A comparison of the postoperative analgesic efficacy of single-dose epidural tramadol versus morphine in children

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**Background.** The aim of this study was to compare epidural administration of single-dose tramadol with morphine in children undergoing urological surgery with respect to preoperative haemodynamic effects, postoperative analgesia and side-effects.

**Methods.** Eighty children aged between 7 and 14 undergoing urological surgery were included in the study. After intubation, in the lateral decubitus position, a single dose of morphine 0.1 mg kg\(^{-1}\) in isotonic saline 0.2 ml kg\(^{-1}\) (morphine group) and tramadol 2 mg kg\(^{-1}\) in isotonic saline 0.2 ml kg\(^{-1}\) (tramadol group) was administered epidurally. During the 24-h postoperative period, heart rate, systolic blood pressure, respiration rate, pain score and sedation level of the patients were monitored. A modified objective pain score of 3 or lower was accepted as an indicator of inadequate analgesia and these patients were given 20 acetaminophen mg kg\(^{-1}\) rectally or orally. Time to first analgesia was noted. Sedation level was evaluated with a four-point sedation scale.

**Results.** In the postoperative period, pain scores and the average time for analgesic requirement were similar in the two groups. However, the incidences of allergic rash, itching, sedation and respiratory depression and sedation score were greater in the morphine group than in the tramadol group.

**Conclusion.** Greater epidural use of tramadol may be preferred to morphine for postoperative analgesia under these circumstances.

Since Jensen first described the use of epidural morphine in 1981, several studies have provided evidence of prolonged analgesia following its use.1-3 Unfortunately, a number of side-effects are associated with the use of epidural opioids. These include nausea and vomiting, pruritis, urinary retention and hypoventilation. Of these, the most serious is respiratory depression. While delayed respiratory depression is well described after epidural injection of morphine in adults (three to four cases per 1000 administrations), the overall risk in children is unknown.4-7

Tramadol, a synthetic 4-phenyl-piperidine analogue of codeine, has been available in the UK since 1994, although it is licensed only for use in children aged >12 yr. Tramadol is a racemic mixture of two enantiomers, (+)-tramadol and (−)-tramadol. The (+)-enantiomer has moderate affinity for the opioid \(\mu\) receptor, which is greater than that of the (−)-enantiomer. In addition, the (+)-enantiomer inhibits serotonin uptake and the (−)-enantiomer is a potent norepinephrine inhibitor. These complementary properties result in a synergistic antinociceptive interaction between the two enantiomers.8 The result is an opioid with a lack of respiratory depressant effects despite an analgesic potency that has been shown to be approximately equal to that of pethidine in some studies.9-11 Furthermore, animal work has suggested that tramadol may have a selective spinal action.12-13 Although not licensed for this indication, tramadol has been shown to provide effective, long-lasting analgesia after extradural administration in children.14-16

The objective of this study was to compare the postoperative analgesic properties and side-effects of a single epidural dose of tramadol with those of morphine in children undergoing urological surgery.
Methods

After obtaining local ethics committee approval and written, informed parental consent, 80 boys (age 7–14 yr, ASA I) scheduled for various types of urological surgery were included. The study design was randomized and double-blind, and patients were allocated by computer-generated randomization. Exclusion criteria included local infection of the epidural region, a history of allergic reactions to opioids, bleeding diathesis, aspirin ingestion during the previous week, pre-existing neurological or obvious spinal diseases, and congenital anomaly of the lower back as determined by physical examination.

No premedication was used. After i.v. cannulation, anaesthesia was induced with thiopental 5 mg kg⁻¹ (Penthal Sodium® 500 mg; IE Ulagay, Istanbul, Turkey) and tracheal intubation was facilitated using atracurium 0.5 mg kg⁻¹ (Tracrium® 25 mg 2.5 ml⁻¹; Glaxo-Wellcome, Philadelphia, USA). Anaesthesia was maintained with sevoflurane 2–2.5% (Sevorane; Abbott, Chicago, USA) and nitrous oxide 50% in oxygen. After the induction of anaesthesia, patients were placed in the lateral decubitus position, and, after disinfecting the skin with an iodine-based solution and draping, an 18-gauge paediatric Tuohy needle (Epican 18G; Braun, Melsungen, Germany) was introduced at the L3 to L4 interspace in the midline. The loss of resistance technique was used to locate the lumbar epidural space with a syringe containing preservative-free saline. After ensuring no cerebrospinal fluid (CSF) or blood backflow from the epidural Tuohy needle, a test dose containing epinephrine (1:200 000 or 5 μg ml⁻¹) was administered. The electrocardiogram was observed for 2–3 min for tachycardia or T wave changes. Morphine or tramadol was then given as a single dose. Patients were randomized into two groups prospectively. The morphine group (Group M) received morphine 0.1 mg kg⁻¹ diluted in saline 0.2 ml kg⁻¹ and the tramadol group (Group T) received tramadol 2 mg kg⁻¹ diluted in saline 0.2 ml kg⁻¹. No other peroperative analgesia was given.

During the recovery period, heart rate, arterial pressure, peripheral oxygen saturation, ventilatory frequency, pain and sedation scores were recorded before discharge to the surgical ward. A modified objective pain score (MOPS), amended to give a maximum score of 10, was used for postoperative pain evolution. Sedation score (0=eyes open spontaneously, 1=eyes open to speech, 2=eyes open when shaken, 3=unrousable) was also recorded after surgery. Assessments of postoperative pain and sedation scores were recorded 30 min after extubation and at 2, 4, 6 and 24 h. A pain score greater than 3/10 was taken as an indication for administering oral or rectal acetaminophen 20 mg kg⁻¹, as deemed appropriate. Episodes of nausea, vomiting, facial flushing or pruritus were recorded.

Patient characteristics were compared by using the unpaired Student’s t-test. Repeated measures ANOVA was used to compare all the other variables within the same group. Differences within the group were assessed using the Tukey-Kramer test, and comparison of the groups was validated using the unpaired Student’s t-test. A group size of 40 was derived based on 98% power to detect a maximum difference of 0.93 in MOP scores (α=0.05, β=0.2). A P-value <0.05 was considered statistically significant.

Results

Age, weight, sex and duration of surgery (P>0.005) of the groups and the names of the operations performed are presented in Table 1.

There were no statistically significant differences between the groups with respect to postoperative pain scores (Table 2). No statistically significant differences in time to first supplementary analgesic administration were observed between the groups. Three patients from both groups needed supplementary analgesics within the first 6 h. Between 6 and 24 h, 11 patients from group M and 12 patients from group T needed supplementary analgesics. Twenty-four patients from group M and 22 from group T did not need supplementary analgesics within 24 h (no significant difference).

Table 1 Demographic data of patients and types of operations performed. Data are mean (range) or mean (SD). NS, not significant (P>0.05)

<table>
<thead>
<tr>
<th></th>
<th>Group M (n=40)</th>
<th>Group T (n=40)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>8.3 (7–14)</td>
<td>8.07 (7–13)</td>
<td>NS</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>25.2 (10.4)</td>
<td>24.5 (11.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male, n)</td>
<td>40</td>
<td>40</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of operation (h)</td>
<td>2.8 (0.9)</td>
<td>2.5 (0.6)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 2 Postoperative pain scores. Median (range); n=40 in each group. NS, not significant (P>0.005)

<table>
<thead>
<tr>
<th></th>
<th>Group M</th>
<th>Group T</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 min</td>
<td>1 (0–2)</td>
<td>1 (0–3)</td>
<td>NS</td>
</tr>
<tr>
<td>2 h</td>
<td>1 (0–2)</td>
<td>1 (0–4)</td>
<td>NS</td>
</tr>
<tr>
<td>4 h</td>
<td>1 (0–3)</td>
<td>2 (0–4)</td>
<td>NS</td>
</tr>
<tr>
<td>6 h</td>
<td>2 (1–4)</td>
<td>2 (1–5)</td>
<td>NS</td>
</tr>
<tr>
<td>24 h</td>
<td>3 (2–6)</td>
<td>3 (2–7)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 3 Postoperative sedation scores. Median (range); n=40 in each group. NS, not significant (P>0.005)

<table>
<thead>
<tr>
<th></th>
<th>Group M</th>
<th>Group T</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 min</td>
<td>2 (1–3)</td>
<td>1 (0–2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>2 h</td>
<td>2 (1–2)</td>
<td>1 (0–2)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4 h</td>
<td>1 (0–2)</td>
<td>0 (0–1)</td>
<td>NS</td>
</tr>
<tr>
<td>6 h</td>
<td>0 (0–1)</td>
<td>0 (0–0)</td>
<td>NS</td>
</tr>
<tr>
<td>24 h</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Postoperative sedation scores at 30 min and 2 h were significantly higher in group M than in group T ($P<0.05$). Sedation scores were similar in other periods (Table 3).

Within the postoperative 0–4 h, nausea and vomiting were observed in eight patients in group M and 10 patients in group T. Allergic rash was observed in eight patients in group M and two patients in group T ($P<0.05$). Itching was observed in 16 patients in group M and none of the patients in group T ($P<0.05$). In two patients of the group M, ventilatory depression was observed during the first postoperative hour, resulting in desaturation ($S_{aO_2}$ 85–90%) and bradypnoea for a few minutes ($P<0.05$). These two cases were handled by maintaining the airway with slight head extension and administering supplementary oxygen via a face mask while repeatedly simulating breathing. Carbon dioxide tension was 42 and 45 mmHg, respectively. Ventilatory parameters normalized without naloxone treatment or intubation. None of the other patients had significant changes in $S_{aO_2}$ or respiratory rate during the follow-up period. Urinary retention and motor block were not observed in any patients (Table 4).

There was a statistically significant reduction in heart rate and systolic arterial pressure after epidural administration in all groups. There was no other statistically significant change in any variable for either within or between the groups. $S_{pO_2}$ remained unchanged in all periods within and between groups. Motor blockade was not seen in any patient postoperatively.

### Discussion

Genitourinary and lower abdominal surgery is often associated with moderate to severe postoperative pain in children. Recognition of this problem has made it desirable to find safe and effective ways of administering peroperative opioids. At the same time, the idea of complementing general anaesthesia and the development of new drugs have increased interest in the concept. Single-dose or continuous application of regional anaesthesia with a catheter decrease the need of general anaesthesia and increase threshold of the post-operative pain.19–22

In a dose–response study using caudal epidural morphine 0.033, 0.067 and 0.1 mg kg$^{-1}$ in children aged 1–8 yr undergoing major surgical procedures below the diaphragm, Krane and colleagues23 showed that the mean duration of analgesia was significantly longer after 0.1 mg kg$^{-1}$. Also, Bozkurt and colleagues24 reported effective safe and prolonged analgesia by using epidural morphine 0.1 mg kg$^{-1}$ in 175 children. Efficacy, safety and longer duration of analgesia with 0.1 mg kg$^{-1}$ were the reasons for our preference in this study.

Naguib and colleagues24 administered tramadol 100 mg and morphine 10 mg intravenously 10 min before induction in two groups of patients undergoing laparoscopic cholecystectomy and found no significant difference between the groups when they compared peroperative haemodynamics (blood pressure, heart rate and $S_{pO_2}$). Baraka and colleagues25 compared the peroperative haemodynamic status of two groups of patients undergoing major abdominal surgery who received morphine 4 mg and tramadol 100 mg epidurally and found no difference. Similar haemodynamic findings occurred in the present study.

Baraka and others25 reported effective analgesia lasting 24 h by using single-dose morphine and tramadol epidurally. On the other hand, Delikan and colleagues26 were able to obtain analgesia lasting 10 h by using tramadol 100 mg epidurally. Fu and colleagues27 reported 12 h of analgesia with tramadol 50 mg and 11.5 h of analgesia with tramadol 75 mg, and found lower visual pain scores in the 75 mg group. Grace and colleagues26 compared tramadol (50–100 mg bolus, 10 mg h$^{-1}$ epidural infusion) and morphine (2 mg bolus and 0.2 mg h$^{-1}$ epidural infusion). Despite using higher equivalent analgesic dosages of tramadol than morphine, they obtained much better results with morphine. In this study supplementary analgesic was not needed for 16 h in the tramadol group and for 18 h in the morphine group. MOPS scores were observed to be similar in two groups.

Vickers and colleagues29 reported that the sedation potential of tramadol was less than that of morphine; the incidence of somnolence was 1.1% in the tramadol group and 1.2% in the morphine group. In our study, statistically higher sedation scores were observed in the morphine group compared with the tramadol group. One patient experienced a decrease in respiratory rate and somnolence in the postoperative period (0–1 h).

The incidence of nausea and vomiting has been reported as 20–80% when opioids are administered i.v. and epidurally.30,31 James and colleagues32 did not report any nausea and vomiting with tramadol i.v., whereas nausea and vomiting was evident in 20% of patients treated epidurally with morphine. On the other hand, Baraka and colleagues25 reported nausea and vomiting in 20% of patients with tramadol and 40% of patients with morphine epidurally. In another study,26 nausea and vomiting was observed in 50% of patients treated with tramadol epidurally; the incidence was less with smaller doses. In our study, nausea and vomiting rates were 25% in the tramadol and 20% in the morphine group.

James and colleagues32 observed i.v. tramadol and epidural morphine and reported that itching was not seen in any group. However, Baraka and colleagues25 found itching in

### Table 4 Incidence of postoperative complications in the two groups of patients.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Group M (n=40)</th>
<th>Group T (n=40)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea-vomiting</td>
<td>8</td>
<td>10</td>
<td>NS</td>
</tr>
<tr>
<td>Iching</td>
<td>16</td>
<td>0</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Allergic rash</td>
<td>8</td>
<td>2</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>2</td>
<td>0</td>
<td>$&lt;0.05$</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Motor block</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
</tbody>
</table>
10% of tramadol-treated patients and in 20% of morphine-treated patients. In this study, itching was not observed in the tramadol group but observed in 40% (16 patients) of patients in the morphine group. Bozkurt and colleagues observed ventilatory depression in 1.1–2% of epidural morphine-treated patients. In our study, ventilatory depression was observed in two patients (4%).

References
7 Gunter JB, Eng C. Thoracic epidural anaesthesia via the caudal approach in children. Anesthesiology 1992; 76: 935–8
17 Wilson GAM, Doyle E. Validation of three paediatric pain scores for use by parents. Anaesthesia 1996; 51: 1005–7