POSTOPERATIVE SPINAL ANALGESIA WITH MORPHINE

K. SAMII, M. CHAUVIN AND P. VIARS

SUMMARY

Patients with pain after operation received morphine hydrochloride intrathecally in doses of 0.02 mg kg⁻¹ (n = 30) and 0.2 mg kg⁻¹ (n = 30). The high-dose group showed slightly longer-lasting and more potent analgesia than the low-dose group. Sedation, decreases in heart rate and systolic arterial pressure, oliguria, nausea and urinary retention were more frequent in the high-dose group. Two patients of the high-dose group showed evidence of respiratory depression which appeared after a late change in posture (7 and 11 h). We conclude that postoperative analgesia with intrathecal morphine 0.02 mg kg⁻¹ must be followed by a prolonged head-up posture and be performed in hospital units where the treatment of respiratory depression is competent.

A direct spinal action of narcotic drugs was demonstrated in animals by Yaksh and Rudy (1976) and confirmed in man by Wang, Nauss and Thomas (1979) who showed that, when given intrathecally, morphine produced analgesia without central depression. However, the dose of morphine used in that study was much less than that used previously by us (Samii et al., 1979) (0.5–1.0 mg and 20 mg respectively). Therefore, it was decided to compare, in a double-blind study, the effects of morphine 0.02 mg kg⁻¹ and 0.2 mg kg⁻¹ administered intrathecally in the treatment of postoperative pain and to determine the dose most appropriate for clinical use.

PATIENTS AND METHODS

A double-blind study was undertaken in which 30 patients received morphine hydrochloride 0.02 mg kg⁻¹ and a further 30 patients received morphine hydrochloride 0.2 mg kg⁻¹. All patients gave informed consent for the study. The inclusion of a third group receiving a placebo intrathecally (10% dextrose solution without morphine) was abandoned after treatment of three patients because of the absence of analgesia and the risks of intrathecal puncture. Morphine was injected intrathecally at least 4 h after the last systemic injection of narcotic (fentanyl), using a 25-gauge spinal needle passed through an introducer. The morphine solution was made hyperbaric by the addition of the same volume of 10% dextrose and the volume of the solution injected was always less than 2 ml. Immediately after the intrathecal injection the patients were placed in a 40-degree head-up position and kept in the recovery room which is open day and night. The following indices were measured at least once every hour for 6 h and then once every 3 h by one of two observers who was unaware of the dose of morphine used: heart rate, systolic arterial pressure, respiratory frequency, urinary output, intensity of pain, upper level of analgesia (pinprick), discrimination of light touch, motor function (active elevation of the lower limbs) and sedation. End-tidal carbon dioxide concentration (infra-red analyser) was always measured when sedation was observed. When pain reappeared the patients were moved from the recovery room to their own room where they were observed for at least 5 days to exclude late side-effects. Comparisons between the two groups were performed using Student's t test for the duration of analgesia, Mann and Whitney test for the intensity of pain and χ² test for the percentage of patients.

RESULTS

The degree of postoperative pain (scored as: nil = 0, very mild = 1, mild = 2, moderate = 3, severe = 4, intolerable = 5), the types of surgical incision and the ages of the patients were similar in both groups (table I). Table II summarizes the effects of the administration of morphine in the two groups.

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TABLE I. Clinical data of the patients studied. No statistically significant differences between groups

<table>
<thead>
<tr>
<th>Age (yr) (mean ± SD)</th>
<th>Laparotomy</th>
<th>Thoracotomy</th>
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<td></td>
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<td>53 ± 8</td>
<td>57 ± 9</td>
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Mean initial intensity of pain (scored 0–5)

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<tr>
<th></th>
<th>Laparotomy</th>
<th>Thoracotomy</th>
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<td>3.9</td>
<td>4.3</td>
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TABLE II. Consequences of intrathecal administration of morphine. Value denotes number of patients unless stated otherwise

| Dose of morphine (mg kg⁻¹) | Mean maximal decrease in pain (scored 0–5) | Duration of analgesia (h) (mean ± SD) | Sedation | Respiratory frequency | End-tidal CO₂ > 5.5% | Decrease in heart rate ≥ 20 beat min⁻¹ | Decrease in systolic arterial pressure ≥ 20 mmHg | Urinary output < 150 ml per 3 h despite plasma volume expansion | Nausea | Urinary retention without previous urethral catheter | Cephalgia |
|---------------------------|------------------------------------------|---------------------------------------|----------|----------------------|----------------------|------------------------------------------|-----------------------------------------------|-----------------|---------------------------------------------|----------|
| 0.02 (n = 30)             | 3.1                                      | 26 ± 3                                | 18       | 0                    | 0                    | 3                                        | 1                                      | 16              | 0                                           | 0        |
| 0.2 (n = 30)              | 4.0                                      | 33 ± 4                                | 28       | 2                    | 2                    | 1                                        | 2                                      | 25              | 5                                           | 1        |
|                           |                                          |                                       |          |                      |                      |                                          |                                        |                 |                                             |          |
| P                        |                                          |                                       |          | < 0.05               | < 0.01               | < 0.01                                   | < 0.02                              | < 0.02           | < 0.02                                      |          |

Analgesia
Following the intrathecal injection, analgesia appeared in both groups after 10–15 min and was maximum after 2–3 h. A segmental limit of hypalgesia to pin-prick, ranging from dermatomes T1 to T7, could be detected in all patients. The moment when there was an increase in the intensity of pain of at least 1 point (scored 0–5) was taken as the end of analgesia.

Sedation, respiratory frequency and end-tidal carbon dioxide concentration
Sedation was more frequent in the morphine 0.2 mg kg⁻¹ group than in the morphine 0.02 mg kg⁻¹ group. Sedation appeared between 2 and 6 h after administration and lasted from 6 to 12 h. All but two patients with sedation had respiratory frequency of less than 10 b.p.m. and end-tidal carbon dioxide concentration greater than 5.5%. Indeed, two patients of the morphine 0.2 mg kg⁻¹ group who were changed to the horizontal position 7 h and 11 h respectively after the injection of morphine had slowing of breathing (8 b.p.m. and 6 b.p.m.) and increases in end-tidal carbon dioxide concentration (6.5% and 7.2%). These effects were immediately reversed by naloxone 0.4 mg i.v. while analgesia persisted (pain score: 1 and 0 respectively). A continuous infusion of naloxone 0.4 mg h⁻¹ was instituted (for 9 h and 6 h respectively) to prevent the recurrence of respiratory depression.

Heart rate, systolic arterial pressure and diuresis
The changes in these vital signs were considered significant if no obvious cause of hypovolaemia such as haemorrhage or fluid loss was observed. Decreases in heart rate equal to or greater than 20 beat min⁻¹ and in systolic arterial pressure of at least 20 mmHg were more frequent in the morphine 0.2 mg kg⁻¹ group than in the other group. However, heart rate and systolic arterial pressure remained always greater than 60 beat min⁻¹ and 100 mmHg respectively. Urinary output of less than 150 ml per 3 h was considered significant if it persisted despite the rapid infusion of lactate Ringer’s solution 1000 ml in 30 min. Oliguria was more frequent in the morphine 0.2 mg kg⁻¹ group than in the morphine 0.02 mg kg⁻¹ group. In all the oliguric patients urinary output could be increased with frusemide 20 mg i.v. Changes in heart rate, systolic arterial pressure and diuresis appeared from 2 to 4 h after morphine injection.

Nausea
Nausea was only observed in five patients of the morphine 0.2 mg kg⁻¹ group. It was treated successfully by the administration of droperidol 2.5–5 mg i.v.

Urinary retention
This was rare in the morphine 0.02 mg kg⁻¹ group and observed in all but one of the patients of the morphine 0.2 mg kg⁻¹ group and required insertion of a catheter in these patients.
Headache

Headache was observed in only one patient in the morphine 0.2 mg kg\(^{-1}\) group, occurring on the day following the intrathecal injection and easing spontaneously.

Sensitivity to light, touch and motor function remained unchanged.

DISCUSSION

Our results show that morphine 0.2 mg kg\(^{-1}\) given intrathecally produced slightly longer-lasting relief of pain, but was associated with more frequent side-effects than the 0.02-mg kg\(^{-1}\) dose.

In this study morphine was given as mg kg\(^{-1}\) of an absolute dose to permit a simultaneous pharmacokinetic study of plasma concentration and urinary elimination of morphine. This study is not yet complete.

The presence of a detectable upper thoracic level of analgesia was not reported in earlier studies of this technique (Wang, Nauss and Thomas, 1979), but constitutes a powerful argument for the direct spinal action of morphine when given intrathecally. However, it does not exclude an action at other sites. On the contrary, several of the side-effects observed suggest a simultaneous involvement of the opiate receptors in the central nervous system. In all but two of the patients who became sleepy, respiratory frequency and end-tidal carbon dioxide concentration were within normal limits. However, the absence of blood-gas data and carbon dioxide response curves in our study does not permit us to eliminate a certain degree of respiratory depression. We can only conclude that, even if present, the respiratory depression was not dangerous except in two patients.

The persistence of analgesia following the injection of naloxone and the improvement in ventilation are a probable result of lower concentrations of morphine near the respiratory centres than in the vicinity of the spinal cord, and may be associated with the local analgesic action of intrathecal morphine. The decrease in heart rate and in systolic arterial pressure may have been caused by analgesia suppressing sympathetic stimulation. However, these cardiovascular changes were more frequent in the morphine 0.2 mg kg\(^{-1}\) group, whereas analgesia was good in both groups. Thus, a direct inhibitor action of morphine on higher sympathetic centres is a possible explanation for these cardiovascular changes. The oliguria we observed may have been caused by renal hypoperfusion. However, the absence of severe hypotension and the persistence of oliguria despite plasma volume expansion eliminate this hypothesis: hypersecretion of antidiuretic hormone from a direct central action of morphine may explain this finding, but a more detailed study is necessary for confirmation. Nausea is another side effect probably caused by the invasion of higher centres by the morphine. Wang, Nauss and Thomas (1979) did not observe similar side-effects with doses of morphine 0.5–1.0 mg, that is doses close to 0.02 mg kg\(^{-1}\). However, that study involved only eight patients and the vital signs were recorded for 1 h, while most of the side effects we observed appeared at least 2 h after the injection. The respiratory depression observed in two patients in the morphine 0.2 mg kg\(^{-1}\) group occurred following a change in posture. Similar respiratory depression has been reported with 15 mg (Liolios and Andersen, 1979), 5 mg and 3 mg of morphine (Glynn et al., 1979). In all these reports two factors were present: a change in posture, even if late, or the previous systemic injection of narcotics (Glynn et al., 1979; Liolios and Andersen, 1979) or both. Urinary retention has been reported following the extradural injection of morphine (Bapat, Kshirsagar and Bapat, 1979). The urinary retention was frequent in the morphine 0.2 mg kg\(^{-1}\) group. A local-anaesthetic effect may occur with high dose of intrathecal pethidine (Cousins et al., 1979) and may be the explanation. On the other hand, a central mechanism can also be invoked. The use of a 25-gauge spinal needle probably explains the occasional occurrence of headache in the patients studied despite the prolonged head-up position. The normal muscular activity that this technique of spinal analgesia permits is particularly useful in the period after laparotomy or thoracotomy because it permits breathing exercises. The extradural injection of morphine also produces analgesia without central depression and may allow repeated injections through a catheter (Behar et al., 1979). The intrathecal procedure has the advantages of being technically easier than the extradural technique and a single injection produces pain relief of sufficient duration for most postoperative patients. Pain following abdominal or thoracic surgery is much less by the 2nd day after operation. However, a prolonged head-up position may be difficult to maintain in the period after

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operation. Thus, the respective indications for extradural and intrathecal methods of analgesia have to be clarified by a comparative study.

We confirm that the intrathecal injection of morphine produces good and long-lasting pain relief after operation without major respiratory depression. However, the intrathecal administration of the dose of 0.02 mg kg\(^{-1}\) of morphine that we recommend must be made at least 4 h after any systemic injection of narcotic and be associated with a head-up position for at least 12 h. Naturally, the management of such patients should be undertaken in an intensive care unit or a recovery room where the assessment and treatment of any respiratory depression is possible.

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REFERENCES


ZUSAMMENFASSUNG

Patienten mit postoperativen Schmerzen erhielten intrathecale Morphinumgaben von 0,02 mg kg\(^{-1}\) (n = 30) und 0,2 mg kg\(^{-1}\) (n = 30). Die Gruppe mit hoher Dosis erfuhr etwas länger und stärker wirkende Schmerzlinderung. In dieser Gruppe waren Sedierung und Abstiege in Herztätigkeit, systolischem Arteriendruck, Harnverhaltung und Übelkeit häufiger. Zwei Patienten dieser Gruppe zeigten Anzeichen respiratorischer Dämpfung nach einer späteren Haltungsänderung (nach 7 und 11 Stunden). Wir schließen, dass postoperative Morphium-Analgesie mit 0,02 mg kg\(^{-1}\) vor einer längeren Haltung mit hochliegendem Kopf gefolgt und in einem Krankenhaus durchgeführt werden muss, in dem man gute Erfahrungen mit der Behandlung respiratorischer Dämpfungen hat.

SUMARIO

Aquellos pacientes que sufrieron dolor después de la operación recibieron hidrocloruro de morfina intratecalmente, en dosis de 0,2 mg kg\(^{-1}\) (n = 30) y 0,2 mg kg\(^{-1}\) (n = 30). El grupo de la mayor dosis mostró una analgesia ligeramente más poderosa y de mayor duración que el grupo que recibió la dosis menor. El grupo que recibió la mayor dosis presentó con más frecuencia casos de sedación, disminuciones del ritmo cardíaco y presión arterial sistólica, oliguria, nauseas y retención de orina. Dos de los pacientes pertenecientes al grupo de la mayor dosis mostraron evidencia de depresión respiratoria, la cual apareció después de un cambio de postura tarde (7 a 11 h). Concluímos que la analgesia posoperatoriva mediante 0,02 mg kg\(^{-1}\) de morfina intratecal debe ser seguida por un prolongado periodo en el que la cabeza esté elevada y que debe efectuarse en las unidades del hospital en las que el tratamiento de la depresión respiratoria es competente.