Use of intrathecal morphine for postoperative pain relief following lumbar spine surgery

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A randomized prospective double-blind trial of intrathecal morphine for postoperative pain relief following lumbar spine surgery is described. Intrathecal morphine significantly reduced the mean pain score in the postoperative period (p < 0.01) and there was a corresponding significant reduction in the need for additional postoperative analgesia (p < 0.05). The possible mechanism of action of intrathecal morphine and the potential advantages of this technique are discussed. Possible side effects are also considered, and caution is urged until wider experience has been obtained.

KEY WORDS • analgesia • intrathecal drug delivery • morphine • pain • lumbar spine surgery

The demonstration of opiate receptors and the discovery of naturally occurring opiate substances (enkephalins) in the central nervous system started a new era in pain control. Opiate receptors have been identified autoradiographically in the brain and the substantia gelatinosa of the spinal cord. In a corollary study, morphine administered directly into the spinal subarachnoid space of the rat produced potent analgesia. Subsequent studies confirmed this finding and demonstrated that repeated intrathecal injections of morphine did not cause adverse tissue reactions of the spinal cord. The results of these animal experiments prompted clinical studies on the use of intrathecal morphine for obstetric analgesia and in patients suffering intractable pain from inoperable cancer.

Since the subarachnoid space is readily accessible during operations on the lumbar spine it seemed probable that intrathecal administration of morphine could be used to provide adequate postoperative analgesia in patients undergoing lumbar spine procedures. In addition, if effective it would obviate the need for an extradural catheter as proposed by others and thereby diminish the potentially increased risk of postoperative infection caused by an indwelling catheter. We are therefore reporting our experience with the use of intrathecal morphine for postoperative pain relief following lumbar spine surgery in a double-blind trial in 24 patients.

Clinical Material and Methods

The investigation was approved by the ethics committee of Walsgrave Hospital, and the patient's informed consent was obtained in the preoperative period. All patients undergoing lumbar spine procedures for either prolapsed lumbar intervertebral disc, lumbar canal stenosis, or extradural nerve root adhesions were included. Advanced age was not considered a contraindication to inclusion in the trial; however, two patients were excluded because of severe respiratory disease. Each patient was shown a 20-cm linear analog pain scale, in which the left end represented no pain and the right end represented the most severe pain imaginable, and was asked to indicate the severity of back and leg pain experienced while lying quietly in bed and after turning. Each agreed to provide similar assessments of pain in the postoperative period.

Patients were allocated at the time of surgery in a randomized prospective double-blind manner to either a treatment or a control group. Each patient in the treatment group received 1 mg morphine in 2 ml of saline injected intrathecally. No injection was made in the control group. The case notes did not record to which group the patient belonged.

After recovery from anesthesia and return to the postoperative ward, the patient was asked to indicate the severity of back and leg pain during rest and on turning, at 2-hourly intervals for the succeeding 24...

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hours. The linear pain scale was read and the results were recorded by a member of the nursing staff who was not aware to which group a particular patient belonged.

Parenteral analgesia (papaveretum, 15 to 20 mg intramuscularly every 4 to 6 hours as required) was available to patients in both groups to control any postoperative pain. The time, frequency, and dosage of all analgesic drugs were carefully recorded, and any drug side effects including respiratory depression, hypotension, pruritis, nausea and vomiting, and difficulty in voiding were also documented.

**Results**

Twenty-two patients comprised the control group of whom 13 were female. There were 24 patients in the treated group of whom 11 were female. The mean age was 40.7 years in the control group (range 24 to 75 years) and 38.7 years in the treatment group (range 21 to 69 years). Both groups were well matched for the type of procedure performed.

The mean pain scores for back and leg pain at rest and on turning are graphically demonstrated in Fig. 1. When the Wilcoxon rank sum test was applied to these values, \( p < 0.01 \) was achieved in all instances. However, the differences in each group failed to remain significant after 16, 12, 12, and 20 hours (unpaired t-test, using \( p \) values corrected for multiple tests).

Forty-six percent of the treatment group and 14% of the control group did not require any additional postoperative analgesia. The mean number of analgesic doses per patient in each group was 1.25 and 2.3, respectively (\( p < 0.05 \) Wilcoxon rank sum test).

All patients were monitored for drug side effects including respiratory depression, hypotension, pruritis, nausea and vomiting, and difficulty in voiding. The only significant difference between the two groups was an increased incidence of pruritis in those given intrathecal morphine. Respiratory depression was not encountered in either group.

**Discussion**

The present study demonstrates that intrathecal morphine produces a highly significant reduction in mean pain scores during the postoperative period, with a corresponding reduction in the need for additional postoperative analgesia. The mean number of analgesic doses per patient in each group was 1.25 and 2.3, respectively (\( p < 0.05 \) Wilcoxon rank sum test).

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The present study demonstrates that intrathecal morphine produces a highly significant reduction in mean pain scores during the postoperative period, with a corresponding reduction in the need for additional postoperative analgesia, such that 46% of those treated did not require any additional analgesia during the trial period. The precise mechanism of action of intrathecal morphine is somewhat controversial; however, there is
Intrathecal morphine for postoperative pain

now a large body of experimental evidence to suggest that morphine can act at a spinal level. In earlier work from Kitahata’s laboratory, intravenous administration of morphine sulfate selectively suppressed spontaneous activity of dorsal horn cells that respond to noxious stimuli while not significantly altering the spontaneous activity of cells known to react best to non-noxious stimuli. Later, Dohi and colleagues, utilizing noxious thermal stimuli in decerebrate cats with transected spinal cords, reported that 1 to 2 mg/kg of intravenous morphine significantly depressed both spontaneous and evoked activity of wide dynamic range neurons. The extent of suppression was related to the dosage of morphine, and the suppression could be reversed by naloxone. In similar studies, Yaksh reported that morphine or etorphine depressed the responses to high-threshold noxious stimuli in all the cells studied and also attenuated the responses to low-threshold stimuli in about 30% of cells.

Calvillo, et al., recorded extracellularly from cells in laminae I, IV, V, and VI of the dorsal horn of cats with spinal cord transection. Intravenous morphine depressed both the spontaneous and the noxiously evoked activity of nociceptive neurons, while having no effect or only a slight depressive action on the response of the same cells to non-noxious stimuli. Similarly, Toyooka, et al., reported that, in cats with spinal cord transection, morphine suppressed both the spontaneous and the noxiously evoked activity of cells in lamina VII. In addition, the threshold intensity of heat needed to activate these cells was increased by morphine and the slope of the temperature versus firing frequency regression line was significantly decreased. These effects were quickly reversed by naloxone.

Grossmann and Jurna demonstrated that morphine reduced the number of impulses discharged by ventrolateral tract axons following electrical stimulation of A delta and C fibers in the sural nerve. They thereby demonstrated for the first time a drug effect on ascending pathways.

In addition to the large body of neurophysiological evidence, Yaksh, et al., provided behavioral evidence supporting the proposition that morphine can act at the level of the spinal cord. Wang confirmed these effects in rats, and reported that gross and microscopic studies of the spinal cord 7 days after injection of 25 μg of morphine in 50 μl of saline produced no adverse tissue reactions. In the discussion section of that article, brief mention is made of a clinical trial of the technique in human subjects. This initial report of the clinical use of intrathecally applied morphine in man was quickly followed by several reports of similar clinical work.

Wang, et al., used a double-blind technique in eight patients suffering intractable pain from inoperable cancer, and found that in all of the patients the administration of intrathecal morphine produced long-lasting pain relief without changing other neurological functions. Similar results were reported by Ventafridda, et al., but in their series there was a higher incidence of drowsiness, orthostatic dizziness, pruritus, sweating, and nausea. Samii, et al., used a high dose of intrathecally administered morphine (20 mg), and found the effects to be similar to those reported in previous work involving lower doses. Baraka and colleagues used intrathecally administered morphine for obstetric analgesia and again achieved excellent pain relief.

The present study is the first report on the use of intrathecal morphine for relief of postoperative pain after lumbar spine surgery. Both Teddy and colleagues using diamorphine and Schmidek and Cutler using morphine have reported on the use of epidurally applied analgesics for pain relief after spinal surgery. It is difficult to compare the results achieved in the present study with those reported in these two previous series, as neither previous study was a randomized prospective double-blind trial. In addition, the epidural approach, while possibly achieving a good analgesic effect, requires that a catheter be left in situ, thereby theoretically increasing the potential risk of postoperative infection. As the intrathecal space is readily accessible during lumbar spine procedures we believe that this route may be more appropriate.

The incidence of pruritis was higher in the treatment group than in the controls. No other untoward complications of intrathecal morphine administration were found in this study with the dosage used. The most potentially serious side effect would be respiratory depression. This has been reported by Glynn, et al., Liolios and Andersen, and Davies, et al., with dosages varying from 15 mg to as low as 1 mg. The respiratory depression frequently occurred approximately 10 hours after administration of the spinal anesthetic, and therefore may be due to the cephalad spread of morphine via the cerebrospinal fluid. Long, commenting on the work of Schmidek and Cutler, also warned about the potential risk of respiratory arrest and pointed out that intraspinal analgesia must still be considered investigational and must be compared with other potential methods of pain control. Although we have been impressed by the level of analgesia obtained in the present study, we consider that Long’s warning is timely, and that much wider experience should be obtained before the usefulness of this technique can be fully established.

References

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