) and with movement (n = 4,454) were 2.2±2.0 and 5.1±2.2, respectively. Table 2 represents the prevalence of patients having each intensity of pain. The majority of the patients (3,940, 70.7%) had none to mild pain at rest (NRS 0-3) and 2,778 of them (62.5%) had none to moderate pain with movement (NRS 0-5).

The intraoperative, recovery room’s and 24-hour postoperative complications (nausea / vomiting, pruritus and respiratory depression as defined as respiratory rate less than 8 bpm) are demonstrated in Table 3. Since the beginning of our use of intrathecal opioids, mainly morphine in parturients undergoing cesarean section, there was no report of respiratory depression defined as respiratory rate less than 8 bpm either with early or delayed onset.
Table 1. Background data of the reviewed population (n = 10,061)

| Data                        | Number (mean±SD) | ASA classification** | Intrathecal opioid | Type of operation | Type of anesthetic technique |
|-----------------------------|------------------|----------------------|--------------------|-------------------|-----------------------------|
| Age (years)                 | 30.5 ± 5.3       | - I                  | - Morphine         | - Elective        | - Regional anesthesia       |
| Body weight (kg)            | 68.1 ± 10.7      | - II                 | - Fentanyl         | - Emergency       | - Regional then general anesthesia |
| Height (cm)                 | 156.0 ± 5.8      | - III                |                    |                   |                             |
| BMI* (kg/m²)                | 28.0 ± 4.0       |                      |                    |                   |                             |
| Data                        | Number (%)       |                      |                    |                   |                             |
| ASA classification**        |                  |                      |                    |                   |                             |
| - I                         | 3,683 (36.6%)    |                      |                    |                   |                             |
| - II                        | 6,220 (61.8%)    |                      |                    |                   |                             |
| - III                       | 158 (1.6%)       |                      |                    |                   |                             |
| Intrathecal opioid          |                  |                      |                    |                   |                             |
| - Morphine                  | 10,051 (99.9%)   |                      |                    |                   |                             |
| - Fentanyl                  | 10 (0.1%)        |                      |                    |                   |                             |
| Type of operation           |                  |                      |                    |                   |                             |
| - Elective                  | 5,246 (52.1%)    |                      |                    |                   |                             |
| - Emergency                 | 4,815 (47.9%)    |                      |                    |                   |                             |
| Type of anesthetic technique|                  |                      |                    |                   |                             |
| - Regional anesthesia       | 10,022 (99.6%)   |                      |                    |                   |                             |
| - Regional then general anesthesia | 39 (0.4%)  |                      |                    |                   |                             |

*BMI: body mass index

**ASA: American Society of Anesthesiologists

Table 2. Prevalence of the patients for each pain intensity within 24 hours after intrathecal injection (n = 10,061)

| NRS* | At rest (n = 5,575) | With movement (n = 4,454) |
|------|---------------------|---------------------------|
|      | Number (%)          | Number (%)                |
| 0    | 1,913 (34.3%)       | 92 (2.1%)                 |
| 1    | 315 (5.7%)          | 74 (1.7%)                 |
| 2    | 889 (15.9%)         | 307 (6.9%)                |
| 3    | 823 (14.8%)         | 657 (14.8%)               |
| 4    | 987 (17.7%)         | 573 (12.9%)               |
| 5    | 408 (7.3%)          | 1,075 (24.1%)             |
| 6    | 110 (2.0%)          | 494 (11.1%)               |
| 7    | 71 (1.3%)           | 486 (10.9%)               |
| 8    | 33 (0.6%)           | 435 (9.8%)                |
| 9    | 4 (0.1%)            | 75 (1.7%)                 |
| 10   | 22 (0.4%)           | 186 (4.2%)                |

Data presented as number and percentage per each NRS (0-10)

*NRS = numerical rating score

Table 3. Intraoperative, recovery room’s and 24-hour postoperative complications (n = 10,061)

| Complications               | Intraoperative | Recovery room’s | Postoperative |
|-----------------------------|----------------|-----------------|--------------|
| Nausea / vomiting           | 1,686 (16.8%)  | 1,075 (10.7%)   | 2,217 (22.0%)|
| Pruritus                    | 188 (1.9%)     | 944 (9.4%)      | 5,749 (57.1%)|
| Respiratory depression (< 8 bpm) | 0 (0%)        | 0 (0%)          | 0 (0%)       |
4. DISCUSSION

From this 11-year retrospective, descriptive analysis in 10,061 patients undergoing cesarean section with majority of them received intrathecal morphine 0.2 mg, we found that their pain scores both at rest and with movement were mild and moderate, respectively. Nausea / vomiting and pruritus were common complications but no patient experienced respiratory depression.

Intrathecal administration of opioids leads to potent and selective analgesia in living creatures including animals and humans [1]. It is widely utilized to relieve postoperative pain in parturients undergoing cesarean section [2-4] and non-obstetrical patients undergoing non-cesarean section [5,6]. Intrathecal morphine has been found to be more superior in terms of postoperative pain relief compared to the more modern technique of ultrasound-guided transversus abdominis plane (TAP) block after cesarean section. However, it has also been found to cause a higher incidence and severity of nausea, vomiting and pruritus [7].

Many trials aimed to compare different doses of intrathecal morphine for postcesarean analgesia [8-12]. Craig et al. [9] and Girgin et al. [12] have discovered that intrathecal morphine 0.1 mg provides similar analgesia in comparison to higher doses including 0.4-0.5 mg. Rathmell et al. [13] recommended 0.1 mg of intrathecal morphine as the optimal dose for cesarean section. Abouleish et al. [14] has demonstrated that a combination of morphine 0.2 mg and spinal hyperbaric bupivacaine prolongs adequate postoperative analgesia in cesarean section patients and is safe in both mothers and babies as evaluated by the Apgar score together with arterial and venous umbilical blood gas tensions plus acid-base status. At our institute, we routinely use 0.2 mg of morphine for intrathecal administration in cesarean section patients and we have found that it produces good analgesic coverage and is safe which is compatible with what demonstrated by Abouleish et al. [14].

Apart from morphine, other opioids such as sufentanil and fentanyl are also intrathecally administered for postcesarean analgesia. However, both of them have been found to provide shorter postoperative analgesia in comparison to intrathecal morphine [15,16]. Moreover, fentanyl has also been found to offer inferior analgesia [16].

From our study, the pain intensity in the first 24 hours after intrathecal administration of 0.2 mg of morphine, as measured by using numerical rating score (NRS) from 0 to 10, indicated that our patients had mild pain at rest and moderate pain while mobilizing. Focusing on pain at rest, one third of our patients reported pain intensity as 0 while one forth of them reported pain intensity as 5 during mobilization. Postoperative pain has significant impacts on patients physically and emotionally. Adequate pain control is essential and beneficial for the patients and the babies as breast feeding is required. With the same intrathecal morphine dose, Terajima et al. [17] demonstrated mild pain intensity at rest and moderate pain intensity with movement in present cesarean section patients.

Intrathecal morphine carries a significant risk of causing adverse effects comprising minor and major events. Many patients in this retrospective study had common adverse effects (nausea / vomiting and pruritus) but none of them experienced life-threatening events (early and late respiratory depression). With the same dose of 0.2 mg of intrathecal morphine in patients undergoing cesarean section, a variety of incidences of various adverse events has been reported. Karaman et al. [15] revealed that 30%, 4% and 0% of their patients had postoperative nausea, vomiting and respiratory depression, respectively. Abouleish et al.
revealed that 29%, 12% and 65% of their patients had postoperative nausea, vomiting and pruritus, respectively while Caranza et al. [18] demonstrated that 73% and 88% of their patients had nausea / vomiting and pruritus, respectively. It is clearly demonstrated that with 0.2 mg of intrathecal morphine, nausea / vomiting and pruritus are common. Our findings also show high incidence of nausea / vomiting and especially pruritus.

It has been found that the various doses of intrathecal morphine (0-0.5 mg) do not cause different incidences of nausea but pruritus is dose-dependent [9]. The other trial has found similar results with a no dose-dependent effect for nausea and vomiting while pruritus has a significant trend of increasing pruritus in direct proportion to the intrathecal morphine doses level (0-0.4 mg) [12]. In all of our patients receiving intrathecal morphine, the same dose of 0.2 mg was given so we cannot demonstrate the differences of side effects according to different doses.

Regarding the most fearful unwanted adverse effect of respiratory depression from intrathecal morphine, we found no patient experienced this event. With an intrathecal dose of morphine as high as 0.4 mg, Girgin et al. [12] did not find any parturients with severe respiratory depression. Kato et al. [4] retrospectively reviewed 1,915 parturients receiving 0.15 mg of intrathecal morphine and identified 6 of them with bradypnea (defined as respiratory rate ≤ 10 bpm) within 24 hours of the injection. Among those six, one of them exhibited severe bradypnea (30-second apnea, respiratory rate 3-8 bpm) requiring treatment with naloxone.

Two studies regarding safety of intrathecal morphine in patients undergoing different kinds of operation have been reported. Yimyaem et al. [5] did a retrospective review and reported no respiratory depression in their 274 patients receiving 0.1-0.4 mg of intrathecal morphine. The large prospective study of 5,969 surgical patients given intrathecal morphine 0.2-0.8 mg found a 3% incidence of respiratory depression (defined as respiratory rate < 8 bpm or an increasing PaCO₂ > 50 mmHg) [6].

Our study included a significant number of patients over a long period of practice and it revealed very good relief for pain at rest and good relief for pain with movement in the first 24 hours after the operation. According to our practice, respiratory rate of less than 8 bpm is defined as respiratory depression and intravenous naloxone will be given. This study showed the safety of intrathecal opioids in cesarean section patients as none of our patients had respiratory rate less than 8 bpm and was given intravenous naloxone.

We are aware that this descriptive retrospective study has some important limitations. Furthermore, we have not designed this study to identify factors related to pain intensity and side effects of intrathecal opioids in parturients undergoing cesarean section. However, this study included a significant number of patients so we believe that its data will partially be useful for other practitioners.

5. CONCLUSIONS

Intrathecal morphine is effective for controlling postcesarean pain. From our study, there was not any patient with respiratory rate of less than 8 bpm.
CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that this retrospective, descriptive study had been approved by the Ethics Committee of our institute.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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