Morphine for post-caesarean section analgesia: intrathecal, epidural or intravenous?

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ABSTRACT

Introduction: Good analgesia is important after a caesarean section but there are no studies to date that compared intrathecal (IT), epidural (EP) and intravenous patient-controlled analgesia (IV PCA) morphine for post-caesarean section analgesia. In this study, we compared the differences in the quality of analgesia and side effects rendered by IT, EP and IV PCA morphine for post-caesarean section analgesia.

Methods: We systematically collected and reviewed the data of 949 women who received IT, EP or IV PCA morphine for post-caesarean analgesia during a six-month period. We reviewed the patients 24 hours after surgery and recorded the type of analgesia, the use of adjuncts, pain scores, side effects and degree of satisfaction with the mode of analgesia. The data was captured in an electronic database and analysed.

Results: IT morphine was the predominant method of post-caesarean analgesia, accounting for 89.5 percent of the cases. Non-steroidal anti-inflammatory drugs (NSAIDs) were more commonly used in the IT and EP group (IT 76 percent, EP 80 percent and IV PCA 49 percent, p-value is less than 0.05). IT morphine group had a significantly lower pain score at rest (p-value is less than 0.001) and on movement (p-value is less than 0.05) when compared with IV PCA group. EP morphine also resulted in a lower pain score than IV PCA on movement (p-value is less than 0.05). There was no difference in pain scores between EP and IT morphine. In the subgroup analysis of patients who did not receive NSAIDs, IT and EP morphine group also registered lower pain scores at rest and on movement than IV PCA group (p-value is less than 0.05). There was no difference in the satisfaction scores among the three groups.

Conclusion: The use of IT and EP morphine was associated with lower pain scores than IV PCA morphine at rest and on movement in the first 24 hours after caesarean section. No severe side effects were found.

Keywords: caesarean section, epidural anaesthesia, morphine, patient-controlled analgesia, spinal anaesthesia

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INTRODUCTION

Good analgesia is important after caesarean section to provide the mother with opportunities for mother-child bonding, early ambulation and discharge, hence leading to greater overall patient satisfaction. Apart from being associated with a decline in anaesthesia-related maternal mortality, the use of regional anaesthesia for caesarean section has also provided an avenue for rendering post-operative analgesia with neuraxial opioids[1,2]. In this respect, the use of intrathecal (IT) and epidural (EP) morphine has gained popularity as it is effective and inexpensive[3]. Alternatively, a parenteral route of administration of analgesics, such as intravenous patient-controlled analgesia (IV PCA) with morphine, may be used if a regional block is contraindicated. Although the ways of counteracting post-caesarean section pain are legion, none has proven to be clearly superior[4].

There are no studies to date that compare IT, EP and IV PCA morphine for post-caesarean section analgesia. In this prospective, non-randomised study, we reviewed the data of patients who had received these three different routes of morphine administration for post-caesarean analgesia. The objective of this investigation is to elucidate the differences, if any, with regard to the quality of analgesia and side effects of these modalities of pain relief.

METHODS

KK Women's and Children's Hospital is a tertiary referral centre for the fields of obstetrics, gynaecology and paediatrics in Singapore. The approximate annual rate of childbirth in this institution is 15,000 and

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some 18% of these deliveries are undertaken abdominally. In our institution, regional anaesthesia is employed for a majority (about 80%) of caesarean sections. IT morphine 0.1 mg is routinely given at the point of IT injection, if a single shot subarachnoid block or combined spinal epidural anaesthesia is used for this surgery. Hyperbaric bupivacaine 9 mg to 12 mg, sometimes in combination with fentanyl 0.01 mg to 0.02 mg, is used to induce spinal anaesthesia. The augmentation of pre-existing intrapartum epidural block is commonly undertaken for caesarean section. In this instance 15 ml to 20 ml of 1.5% lidocaine in a 1/200 000 solution of adrenaline (with or without fentanyl 0.05 mg to 0.1 mg) would be injected epidurally to effect anaesthesia.

If EP anaesthesia is employed for caesarean section, a single dose of EP morphine 3 mg to 4 mg is injected prior to removal of the EP catheter at the end of surgery for post-operative analgesia. If general anaesthesia has been performed for abdominal delivery, IV PCA morphine (1 mg boluses, lockout time five minutes and maximum dose 8-12 mg/hr) would be the method of choice for post-operative pain relief. Intraoperatively, these patients would receive 0.1 mg/kg to 0.2 mg/kg of IV morphine post-delivery. Antiemetics (IV metoclopramide, ondansetron, dexamethasone or a combination of any of the three) are routinely used intraoperatively. Supplemental non-steroidal anti-inflammatory drugs (NSAIDs), such as suppository diclofenac 100 mg and IV ketorolac 30 mg, are commonly used prior to discharge from the operating room for all post-caesarean section patients.

With the approval of the hospital ethics committee, a database had been established in our institution since August 2002 to capture the data of all American Society of Anesthesiologists Physical Status Classification (ASA) I-II post-caesarean patients, who had consented to be included in the acute pain service. For this prospective, non-randomised study, information related to the mode of post-caesarean analgesia was recorded for a six-month period from August 1, 2002 to January 31, 2003 for this study. We included only patients who had received IT morphine 0.1 mg, EP morphine 3 mg to 4 mg or IV PCA morphine, with or without NSAIDs, for our analysis. The anaesthetic technique was left to the discretion of the attending anaesthetist, in consultation with the patient. Patients who had had other unplanned procedures, such as repair of accidental perforations of viscera or caesarean hysterectomy, were excluded from the study. Patients who had required a conversion to general anaesthesia due to inadequate neuraxial blocks were also excluded from analysis.

The time of administration of IT and EP morphine or the time of initiation of IV PCA morphine was recorded by the attending anaesthetist. The use of NSAIDs during or just prior to the completion of surgery was also recorded. In the recovery room, post-operative pain at rest was assessed by using a 0-4 verbal analogue scale (VAS, 0=no pain, 1=mild pain, 2=moderate pain, 3=severe pain, 4=very severe pain). Only patients who had reported VAS <1 were discharged from the recovery room half an hour post-surgery. IV PCA would be started at that time provided that pain was adequately controlled with boluses of IV fentanyl and morphine. No further parenteral opioids would be prescribed for patients who had received IT and EP morphine. Instead, diclofenac suppository 50 mg would be given every six- to eight-hourly to supplement post-operative analgesia.

Apart from cardio-respiratory vital signs, the patients were assessed hourly by ward nurses for the next 12 hours, then two-hourly for the next 12 hours, on the following:

1. Pain score at rest and on movement based on 0-4 VAS. Additionally, for patients in the IV PCA group, the total drug consumption was also recorded. (movement was defined as change from supine to sitting/standing position)
2. Sedation (0=no sedation, 1=drowsy, easily roused, 2=somnolent, difficult to rouse)
3. Nausea + vomiting (0=none, 1=mild, 2 =severe)
4. Pruritus (0=none, 1=yes)

IV naloxone was readily available to be administered in the event that patients suffered from respiratory depression (respiratory rate <8) and sedation score = 2. Nausea and vomiting would be treated with IV metoclopramide on patients' request. Anti-histamines, such as chlorpherinamine, would be prescribed for patients who had requested for treatment for itch.

All the patients would be followed up in the next 24 hours after discharge from the operating room by a dedicated pain service team comprising an anaesthetist and a pain nurse. The team would review the patients' record, and data on the following would then be retrieved:

1. Worst pain score at rest and on movement
2. The total number of IV PCA attempts and drug consumption
3. The highest scores for sedation, nausea/vomiting and pruritus. Additionally, the number of times the patients had vomited was also recorded.

Table I. Pain scores of the various modes of analgesia.

	Group IT n=850	Group EP n=52	Group PCIA n=47
Pain score at rest (all patients)	0.04 (0.01)	0.05 (0.03)	0.14 (0.06)*
Pain score on movement (all patients)	0.26(0.1)	0.21(0.06)	0.84 (0.11)**
Pain score at rest (with NSAIDs)	0.03 (0.01)	0.06 (0.03)	0.11 (0.07)
Pain score on movement (with NSAIDs)	0.24 (0.02)	0.20 (0.03)	0.83 (0.14)**
Pain score at rest (without NSAIDs)	0.07 (0.02)	0.06 (0.02)	0.16 (0.08)
Pain score on movement (without NSAIDs)	0.35 (0.05)	0.20 (0.02)	0.84 (0.16)**

Values in mean (SEM); * Significant difference found between IT vs PCIA, $p<0.05$; ** Significant differences found between IT vs PCIA and EP vs PCIA, $p<0.05$.

Table II. Side effects of the various modalities of pain relief.

	Group IT n=850	Group EP n=52	Group PCIA n=47
Pruritus	422 (50)	30 (58)	10 (21)*
Nausea + vomiting (no patient had score>1)	131 (15)	19 (36)	13 (28)
Backache	14 (0.2)	0 (0)	1 (0.2)
Headache	13 (0.2)	0 (0)	0 (0)

Values in n (% of total in the group); * Significant differences found between IT vs PCIA and EP vs PCIA, $p<0.05$.

The patients were also directly asked whether they had experienced complications such as headache and backache at that point in time. Overall satisfaction score with post-operative analgesia (4=excellent, 3=good, 2=satisfactory, 1=poor) was also obtained during the ensuing interview. At the same time, oral analgesics such as NSAIDS would be prescribed. IV PCA morphine could be continued for the second day, if required.

The data were entered systematically into the Statistical Package for Social Sciences (SPSS) version 9.0 (Chicago, IL, USA) formatted databank. Ordinal data (pain scores, satisfaction scores and sedation scores) of the EP, IT and IV PCA morphine groups were compared using the Kruskall Wallis test. Post-hoc Mann U Whitney test with Bonferroni correction was used for pairwise comparison when appropriate. For comparison of proportions, χ^2 tests were used. A p-value <0.05 was considered statistically significant.

RESULTS

During the six-month period of the study, a total of 949 cases were collected. IT morphine was the predominant method of post-caesarean analgesia practised in our institution. Of these cases, 89.5% (n=850) received IT morphine, 5.5% (n=52) EP morphine and 5% (n=47) IV PCA morphine. More patients in the IT (76%) and EP (80%) groups received NSAIDs than IV PCA (49%), $p<0.05$. IT morphine group had a significantly lower pain score at rest ($p<0.05$) and on movement ($p<0.05$) when compared with IV PCA group. EP morphine resulted in a lower pain score on movement ($p<0.05$) but not at rest than IV PCA. There was no difference in pain scores between EP and IT morphine.

When analysis was limited to the patients who had not received NSAIDs, pain scores on movement in IT and EP groups were still lower than IV PCA ($p<0.05$) (Table I). Within the IT morphine group, patients who had received NSAIDs also registered lower pain scores at rest and on movement ($p<0.05$). This difference was not detected in the EP group but the sample size was small.

Over the 24-hour study period, the total dose of IV PCA morphine used was mean 14 mg + standard error [SE] 2 mg. The use of intra-operative NSAIDs did not affect pain scores in this group of patients. However, patients who received intra-operative NSAIDS required less morphine when compared with patients who were not given NSAIDS (mean 7 mg, 95% confidence interval [CI] 2-12 versus mean 20 mg 95% CI 12- 28, $p<0.05$).

Apart from itch which occurred more frequently in EP and IT groups than IV PCA group (58% and 50% versus 21%, $p<0.05$), there was no difference in the other side effects or complications (Table II). None of the patients experienced any respiratory

depression. Sedation was observed in two patients from Groups IT and IV PCA (score=1) but not EP ($p>0.05$). There was also no residual motor block detected in the patients 24 hours after neuraxial block in our study cohort. None of the patients had had a nausea/vomiting score of >1. There was no difference in the satisfaction scores among the three groups (median 3. [minimum 2-maximum 4] for Group IT, 3(2-4) for EP and 3(1-4) for IV PCA, $p>0.05$).

DISCUSSION

Our results suggest that in the first 24 hours after caesarean section, IT morphine provided more effective analgesia at rest and on movement than IV PCA. EP morphine also resulted in a lower pain score than IV PCA on movement. Therefore, we could infer that collectively, neuraxial morphine produces analgesia of a greater reliability than the parenteral route. This has been previously recognised, although the contribution of an existing conduction block from local anaesthetics to the superiority of EP and IT morphine cannot be excluded[5]. In our cohort of patients, NSAIDs were used more commonly in conjunction with neuraxial opioids. On the other hand, even after having excluded patients who had received NSAIDs, pain scores on movement in IT and EP groups were still lower than their parenteral counterpart. We could view this as neuraxial block with opioids playing a critical role in effecting favourable pain scores independently of NSAIDs.

Nevertheless, we like to emphasise the importance of the multimodal approach to analgesia rendered by the concurrent use of NSAIDs with neuraxial opioids. Although we used an "optimal" dose of IT morphine 0.1 mg, a previous study had shown that no patient was completely pain free in the first 24 hours post-caesarean section and supplemental analgesia was required[6]. In our study, the patients in the IT morphine group who received NSAIDs reported lower pain scores at rest and on movement. Therefore, in the context of enhancing pain relief, strictly "round-the clock" order of NSAIDs post-operatively in patients who had received IT and EP morphine can increase duration of analgesia[7-9].

Neuraxial morphine employed under the current circumstances has also been found to be more cost effective than the patient-controlled analgesic set-up[3]. In that study, the set-up of patient-controlled epidural analgesia has been shown to substantially increase the cost of providing post-caesarean section analgesia. Even though the use of neuraxial morphine is inexpensive but effective, the risk of respiratory depression remains a concern for many[6,10]. The use of IT 0.2 mg morphine for post-caesarean analgesia was found to cause respiratory depression (respiratory rate of <10/min and/or arterial oxygen saturation <85% from pulse oximetry), albeit in less than 1% of the patients[11].

We did not encounter any clinically-detectable respiratory depression in our study by using IT morphine 0.1 mg but we did not routinely use pulse oximetry for post-operative monitoring. Similarly, we did not detect any respiratory depression from EP morphine in our study but our sample size for patients receiving this mode of analgesia was small. However, the use of EP morphine 2 mg to 5 mg for post-caesarean section analgesia was previously found to cause bradypnea but without serious sequelae in 0.25% of the patients[12]. Therefore, it was imperative to closely monitor the respiratory status, even in this young and healthy adult population, for at least 24 hours after the administration of neuraxial morphine.

Even though the exact potency ratio of IT versus EP morphine remains undetermined, we found the currently-employed doses to be comparable. A previous study had also found the potency difference between the two routes of administration to be of a similar order of magnitude[3]. A recent study comparing 2 mg of epidural morphine versus 0.075 mg of IT morphine found the former to be more effective in providing post-operative analgesia after caesarean section[13]. However, this study used a lower dose of morphine and so direct comparison cannot be made with our study.

Addition of IT fentanyl to local anaesthetic to enhance subarachnoid block is a widely-accepted practice[14,15]. However, their analgesic effect is about 30 minutes with an elimination half-life of 1.5-6 hours[16], and we believe the effect of fentanyl on the post-operative pain scores is minimal. In a randomised trial comparing IT morphine with IT fentanyl and a combination of IT morphine and fentanyl, the quality of post-operative analgesia with fentanyl, when used alone, was found to be inferior to that with morphine. The investigators concluded that the combination of opioids offered no advantage over morphine alone in management of post-caesarean pain[17].

Both EP and IT morphine were associated with a greater risk of pruritus than IV PCA. The presence of pruritus associated with neuraxial morphine has been shown to have a negative impact on patient satisfaction in a previous study[18]. We were unable to determine if this contributed to the lack of differences in the overall satisfaction scores despite lesser pain scores in the IT and EP groups when compared

with the IV PCA group because we had used a one-dimensional overall satisfaction scoring system to assess our post-operative patients. The lack of difference in the overall satisfaction scores could be multifactorial, including patients' willingness to accept the presence of post-operative pain and having realistic expectations[19].

As with all non-randomised studies, certain pitfalls exist. The main reason for general anaesthesia for caesarean section in our centre is due to maternal requests[20] and this reflects the true clinical practice in our institution. With overwhelming data supporting the benefits of regional anaesthesia over general anaesthesia for caesarean section, it would unethical to conduct a randomised prospective study[1]. We took all the patients that came under our purview over a six-month period and vigilantly collected their data post-operatively, hence the results are reflective of the current obstetrics anaesthesia practice in our institution.

In conclusion, our study showed that the use of IT and EP morphine was associated with lower pain scores at rest and movement when compared with IV PCA. The use of NSAIDs enhanced the efficacy of analgesia of IT morphine. We did not detect any severe side effects (e.g. respiratory depression and sedation) with the doses of neuraxial morphine used. Even though EP and IT morphine resulted in pruritus more frequently than IV PCA, we did not find any significant differences in the overall patient satisfaction scores among the three groups of patients. EP and IT morphine are good alternatives to IV PCA morphine for post-caesarean section analgesia.

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