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Audits

An Audit of Intrathecal Morphine Analgesia for Non-Obstetric Postsurgical Patients in an Adult Tertiary Hospital

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SUMMARY

We conducted a retrospective audit of adult non-obstetric patients who had received a single dose of intrathecal morphine for postoperative analgesia. These patients were predominantly admitted to a regular postsurgical ward with strict hourly nursing observations, treatment protocols in place and supervision by an Acute Pain Service for the first 24 hours after intrathecal morphine administration. A total of 409 cases were examined for sedation score, incidence of respiratory depression and other side-effects, admission to the high dependency or intensive care unit and opioid-tolerance. Respiratory depression was defined as requiring treatment with naloxone (implying a sedation score of 3 irrespective of respiratory rate), or a sedation score of 2 with a respiratory rate less than six breaths per minute. The patients were predominantly elderly (57.2% were over the age of 70 years) and 84.8% had undergone vascular surgery. Of the total of 409 cases, only one case of respiratory depression was observed. A total of 77 patients were admitted to high dependency or intensive care unit for various reasons including management of postsurgical complications and patient co-morbidities. Our findings suggest that elderly patients who receive intrathecal morphine analgesia can be safely managed in a regular postsurgical ward.

Key Words: intrathecal, morphine, audit, elderly, respiratory depression, sedation

Single dose intrathecal morphine in combination with spinal (subarachnoid) local anaesthetic injection, providing intraoperative anaesthesia and postoperative analgesia, has been utilized for the last 25 years or more[1]. However some clinicians view this technique as unsafe because of concerns of delayed respiratory depression[2]. The perception of increased opioid-related side-effects and lack of titratability of analgesia with this technique may lead some clinicians to favour systemic opioids, including patient-controlled analgesia (PCA) and other methods of pain relief. It has been argued that all patients given intrathecal morphine must be admitted to a high dependency or intensive care unit (HDU or ICU) for closer nursing observations[3, 4].

For more than ten years intrathecal morphine and other intrathecal opioids have been popular analgesic techniques after caesarean section. Most studies of efficacy and safety after intrathecal morphine have been conducted in women after caesarean section[5,6]. Fewer studies have reported on the safety of this technique in elderly post-surgical patients after non-obstetric surgery; for example after urologic, orthopaedic, vascular, non-obstetric gynaecological and general surgery. Gwirtz et al[7] conducted a prospective clinical observational study of more than 5000 patients who received intrathecal opioids for analgesia after such operations. They reported a high degree of patient satisfaction and a low incidence of adverse effects including respiratory depression. However, the incidence of respiratory depression in their study was 3%, which many would not regard as low. The investigators suggested that low-risk adult patients less than 70 years of age who received intrathecal opioids after non-obstetric surgery could be safely managed in a regular hospital ward.

The Royal Adelaide Hospital (RAH) is an adult tertiary referral centre of some 700 beds. The RAH Acute Pain Service (APS) was established in 1989 to provide and supervise advanced analgesic techniques for predominantly postoperative patients. The APS is a 24-hour service run by anaesthetists. In our

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institution, additional opioid administration is strictly forbidden for the first 24 hours after administration of intrathecal morphine, unless approved by the APS. We admit patients given intrathecal morphine after vascular surgery to our regular vascular unit ward, where there are APS-accredited nursing staff and strict protocols in place for monitoring and early treatment of any adverse effects. However, we plan to admit other postsurgical patients who have been given intrathecal morphine to our HDU or ICU. The RAH has a high proportion of elderly patients with significant co-morbidities, as well as patients who are opioid-tolerant. The aim of this audit was to assess the incidence of respiratory depression and other complications with intrathecal morphine use in our institution.

METHOD

Approximately 26,000 RAH APS data sheets from March 1989 to December 2003 were retrospectively reviewed and the information from patients who had been given a single dose of intrathecal morphine in combination with spinal (subarachnoid) anaesthesia was examined. Patients who were given other intrathecal opioids (such as fentanyl and pethidine) and patients with in-dwelling intrathecal catheters were excluded.

The information from the APS data sheets was reviewed for age and gender of patient, type of surgery, dose of intrathecal morphine, sedation scores, respiratory depression, ward admitted to after the recovery unit and any opioid administration within 24 hours after intrathecal morphine. Incidence of nausea or vomiting and pruritus were also recorded.

After approval from the hospital Research Ethics Committee, patients' medical records were also checked to obtain any incomplete data regarding intrathecal morphine dose, further opioid administration within the first 24 hours and ward of discharge.

Respiratory depression as an adverse effect of intrathecal morphine was of particular interest in this audit. Respiratory depression requiring treatment with naloxone is defined by the Acute Pain Service as a sedation score of 3, irrespective of respiratory rate, or a sedation score of 2 plus a respiratory rate of less than six breaths/minute. Sedation is a more reliable early sign of opioid-induced respiratory depression than a decrease in respiratory rate (see Discussion). The sedation scoring system used at our hospital is outlined in Table 1. Any respiratory depression, administration of naloxone, further resuscitative management and transfer to the HDU were also noted.

TABLE 1
Definition of sedation scores

Sedation score	*Clinical features*
0	None
1	Mild, occasionally drowsy, easy to rouse
2	Moderate, constantly drowsy, easy to rouse
3	Severe, somnolent, difficult to rouse
S	Asleep, easy to rouse

Patients who were opioid-tolerant preoperatively and who subsequently received intrathecal morphine were of particular interest in this audit. These patients were defined as having received opioid agonists regularly for at least seven days before their surgery and were identified from the APS data sheets. Information about any additional opioid administration within the first 24 hours after intrathecal morphine administration was collected from the APS data sheet or the patient's medical records. Respiratory depression, using the same definition as above, was also looked for closely.

As elderly patients may have an increased risk of respiratory depression following intrathecal morphine, patients in this audit were arbitrarily divided into two age groups; those aged 70 years or more and those under the age of 70 years. A reduced opioid dose for elderly patients is used by the APS regardless of the technique involved, for example halving the initial bolus dose of PCA morphine to 0.5 mg.

RESULTS

A total of 409 patients were identified over the 13-year period; 272 were male and 137 female (66.5% and 33.5% respectively). More than half the patients (57.2%) were aged 70 years or older. The majority of patients (84.8%) had undergone vascular surgery. Table 2 summarizes patient and surgical data.

The doses of intrathecal morphine used ranged from 0.05 mg to 0.3 mg; the majority were 0.1 mg, 0.15 mg or 0.2 mg (22.9%, 30.2%, and 45.3% respectively of all doses). Pain scores within the first 24 hours are measured using a verbal numerical scale (between 0 to 10), however only 54% of APS record sheets provided this information. Table 3 summarizes the adverse effects recorded following administration of intrathecal morphine.

Only one patient out of the total 409 cases developed respiratory depression by our APS criteria (0.24%). This was a 74-year-old male with a past history of cerebrovascular accidents resulting in dysarthria and epilepsy. Preoperatively he was managed with an intravenous ketamine infusion

TABLE 2
Patient details and type of surgery

Patient age	
<70 years	171
70 years or more	234
Not recorded	4
Patient gender	
Male	272 (66.5%)
Female	137 (33.5%)
Opioid-tolerant	28
Given additional opioid within 24 hours	47
Given a concurrent IV ketamine infusion	12
Ward after discharge from recovery	
HDU/ICU	77
General vascular ward	324
Other general surgical ward	8
Type of surgery	
Vascular surgery	347
Orthopaedic surgery	50
Urology	6
General surgery	6

TABLE 3
Adverse effects

Respiratory depression (sedation score of 3)	1 (in recovery)
Sedation score 2 but respiratory rate ≥6 breaths/minute (not considered to be respiratory depression)	5
Nausea/vomiting	67 (16.4%)
Pruritus	30 (7.3%)
Mortality (not related to intrathecal morphine)	1

of 4 mg/h for intractable ischaemic leg pain that was not responding well to opioids. Subsequently his ischaemic leg was amputated under spinal anaesthesia with bupivacaine and 0.1 mg intrathecal morphine. Postoperatively his ketamine infusion was continued. Two hours after admission to the recovery unit he became unrousable (sedation score 3). He remained spontaneously ventilating on 6 litres per minute of oxygen with a respiratory rate of 16 breaths per minute and an oxygen saturation of 96%. Following our APS protocol, naloxone 100 μg was administered intravenously and the ketamine infusion was ceased, rapidly effecting a reversal of his sedation. He was closely monitored in the recovery unit for 24 hours postoperatively with no further sedation or respiratory depression. The ketamine infusion was recommenced and he was discharged to the vascular surgical ward with no further events.

There were five patients who had a sedation score of 2 (see Table 3). However their respiratory rate remained above six breaths per minute throughout the hourly nursing observations in the first 24 hours. These cases included two opioid-tolerant patients. The first patient was a 58-year-old man given 0.15 mg intrathecal morphine at the time of spinal anaesthesia for leg amputation. Seven hours later, due to inadequate analgesia, he was ordered an intravenous morphine PCA and an intravenous ketamine infusion (initially at 4 mg/h increased to 8 mg/h one hour later). This was followed by 25 mg of oral amitriptyline 12 hours after intrathecal morphine administration. Although a sedation score of 2 was not recorded until 25 hours after the intrathecal morphine dose, the ward nursing staff had documented the patient's sedation score as "S" (sleeping) from 18 hours after administration. Thus we cannot be sure that the patient did not have a sedation score of 2 at this earlier time, especially as he had not used the PCA since "S" was first noted. Total PCA morphine dose at that time was 16 mg. The nurses are supposed to wake the patient if asleep, but we suspect this sometimes did not happen.

The second opioid-tolerant patient with a sedation score of 2 was a 75-year-old man who received 0.2 mg intrathecal morphine. Six hours later, again due to inadequate analgesia, the patient was given his usual slow-release oral morphine 60 mg (which would normally have been continued) and commenced on intravenous morphine PCA. Thirteen hours after the intrathecal morphine, the patient was noted to have a sedation score of 2. The total intravenous morphine used via PCA was 18 mg. The patient did not start morphine PCA again until 18 hours after the intrathecal morphine dose had been given, by which time his sedation score had returned to 0.

Of the other three patients noted on the APS data sheets to have had sedation scores of 2, one had suddenly became sedated; this was noticed by his family and believed to be another of his transient ischaemic attacks (TIA). Another patient had a single recording of a sedation score of 2 at 13 hours after intrathecal morphine; all other sedation scores were 1 or 0 and he had not been given any additional opioids or sedatives. The third patient was now deceased and his case notes could not be found for retrospective review, hence no information is available for the timing of the sedation score of 2 or administration of concurrent sedatives.

There were a total of 28 patients identified as opioid-tolerant (Table 4). Of these, only ten had their opioids withheld during the first 24 hours after intrathecal morphine. The remaining 18 patients were given further opioids in the following manner: continuation of their usual opioid regimen of oral slow-release morphine, oral methadone or oxycodone; co-administration of intravenous morphine via PCA; or subcutaneous morphine administered by nursing staff as required for rescue analgesia. All cases of additional opioid within the first 24 hours were approved and supervised by the APS. Only two patients had sedation score of 2 as reported above; no patient developed respiratory depression (by our definition) in the postsurgical ward.

TABLE 4
Additional analgesia in first 24 hours after surgery

	Opioid-tolerant patients	Opioid-naïve patients
Oral morphine slow-release	6	0
Oral oxycodone	2	4
Oral methadone	1	0
PCA morphine	6	18
Subcutaneous opioids	3	7
Ketamine infusion	2	2

Of the patients who were opioid-naïve, 29 were given opioids for rescue analgesia within 24 hours after intrathecal morphine (Table 4). In all but one patient, this additional opioid administration was approved and supervised by the APS. In this one exception, the patient was given intramuscular pethidine without APS approval and in violation of APS protocols. Most cases of rescue opioid utilized intravenous morphine via PCA for post-orthopaedic joint replacement surgery; however subcutaneous morphine or fentanyl, and oral oxycodone were also used. Of these opioid-naïve patients, 14 (4.4%) were vascular patients compared to 15 (24.2%) non-vascular patients.

A total of 77 patients were admitted to HDU/ICU postoperatively following intrathecal morphine administration. Of these patients, 54 were non-vascular postsurgical cases who could not be nursed in the general surgical wards according to our APS protocols, which do not allow patients given intrathecal morphine to go to wards where the nursing staff are not accredited for this technique.

The remaining 23 patients admitted to HDU/ICU had undergone vascular procedures. Of these patients, five had returned to the operating theatre for surgical control of postoperative bleeding. These patients were given general anaesthesia and intravenous opioids within the 24 hours after intrathecal morphine. One patient had intrathecal morphine followed by intravenous morphine PCA for abdominal aortic aneurysm repair, and hence required several days of ICU management. Three other patients also had significant cardiac co-morbidities which led to admission into HDU/ICU postoperatively for more intensive monitoring and management. One of these three patients suffered a fatal cardiac arrest secondary to an arrhythmia within 24 hours postoperatively and resulted in the only mortality of this audit. He was not sedated prior to the cardiac arrest. Another 14 vascular surgical patients were admitted to HDU/ICU after intrathecal morphine for no apparent reason; we presume the anaesthetists concerned took extra precautions.

A total of eight patients had undergone non-vascular surgical procedures and were not admitted to HDU, ICU or the vascular surgery ward. This was a violation of the APS protocol in this institution. Five of these patients had orthopaedic joint replacement surgery, received no opioid analgesia within the first 24 hours after intrathecal morphine and their postoperative analgesia thereafter was managed by the surgical team. There was one patient who had undergone a radical prostatectomy with analgesia managed by intrathecal morphine and intravenous PCA morphine; and the last patient had superficial leg surgery with no further requirements for opioid analgesia.

DISCUSSION

Our ability to look at the efficacy of intrathecal morphine as an adequate postsurgical analgesic technique is limited in this audit. Recordings of patient pain score as measured by verbal numerical rating scale or a patient's verbal report in terms of "no pain, mild, moderate, or severe pain" were incomplete on many APS data sheets, which may partially reflect the problems in the assessment of pain in some elderly patients. Although we found that 24.2% of non-vascular opioid-naïve patients received additional opioid compared with 4.4% of their vascular counterparts, we cannot conclude from our small numbers that non-vascular patients had significantly poorer analgesia after intrathecal morphine.

The incidence of nausea/vomiting and pruritus in our audit was 16.4% and 7.3% respectively. These are low compared with the incidence reported in other publications[8,9], especially in that by Vercauteren and co-workers who recorded an incidence of up to 48% each for nausea and pruritus in obstetric practice[11].

Our lower incidence of these intrathecal morphine adverse effects may be due to the retrospective nature of this audit or it may be because of the number of elderly patients. A reduced incidence of these adverse effects in the elderly age group compared with the obstetric group has been found by other investigators[8,12].

In the early 1980s, reports of delayed respiratory depression after intrathecal morphine in high doses of 0.5 mg to 2.0 mg began to emerge[10]. Since the mid-1980s smaller doses of intrathecal morphine (0.1 mg to 0.2 mg) were used and reported to be safe and effective. However the debate continued. This led to the publication by Gwirtz et al[7] of a prospective seven-year audit of more than 5000 patients who received intrathecal opioid analgesia. Their protocol allowed for most of the 5000 patients to be cared for in regular postsurgical wards. Only high-risk patients such as the elderly (age >70 years), those with poor pulmonary function, or those who had undergone major thoracic or aortic surgery were admitted to the ICU. The main finding of their study was a respiratory depression incidence of 3%, which was detected by routine nursing observations that mandated hourly observations for 24 hours postoperatively. Gwirtz et al[7] did not report on which of these patients had respiratory depression; it would be of interest to know whether these were the patients admitted to regular postsurgical wards, or those who received higher doses of intrathecal morphine, or the elderly or the respiratory compromised.

We were able to show that our incidence of respiratory depression was much less than reported by Gwirtz et al[7]. In our audit of 409 cases, only one patient developed respiratory depression by our definition. This patient had a sedation score of 3 (unrousable), which was recognised at an early stage, prior to any drop in respiratory rate or oxygen desaturation, and easily treated with just a single dose of naloxone 100 μg intravenously. That respiratory depression would occur at this early stage is probably unusual, given that the intrathecal morphine dose was small and that the onset of respiratory depression after intrathecal morphine is typically delayed by some hours. In addition, if respiratory depression did occur, it is likely to persist for some time. In this situation, repeat doses of naloxone would be required as the duration of its effect is relatively short. In our patient, re-sedation and a recurrence of respiratory depression did not occur and further doses of naloxone were not needed. Given the patient's past history, it could also be possible that the patient may have suffered a transient ischaemic attack.

It has also been suggested that ketamine, an NMDA receptor antagonist, may increase the risk of respiratory depression when given with opioid analgesic agents. Concurrent administration of NMDA receptor antagonists and opioids in the rat resulted in an increased incidence of respiratory depression compared with opioids alone[13]. However it may not be possible to extrapolate these results to low-dose ketamine administration in humans. Other than this patient, where the diagnosis of intrathecal opioid-induced respiratory depression is possibly questionable, respiratory depression was not seen.

Of those patients who had sedation score of 2 but no reduction in respiratory rate to less than six breaths/min, two were given intravenous morphine via PCA because of inadequate analgesia. In one of these patients, an intravenous ketamine infusion and oral amitriptyline were also used as co-analgesics. As noted earlier, although a sedation score of 2 was first documented 25 hours after the intrathecal morphine had been given, the patient could have been sedated for some hours before when the nurses scored him as "S". By APS protocol, nursing staff are supposed to check if a sleeping patient can be roused, but this may not have been done. Furthermore, in both of these cases, the initial PCA morphine bolus dose was not halved. APS guidelines note that this should be done until the peak rise of delayed respiratory depression has passed (16 hours) unless an increase is needed because of inadequate analgesia. Amitriptyline, given at a dose of 25 mg orally in the evening, may have been another contributing factor to the sedation.

We suggest caution in prescribing concurrent sedatives and co-analgesics to patients who have been given intrathecal morphine and, that if they are needed, lower doses should be used in the first instance. These doses can be increased later if found to be inadequate and the patient known not to be sedated. Vigilant nursing observations are required and nursing staff need to be aware of the important difference between normal sleep (when the patient is easily rousable) and opioid-induced sedation. We have now deleted the "S" from our sedation scoring system.

The situation regarding management of opioid-tolerant patients given intrathecal morphine is potentially difficult. The main aim is to provide adequate analgesia for the acute postoperative pain whilst preventing opioid withdrawal as well as respiratory depression. In our audit we found that three different strategies were used in these patients: administration of intrathecal morphine alone within

the first 24 hours (depending on their preoperative opioid dose); intrathecal morphine and continuation of regular oral opioid (most commonly slow-release morphine); and intrathecal morphine together with parenteral opioids. We cannot say from our audit and small patient numbers whether an advantage is offered by any one of the above strategies. It is clear however, that with strict monitoring guidelines in a regular postsurgical ward and with co-administration of only APS-approved opioid, those opioid-tolerant patients can be safely given intrathecal morphine as well as additional opioids.

A major problem in comparing studies of opioid-induced respiratory depression, including after intrathecal morphine, is the lack of agreement for the best definition of respiratory depression. Gwirtz et al[7] used the criteria of increasing P_aCO_2. This has an important impact on interpreting results of different studies that look at the incidence of respiratory depression. Several arbitrary indices have been used to define respiratory depression, such as respiratory rate less than 8 or 10 breaths/min, oxygen desaturation to less than 95% or 90%; reduced nasal air flow; arterial blood gas analysis for acidosis or hypercarbia with P_aCO_2 >50 mmHg; and sedation scores[9,14,15]. Regular postsurgical wards would find monitoring nasal airflow and arterial blood gas analyses impractical. Oxygen desaturation as measured by pulse oximetry has several problems which make it unreliable as a sign of respiratory depression, especially if the patient is receiving supplemental oxygen. Continuous pulse oximetry monitoring would also be required. Sedation has been shown to be a more reliable earlier sign of depression than a decrease in respiratory rate[16]. Hence we rely primarily on sedation scores as our measure of respiratory depression.

In summary, our regimen for the management of patients given intrathecal morphine appears to be safe for our predominantly elderly patients in a regular postsurgical ward provided there is a strict adherence to protocols. These protocols should include a minimum of the following: registered nurses appropriately trained and accredited by the APS; hourly nursing observations of sedation score, respiratory rate and other vital signs for 24 hours after intrathecal morphine administration; an intravenous naloxone standing order for reversal of respiratory depression; 24-hour cover provided by on-site anaesthetists; and no further opioid administration within the first 24 hours unless approved by the APS.

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