The demonstration of opiate receptors in the substantia gelatinosa of the spinal cord (Yaksh and Rudy, 1976) has stimulated interest in the intrathecal administration of morphine in the management of chronic pain and of pain following surgery (Gjessing and Tomlin, 1981; Wang, Nauss and Thomas, 1979). Although the dose of morphine has varied between 0.5 and 20 mg (Samii et al., 1979; Wang, Nauss and Thomas, 1979), good analgesia has been achieved with the smaller doses.

Since orthopaedic operations are performed frequently under subarachnoid blockade, it was decided to assess the efficacy of a small dose of morphine (0.2 or 0.4 mg), administered with the subarachnoid anaesthetic agent, in the control of postoperative pain. Whether the morphine affected the subarachnoid anaesthesia, per se, was studied also.

**Patients and Methods**

**Patients**

The programme of the investigation was approved by the hospital Ethics Committee. Informed consent was obtained from 50 orthopaedic patients (table I) in two different age groups: group A (60–80 yr, ASA I–III) and group B (30–50 yr, ASA I). All patients had normal respiratory function. Chest x-ray, ECG, spirometry and capillary blood-gas analysis were performed before operation on the older patients. Premedication was with diazepam 5–20 mg orally 1.5–2 h before anaesthesia and atropine 0.01 mg kg⁻¹ i.m. about 1 h before anaesthesia.

**Subarachnoid anaesthesia and concomitant medication**

Before the spinal injection, Ringer's solution 8 ml kg⁻¹ was infused rapidly i.v. A similar volume was also administered over a period of about 20 min after the subarachnoid injection of the local anaesthetic. With the patients in a lateral horizontal position the subarachnoid injection was made over about 10 s into interspace L₃–₄ using a 25-gauge needle and barbotage.

The patients were randomly divided into five groups (10 patients in each) according to the amount of morphine hydrochloride (free from preservative) injected with 3 ml of isobaric 0.5% bupivacaine (double-blind):

<table>
<thead>
<tr>
<th>Group</th>
<th>AI</th>
<th>AII</th>
<th>AIII</th>
<th>BI</th>
<th>BII</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F/M)</td>
<td>7/3</td>
<td>5/5</td>
<td>9/1</td>
<td>2/8</td>
<td>1/9</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>(2.1)</td>
<td>(1.7)</td>
<td>(2.0)</td>
<td>(2.0)</td>
<td>(2.6)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73</td>
<td>69</td>
<td>63</td>
<td>76</td>
<td>77</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>(3.0)</td>
<td>(4.5)</td>
<td>(3.1)</td>
<td>(4.4)</td>
<td>(4.9)</td>
</tr>
<tr>
<td>Arthroplasty of hip</td>
<td>164</td>
<td>167</td>
<td>160</td>
<td>173</td>
<td>175</td>
</tr>
<tr>
<td>Arthroplasty of knee</td>
<td>(3.7)</td>
<td>(2.7)</td>
<td>(2.7)</td>
<td>(4.3)</td>
<td>(3.1)</td>
</tr>
<tr>
<td>Meniscectomy</td>
<td>7</td>
<td>5</td>
<td>9</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>2</td>
<td>6</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table I. Characteristics of the patients and types of operation. Mean ages, weights and heights are given (SEM in parentheses)**
Group A I  saline 0.2 ml (older control patients)
Group A II morphine hydrochloride 0.2 mg
(older low-dose patients)
Group A III morphine hydrochloride 0.4 mg
(older high-dose patients)
Group B I  saline 0.2 ml (younger control patients)
Group B II morphine hydrochloride 0.4 mg
(younger morphine patients)

The volume added to the bupivacaine before injection was made up with physiological saline to a final volume of 0.2 ml. If a tranquillizer or an analgesic was required, lorazepam 1–4 mg i.v. or fentanyl 0.05–0.1 mg i.v. was given.

Sensory and motor blockade, haemodynamics
The segmental spread of analgesia was studied by pinprick at 2-min intervals from 4 min after the injection up to 30 min. Regression of analgesia after surgery was tested at 30-min intervals until the first sacral spinal segment had recovered. Motor nerve blockade was evaluated simultaneously using Bromage’s score (0–3) (Bromage, 1965).

Arterial pressure and heart rate were measured at 5-min intervals during the induction of anaesthesia and surgery, and at 15-min intervals in the recovery room. ECG was monitored continuously.

Postoperative analgesia
The intensity of pain was tested with a visual analogue scale (a red-coloured wedge, 10 cm × 30 cm, which was divided on the other side to a scale from 0 = no pain to 10 = unbearable pain) (Houde, 1982) 6, 10 and 24 h after the injection of the anaesthetic and every time the patient required an analgesic drug. The test was performed in the recovery room by the researcher and in the ward by trained nurses. Indomethacin suppositories 50–100 mg or oxycodone 0.13 mg kg⁻¹ i.m., or both, were prescribed for postoperative pain. The need for analgesics was assessed in the ward by trained nurses and it was recorded for 48 h. All observations were double-blind.

Respiratory function and side-effects
The respiratory function was observed carefully in the recovery room and later in the ward. Capillary or venous blood-gas analysis was performed on all older patients 3 and 10 h after the subarachnoid injection.

About 4–5 h after injection the patients were given 100–200 ml of water to drink. Any nausea or vomiting was recorded.

All patients were interviewed by the researcher on the 1st and 2nd days following surgery to detect any side-effects. Pinprick sensation and motor function were tested.

Statistical analysis
The statistical significance of the differences between the means was estimated using Student’s t test.

RESULTS

Patients and subarachnoid blockade
The characteristics of the patients are shown in table I. The operations were mainly arthroplasties in the older age group and meniscectomies in the younger age group (table I).

Sensory blockade was sufficient for surgery except for one older low-dose and one older high-dose morphine patient, who felt pain on incision of the skin, although not thereafter. The mean maximum cranial level of analgesia varied between T8 and T6 and there were no significant differences between the groups (table II). Motor blockade was complete, with one exception in the older control group. This patient was lying on the left side during the whole operation and the left leg was not blocked completely. The duration of analgesia was longer (P<0.01) in the younger patients and slightly longer in the older high-dose than in the older control patients (n.s.). None of the other determinants of the regional block differed significantly.

Systolic arterial pressure decreased moderately during the induction of anaesthesia (fig. 1). During surgery greater decreases in pressure were observed in the older patients, but these were transient and there was no evidence of hypovolaemic shock. Decreases exceeding 30% of the value before operation were noted in older patients only: eight control patients, seven low-dose and six high-dose patients.

Bradycardia (fig. 1) requiring medication with atropine occurred twice in the control group and once in each of the morphine groups.

Postoperative pain and its treatment
Older patients. The need for analgesic drugs and the intensity of pain at the time of first request in different groups are shown in figure 2. The mean maximum intensities of pain as measured by the visual analogue scale during the first 24 h in different groups were: 7.3±0.7 in the control patients, 4.6±0.9 in the low-dose and 1.5±0.7 in the high-
### Table II. Characteristics of spinal blockade

<table>
<thead>
<tr>
<th>Group</th>
<th>Max. analgesic block (segment)</th>
<th>Time to max. analgesic block (min)</th>
<th>Time to max. motor block (min)</th>
<th>Time from max. analgesic block to recovery of S1 segment (min)</th>
<th>Duration of motor block (score 3–0) (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SEM</td>
<td>Range</td>
<td>Mean</td>
<td>SEM</td>
</tr>
<tr>
<td>AI</td>
<td>T6</td>
<td>0.9</td>
<td>T10–T2</td>
<td>21</td>
<td>2.2</td>
</tr>
<tr>
<td></td>
<td>T7</td>
<td>1.0</td>
<td>T11–T2</td>
<td>15</td>
<td>2.0</td>
</tr>
<tr>
<td>AII</td>
<td>T6</td>
<td>0.8</td>
<td>T10–T3</td>
<td>20</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>T8</td>
<td>1.1</td>
<td>L1–T3</td>
<td>19</td>
<td>2.1</td>
</tr>
<tr>
<td>AIII</td>
<td>T7</td>
<td>0.9</td>
<td>T11–T2</td>
<td>12</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>T7</td>
<td></td>
<td></td>
<td>14</td>
<td>2.3</td>
</tr>
<tr>
<td>B1</td>
<td>T6</td>
<td></td>
<td></td>
<td>4–30</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>T7</td>
<td></td>
<td></td>
<td>8–30</td>
<td>2.1</td>
</tr>
<tr>
<td>BII</td>
<td>T8</td>
<td></td>
<td></td>
<td>6–30</td>
<td>2.1</td>
</tr>
</tbody>
</table>

**Group**

- **AI**
- **AII**
- **AIII**
- **B1**
- **BII**

**Fig. 1.** Mean changes (± SEM) in systolic arterial pressure and heart rate from preoperative values during induction and surgery in the older patients.
dose patients. The differences between the groups were statistically significant: between high-dose and control groups \((P<0.001)\), low-dose and control group \((P<0.05)\) and between high-dose and low-dose \((P<0.02)\). In the control group, eight patients required analgesics within 6 h of the injection of the spinal anaesthetic. The two patients who did not need any analgesics during that time had a long sensory block (380 and 345 min) and both required analgesics within the subsequent 2 h. No patients in the morphine groups needed any analgesics during this time. During the next 18 h eight patients in the low-dose group needed analgesics, two of these managing with indomethacin only. In the high-dose group only two patients (one for an aching back) needed analgesics within the first 24 h. Four patients in the high-dose group managed 48 h without any analgesic and two required indomethacin once.

On average, the control group required \(3.7\pm0.5\) doses of systemic analgesics per patient in the first 48 h, the low-dose morphine patients \(3.0\pm1.0\) doses and the high-dose morphine patients \(1.0\pm0.5\) doses per patient. The differences were significant \((P<0.001)\) between the control and high-dose morphine patients and between the high-dose and low-dose morphine patients \((P<0.02)\). There was no statistical difference between the control and low-dose morphine patients.

Interestingly, one patient (older high-dose group) had undergone a similar surgical procedure (total hip arthroplasty) 7 months previously. On that occasion she needed oxycodone five times in 24 h after spinal anaesthesia with bupivacaine. On this occasion, after the addition of morphine 0.4 mg, she managed with only one dose of oxycodone (fig. 2).

Younger patients. The mean maximum intensities of pain during the first 24 h were \(5.9\pm1.0\) in the control and \(2.9\pm0.9\) in the morphine group \((P<0.05)\). As the duration of sensory blockade was longer in the younger patients only three patients in the control group and none in the morphine group required analgesics within the first 6 h after the subarachnoid injection. Within 10 h of the injection eight patients in the control group required analgesics whereas none in the morphine group requested analgesics (fig. 3). The control patients needed on average \(3.5\pm0.6\) doses of systemic analgesics per patient in the first 48 h, while the
morphine group patients received $2.0 \pm 0.6$ doses per patient. The difference was not significant. One control patient and three morphine group patients managed without any analgesics during the first 48 h. The patient with the greatest need for analgesics in the morphine group complained of severe pain each time he needed analgesics.

**PCO$_2$ and side-effects**

The PCO$_2$ (venous or capillary) was significantly greater ($P<0.01$) 3 h after the spinal injection than before the operation in all groups (fig. 4). The increase was greatest in the older high-dose morphine group, but the differences between the groups were not significant. No cases of severe respiratory depression were noted although one patient each in the older high-dose (venous PCO$_2$ 8.5 kPa) and younger morphine groups ($PCO_2$ 7.3 kPa) was cyanotic when observed in the recovery room although the frequency and depth of respiration appeared adequate in both patients. The older high-dose patient had received lorazepam 4 mg during surgery. About 3 h later her PCO$_2$ was 6.7 kPa. Ten hours after the injection the average PCO$_2$ had decreased to within physiological limits in each group, with the exception of two patients in the older low-dose group (PCO$_2$ 8.1 kPa and 7.3 kPa, respectively). One of these patients had received oxycodone about 2 h earlier, while the other one had not received any analgesic up to this time.

As many as seven patients in each of the older control and high-dose morphine groups and five patients in the older low-dose morphine group experienced nausea or vomiting. As many as 14 of these patients had an episode of hypotension (decrease in arterial pressure > 30%) and four patients received fentanyl during the procedure. Five patients had received oxycodone following operation. In the younger patients there was a greater frequency of postoperative nausea and vomiting in the morphine group (table III). Itching occurred only in the morphine groups (three patients, one in each group). Postoperative headache was manifest in the older groups only, but in no instance was it typical post-spinal headache.

Micturition difficulties were recorded in both the morphine and control groups during the first 24 h, but not thereafter. Seven patients in the older group...
already had a urinary catheter in situ before the operation. Five of these had a fractured femoral neck and in two the catheter had been inserted to achieve a better control of fluid balance during rearthroplasties. Five patients in the younger control group had difficulties with micturition, while seven in the younger morphine group complained about voiding difficulties, and three of those needed catheterization on one occasion (table III).

DISCUSSION

Small doses of morphine administered with bupivacaine into the subarachnoid space were found to produce good postoperative analgesia for at least 24 h after orthopaedic surgery. Gjessing and Tomlin (1981) arrived at the same result when they used morphine 0.8 mg in conjunction with tetracaine intrathecally for total hip replacements. Four of 10 patients in the present study who received morphine 0.4 mg managed 48 h without any analgesic. In all morphine groups (both older and younger patients) the time interval to the first request for analgesic was longer than in the corresponding control groups. The smaller dose (0.2 mg) did not appear to be totally adequate in relieving pain for the first 10 h, the period of time during which the maximum degree of pain following this type of surgery (performed under regional anaesthesia) is experienced (Gjessing and Tomlin, 1979). However, there was a marked difference in the maximum intensity of pain as well as in the need for analgesics between the control and morphine groups.

The respiratory depression reported in connection with intrathecal morphine has occurred 10–11 h after the spinal injection (Paulus, Paul and Munson, 1981). This may reflect the time necessary...
for morphine to reach the rostral areas of the CNS. Two patients who had received morphine 0.2 mg had an increased $P_cO_2$ 10 h after the spinal injection, but no clinical evidence of difficulty with respiration was observed. The fact that the $P_cO_2$ at 3 h after the injection was increased in both the morphine and control groups suggests an effect of several factors: lorazepam or fentanyl, or both, during surgery, blood transfusion, episodes of hypotension as a result of blood loss and relative hypothermia caused by major surgery. In fact, the two older high-dose patients with the greatest $P_cO_2$ values at 3 h had been given fentanyl and lorazepam, respectively, during surgery.

One patient in each of the morphine groups complained of itching. In two the site was the face, especially the nose, and the itching may have been caused by the CNS effects of morphine (Jaffe and Martin, 1975).

Nausea or vomiting was more frequent in the older than in the younger patients, which may be a result of the different sex-distribution and types of operation in these groups. The older patients had more major operations which caused more blood loss and a greater frequency of hypotension, both of which cause nausea (Lund, 1971). No correlation was found between the occurrence of nausea and the use of analgesics. Four younger patients who had received morphine and only one younger control patient suffered from nausea or vomiting. Because of the small numbers involved any conclusions about the possible role of morphine may not be justified.

Surprisingly, many patients in the younger group had minor difficulties with micturition. The prolonged subarachnoid block together with prolonged maintenance of a supine position (until next morning) certainly had an effect, as five patients out of 10 in the younger control group had difficulties with micturition in the first 24 h. Nelson and Katz (1980) found no instances of urinary retention in their control group (hyperbaric 1% tetracaine), but five out of seven of those who also received morphine 0.5 mg had urinary retention.

The maximum decreases in the systolic pressure in all older groups were transient and related to blood loss during surgery. It has been suggested that the decreases in systolic and diastolic pressures associated with intrathecal morphine in monkeys (Abouleish et al., 1981) are the result of the direct effect of morphine on the vasomotor centre, a vasodilator effect on the blood vessels or histamine release (Jaffe and Martin, 1975). There were, however, no significant differences in the decreases in systolic pressures between the morphine and control groups during the induction, or during the intra-operative or recovery room periods.

Doses of 0.2 mg and 0.4 mg of preservative-free morphine hydrochloride seem to have no marked effect on the subarachnoid block when given simultaneously with isobaric 0.5% bupivacaine. The duration of blockade was slightly longer (n.s.) in the older morphine groups than in the control group. This difference was not found in the younger patients. All other indices were similar in the morphine and control groups. Interestingly, the duration of spinal analgesia (recovery of S1 segment) was longer in the younger groups than in the older ones. The reason for this is unclear and deserves further study.

ACKNOWLEDGEMENTS

I wish to express my great gratitude to Drs Per Rosenberg and Marjatta Tuominen for the fruitful discussions during this study.

REFERENCES


EFFETS DE LA MORPHINE INTRATHECALE,
INJECTEE AVEC DE LA BUPIVACAINE,
SUR LA DOULEUR CONSECUTIVE A LA
CHIRURGIE ORTHOPEDIQUE

RESUMEN
Du chlorhydrate de morphine 0,4 mg a été administré en même
temps que de la bupivacaine isobare à 0,5% par voie intrathécale
pour des interventions orthopédiques. Elle a permis d’obtenir
une bonne analgésie postopératoire pendant près de 24 h tant chez
des patients âgés (60–80 ans) que chez des patients d’âge moyen
(30–50 ans). La dose de 0,2 mg de morphine (utilisée seulement
chez les patients plus âgés) n’a pas été aussi efficace pour prévenir
la douleur postopératoire, mais a tout de même permis de retarder
la demande d’analgésiques. La morphine n’a pas modifié la
qualité de la rachianesthésie. Dans les groupes d’âges les plus
elevés, la $\text{PCO}_2$ capillaire s’est élevée chez deux patients recevant
morphine 0,2 mg et chez un patient recevant 0,4 mg. Nous
n’avons pas noté de dépression respiratoire sévère prolongée. Les
effets secondaires les plus gênants ont été une rétention urinaire et
des difficultés mictionnelles discrètes. Cette complication n’est
pas apparue comme dose-dépendante, et s’est rencontrée égale-
ment chez des patients n’ayant pas reçu de morphine.