EPIDURAL MORPHINE FOR ANALGESIA AFTER CAESAREAN SECTION

F.J. CARMICHAEL, STEPHEN H. ROLBIN AND ERNEST M. HEW

ABSTRACT

A randomized double blind placebo controlled study of the efficacy, duration and safety of epidural morphine for the management of pain after Caesarean section is reported. Three similar groups of patients received either 0, 4 mg or 8 mg of morphine sulphate in 10 ml of normal saline through an epidural catheter at the completion of the operation. Compared to the saline controls, both the 4 mg and 8 mg epidural morphine groups had significant pain relief as judged by an analogue pain scale ($p < 0.001$), the time to the first administration of narcotic analgesics ($p < 0.001$) and the amount of supplemental analgesic required in the first 36 hours after operation ($p < 0.001$). The side effects occurred in a dose-dependent fashion. Two patients who received epidural morphine 8 mg plus additional narcotic or antihistamine had reduced respiratory rates but were easily rousable. Our experience suggests that the epidural administration of morphine 4 mg may be a safe and reliable method of obtaining prolonged analgesia following Caesarean section.

KEY WORDS: EPIDURAL MORPHINE, postoperative analgesia, caesarean section.

THE IDENTIFICATION of opiate receptors in the central nervous system[1-3] has led to a new method of pain management in patients. The introduction of morphine into the epidural space has provided dramatic relief of acute and chronic pain with few side effects.[4-7]

Epidural morphine relieves postoperative pain, but the dose and volume required for specific situations are not well established. The present investigation was a randomized double blind placebo controlled study of the efficacy, duration and safety of epidural morphine for the management of pain after Caesarean section. We hoped to shed further light on the dose and volume required for this specific situation.

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METHODS

Postoperative pain relief was studied in 29 women of ASA I physical status, undergoing elective Caesarean section. The protocol was approved by the Human Experimentation Committee of the University of Toronto and by the Pharmacy and Clinical Trial Drug Sub-Committee at Mount Sinai Hospital. All patients gave informed consent and a randomized double blind placebo controlled study was done.

Following an intravenous pre-load of 1000 ml of balanced salt solution, patients were placed in a lateral position and the epidural space was located using a 16-guage Tuohy needle at the L2–3 or L3–4 interspace. Ten ml of two percent carbonated lidocaine containing epinephrine 1:200,000 were injected. A catheter was inserted 3–4 cm into the epidural space and after waiting five minutes a further 10 to 16 ml of lidocaine was added. The patients were maintained at 10°–15° of left lateral tilt. Adequacy of analgesia was tested five minutes after the second injection, following which the surgical procedure was commenced. The use of supplementary intravenous drugs for anxiety or analgesia was based on the usual clinical judgements and not influenced by the study protocol.

At the time of skin closure 10 ml of sterile perservative-free saline containing zero, 4 mg, or 8 mg of morphine sulphate were administered

through the epidural catheter, which was then removed. Morphine was prepared aseptically in a laminar flow hood and passed through a 0.22 mμ filter. All solutions were made by the hospital pharmacy within 24 hours before use and were refrigerated at 4° C.

Following the injection of the epidural test solution, blood pressure, heart rate and respiratory rates were determined every 15 minutes for two hours, while the patient was in the delivery suite. After transfer to the ward vital signs were recorded hourly for a further six hours. Skin sensation was tested by pinprick after 30 minutes, then hourly for eight hours. Motor function was assessed a the time of sensory testing using the scale described by Bromage, *et al.*[8] After eight hours the patient's vital signs were followed by the nursing staff.

Pain relief was determined by direct questioning of the patient and by a visual analogue scale.[9]

Data are presented as means ± standard error of the mean. The data were subjected to Chi-Square Analysis or to an Analysis of Variance with significant differences between mean values being calculated by the Least Significant Difference method.[10]

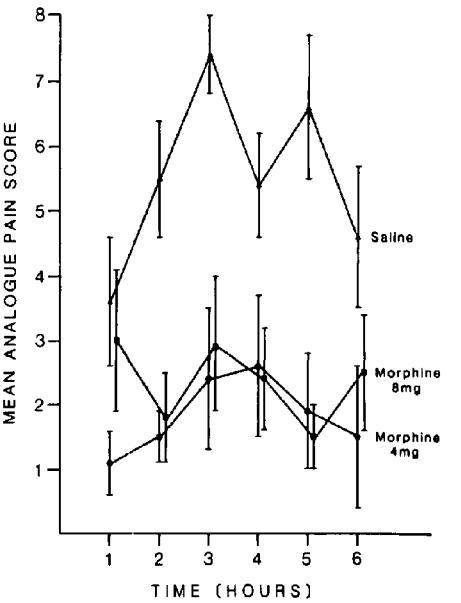

FIGURE 1 Pain relief in patients receiving saline placebo, (▲—▲), 4 mg morphine sulphate (●—●) or 8 mg morphine sulphate (■—■) into the epidural space. Results are expressed as mean ± S.E.

RESULTS

The three groups studied were comparable with respect to age and parity. Seventeen of 29 patients received supplementary intravenous drugs for relief of anxiety or pain during operation. Nine patients received diazepam and the remaining patients received either Innovar®, or fentanyl either alone or in combination with diazepam. One patient received ketamine 15 mg. The three groups had similar rates of regression of the local anaesthetic block with numbness to pinprick disappearing in 3.3 ± 0.4 hours in the placebo group, 3.8 ± 0.3 hours in the 4 mg group and 4.1 ± 0.5 hours in the 8 mg group. As well, the ability of the patients to lift their legs off the bed reappeared in 2.0 ± 0.3 hours in the placebo group, 1.7 ± 0.3 hours in the 4 mg group and 1.5 ± 0.3 hours in the 8 mg group.

Pain relief as assessed subjectively by the analogue pain scale method (Figure 1) demonstrated a significant difference between placebo and the epidural morphine groups ($p < 0.001$). However, there was no difference between the groups receiving 4 mg or 8 mg of morphine. Pain relief was also assessed by comparing the time of the first administration of supplemental narcotic analgesics following the epidural test drug. Requests for analgesia occurred much late in the epidural morphine groups ($p < 0.001$), but again there was no significant difference between patients receiving 4 mg or 8 mg of epidural morphine (Table I). Patients who received placebo required significantly more analgesia during the subsequent three 12 hour periods ($p < 0.001$), than those who had received epidural morphine (Table I).

The incidence of side effects in each of the groups is shown in Table II. Mild to moderate pruritis occurred in 9 of 10 patients receiving 4 mg morphine and moderate to severe pruritis occurred in eight of nine patients who received 8 mg morphine. Nausea and vomiting occurred in all groups, but it was more common in the morphine groups, the highest incidence being in the 8 mg group. Dizziness occurred in only one patient receiving 4 mg of epidural morphine and in three of the nine patients receiving 8 mg. We were unable to assess ability to void spontaneously, as most of our obstetricians electively catheterize patients for 24 hours postoperatively.

Significant cardiovascular or respiratory depression was not seen in any of the patients in the placebo or 4 mg groups; however, two patients

TABLE I

ANALGESIC REQUIREMENTS FOLLOWING EPIDURAL MORPHINE

	Epidural morphine dose		
	0 mg	4 mg	8 mg
Time to First Analgesic			
Mean	2.75 ± 0.5	22.5 ± 4.0*	26.5 ± 4.0*
Range	1.0 to 9.1	2.7 to 38.3	1.3 to > 7 days
Number of Analgesic doses given to each patient			
Hours			
0–12	2.6 ± 0.4	0.1 ± 0.1*	0.2 ± 0.1*
12–24	4.9 ± 0.4	0.7 ± 0.3*	0.6 ± 0.3*
25–36	4.0 ± 1.1	1.8 ± 0.4*	1.0 ± 0.4*
Number of Patients Requesting Pain Relief	10/10	10/10	7/9†

*Significantly different from 0 mg morphine ($p < 0.001$).

†Two patients received no narcotics during 7 days in hospital.

TABLE II

SIDE EFFECTS OF EPIDURAL MORPHINE

	Epidural morphine		
Side Effects	0 mg	4 mg	8 mg
Respiratory Rate < 10 per minute	0/10	0/10	2/9
Pruritis	1/10	9/10††	8/9††
Nausea	2/10	3/10	6/9*
Vomiting	1/10	3/10	7/9††
Dizziness	1/10	1/10	3/9

*Significant difference from placebo $p < 0.05$.

††Significant difference from placebo $p < 0.01$.

in the 8 mg group had a respiratory rate of less than 10/minute. One patient who had received 100 mg of meperidine three hours after 8 mg of epidural morphine had a respiratory rate of 6/minute. Two doses of naloxone 0.1 mg intravenously and 0.2 mg intramuscularly reversed the respiratory depression without loss of the analgesic effect. One other patient who had received only the 8 mg of epidural morphine developed a respiratory rate of 8–9/minute. Arterial blood gases measured with the patient breathing room air revealed $[H^+]a$ 47.86 nmol/l (pH 7.32), $Paco_2$ 5·3 kPa (40 torr), Pao_2 12·8 kPa (96 torr) and bicarbonate 20 mmol/l. This patient had also received diphenhydramine 50 mg intramuscularly, 25 mg by mouth and 50 mg intramuscularly over a five hour period. Both patients appeared sedated but were easy to arouse. The peak respiratory depression occurred seven hours after giving the epidural morphine in both patients. The use of intravenous drugs during anaesthesia did not influence the occurrence of respiratory depression.

DISCUSSION

The effectiveness of epidural morphine in the management of pain after Caesarean Section has been reported by several authors as part of larger studies.[11–14] Yu, *et al.*[15] presented preliminary results of a double blind study comparing 4 mg of morphine by either the intramuscular or epidural route. They found epidural morphine to be more effective in the management of pain after Caesarean section. Hughes, *et al.*[16] presented preliminary results of a double blind randomized study comparing 2, 5, and 7.5 mg of epidural morphine with 7.5 mg of intramuscular morphine for relief of pain after Caesarean section. These authors found 5 and 7.5 mg of epidural morphine to be more effective and to have a prolonged analgesic effect.

Our study differs from other published data in that we used a control group and the routine we followed was applicable to our clinical situation (i.e. intravenous supplementation was given when the patient required it). Four and 8 mg of epidural morphine provided excellent analgesia for patients following Caesarean section. The pain relief was effective for an average of 23 hours following 4 mg of epidural morphine and 27 hours following 8 mg of epidural morphine. Two of the 9 patients in the 8 mg group did not request or receive any other analgesia during the seven days in the hospital. It is of interest that the placebo group, even when given intramuscular morphine or meperidine on request, never achieved the same degree of pain relief as did the epidural morphine groups. This confirms the findings of Yu, *et al.*[15] and Hughes, *et al.*[16] There was no discernible difference in the analgesia provided by the 4 mg or the 8 mg epidural morphine doses.

Although the side effects of epidural narcotics are less pronounced than those following parenteral administration [7,17] some patients have had significant respiratory and cardiovascular depression.[18–20].

In the present study, the most commonly noted side effect was pruritis, which occurred in 90 per cent of the patients receiving 4 mg of epidural morphine, with two patients receiving antipruritic medication. Most patients receiving 4 mg were not distressed by this pruritis. Six of

the nine patients who received 8 mg of epidural morphine were given antipruritic medication. A dose dependent relationship has previously been noted by other authors.[7,13,16] Pruritis occurred despite the use of preservative-free morphine sulphate. This is in contrast to the report of Reiz and Westberg.[7]

The incidence of nausea and vomiting was higher than in previously reported studies[7] (Table II). This may reflect the encouragement of early oral intake in our patients, since it was also common in the placebo group.

With the two notable exceptions, there were no significant reductions in respiratory rates or in blood pressure in the present study. This agrees with other authors.[6,11,13,15,16,21–23] The two patients who developed respiratory depression had received supplemental narcotic or antihistamine and perhaps these contributed. Delayed respiratory depression following epidural morphine has been reported and appears to be more frequent in the elderly and severely ill patient.[7,18–20] Although the incidence in the present study was greater, this may be due in part to altered epidural distribution seen in the postpartum patient. The code was broken after these two "problem" patients. Both involved the 8 mg group and since the last patient was to receive an 8 mg dose, the study was discontinued.

The present study made no attempt to determine the time of onset of analgesia following epidural administration of morphine, since the drug was given while there was still an effective local anaesthetic block present. Thus the results may have been influenced by the presence of 25 ml volume of lidocaine with epinephrine 1:200,000. Two patients who had received 8 mg epidural morphine complained of pain about one hour after receiving this drug. They were given a single intramuscular narcotic injection which required no supplementation for 16 to 20 hours. This may reflect the slower onset of action noted by some authors for morphine given by this route.[6,13,16,22]

In conclusion, epidural morphine provided profound analgesia for prolonged periods following Caesarean section. It increased patient comfort and probably improved mother-infant interaction. Both patients and nurses were pleased with the pain relief associated with epidural morphine. This technique of pain management is reliable and safe using a 4 mg dose. However, the 8 mg dose had more pronounced side effects.

Since this technique is relatively new, its safety is still in doubt. Our experience suggests that patients would be adequately monitored postpartum on the ward if vital signs were taken hourly for the first 8 to 12 hours after each epidural dose of morphine. This would be practical even in a busy obstetrical unit because of the marked improvement of patient comfort and decreased nursing care required. If the patient became unduly sedated or hypotensive, or if the respiratory rate fell to less than 10/minute, then the anaesthetist should be notified. Further assessment including arterial blood gases would then be indicated.

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RÉSUMÉ

On a étudié l'efficacité, la durée et la sécurité de l'analgésie épidurale à la morphine lors de la césarienne en utilisant une méthode randomisée à double insu avec placebo. A trois groupes comparables de patientes on a administré un placebo ou du sulfate de morphine 4 mg ou 8 mg dans 10 ml de soluté physiologique à la fin de l'intervention par un cathéter épidural. Comparés au groupe contrôle, les deux groupes qui avaient reçu morphine 4 mg et 8 mg ont été soulagés de façon significative comme le montre l'échelle analogique d'évaluation algique ($p < 0.001$), le temps écoulé avant l'administration d'un narcotique additionnel ($p < 0.001$) et la quantité totale d'analgésique supplémentaire requise dans les des preières 36 heures qui ont suivi l'intervention. L'importance des effets secondaires a été proportionnelle à la dose. Deux patientes qui avaient reçu morphine respectivement 8 mg par la voie épidurale une dose narcotique supplémentaire ou un anti-histaminique ont présenté une diminution de la fréquence respiratoire mais pouvaient être facilement réveillées. Notre expérience suggère que morphine 4 mg en injection épidurale est une dose adéquate et sans danger pour l'obtention d'une analgésie prolongée après une césarienne.