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RANDOMIZED TRIAL

# Patient-controlled Intermittent Epidural Bolus *Versus* Epidural Infusion for Posterior Spinal Fusion After Adolescent Idiopathic Scoliosis

*Prospective, Randomized, Double-blinded Study*

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**Study Design.** A prospective, randomized, double-blinded study.

**Objective.** The aim of this study was to compare the efficacy and side effects of patient-controlled intermittent bolus epidural analgesia (PCIEA) and patient-controlled continuous epidural analgesia (PCCEA) for postoperative pain control in adolescent idiopathic scoliosis.

**Summary of Background Data.** Epidural analgesia is an accepted efficacious and safe procedure for postoperative pain management in scoliosis surgery. However, the PCIEA has not been adequately investigated for postoperative pain control in adolescent idiopathic scoliosis.

**Methods.** Forty-seven patients, 8 to 18 years of age, who were undergoing posterior spinal fusion for idiopathic scoliosis were randomized to either the PCIEA or PCCEA group. An epidural catheter was inserted by a surgeon under direct visualization. The PCIEA group received 0.2 mg/mL of morphine, 0.25 mL/kg of morphine bolus, additional doses of 0.25 mL/kg morphine with a 1-hour lockout given by patient-controlled demand, and no infusion. The PCCEA group received the following: 0.2 mg/mL morphine, an initial morphine loading set at 0.1 mL/kg, followed by a 0.05 mL/kg/h continuous infusion of morphine, and a 0.025 mL/kg bolus dose of morphine. There was a 30-minute lockout interval. The primary outcome was morphine usage. The secondary outcomes were pain score, postoperative nausea and vomiting, and pruritus.

**Results.** Cumulative morphine consumption was lower in the PCIEA group than in the PCCEA group. Both methods provided effective pain control. There were no differences in pain scores between the groups. Postoperative nausea, vomiting, and pruritus were lower in the PCIEA group.

**Conclusion.** The two epidural analgesia techniques studied are both safe and effective methods for postoperative pain control after posterior spinal fusion in idiopathic scoliosis. Nausea, vomiting and pruritus were considerably higher in the PCCEA group. Concerns regarding side effects associated with epidural opioids can be avoided by an intermittent bolus with a relatively lower amount of opioid.

**Key words:** pain management, patient-controlled epidural analgesia, scoliosis.

**Level of Evidence:** 2

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Scoliosis surgery is commonly performed in adolescents due to idiopathic scoliosis. It has been reported that postoperative pain, due to surgical trauma and severe reflex muscle spasms after scoliosis surgery, can be severe and excruciating[1] and that surgical incision length and any large tissue trauma increase the severity of postoperative pain.

Many methods are often used in the management of postoperative pain, such as opioids, paracetamol, and nonsteroidal anti-inflammatory drugs with patient-controlled intravenous analgesia (IV-PCA). In addition, intrathecal opioids, one catheter epidural with intermittent dosing bolus of morphine or continuous infusion (opioids, local anesthetics, or both), double epidural catheters with continuous infusion, and intravenous ketamine infusion are other preferred postoperative pain management models.[2,3]

Epidural analgesia is widely accepted as a safe and effective procedure for the management of postoperative pain in major

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The device(s)/drug(s) that is/are the subject of this manuscript is/are being evaluated as part of an ongoing FDA-approved investigational protocol (IDE) or corresponding national protocol for an epidural catheter/morphine.

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orthopedic surgery, including scoliosis surgery.[4] Compared with IV-PCA, epidural analgesia has been demonstrated to provide a significantly lower pain score, return faster bowel sounds, and to be safe and effective.[4–8]

Epidural analgesia techniques have commonly been used in the continuous infusion of local anesthetics with or without opioids.[1–3,6] It has been emphasized that there are not enough data reported in the literature to support an argument for the use of epidural opioids after spinal surgery.[1] The objective of the present study was to compare the efficacy and side effects in patient-controlled intermittent bolus epidural analgesia (PCIEA) and patient-controlled continuous epidural analgesia (PCCEA) with morphine for postoperative pain control in adolescent idiopathic scoliosis patients after posterior spinal fusion.

## MATERIALS AND METHODS

The study was conducted after obtaining written consent from all patients and their guardians as well as approval from the Inonu University Faculty of Medicine Ethics Committee (No 2015/189). This prospective, randomized, controlled, double-blind study was conducted in 47 patients between the ages of 8 and 18 years, who were diagnosed according to the American Society of Anesthesia Classification (ASA) I-II with idiopathic scoliosis and who were scheduled for elective posterior spinal fusion.

Patients with a history of allergy to the drugs used in the study protocol, drug abuse, preoperative neurological deficits, the inability to use a visual analogue scale, or pulmonary, cardiac, or neuropsychiatric disorders were excluded. Exclusion criteria during the study were the accidental perforation of the dura, faulty epidural catheter placement, postoperative neurologic deficit or uncontrollable nausea, vomiting, and pruritus.

Patients who were not premedicated were instructed on how to use the visual analog scale (VAS) and the patient-controlled analgesia (PCA) device that was implanted during the postoperative period.

Patients were premedicated with intravenous (IV) (0.1–0.2 mg /kg) or oral (0.5 mg /kg) midazolam. Peripheral vascular access was available in the preoperative room or the operating room.

Patients were divided into two groups using the simple randomization method, based on the web-based generation of a random allocation sequence and a reference was cited.[9] Patients who received epidural morphine with PCIEA represented Group 1, and those who received epidural morphine with PCCEA represented Group 2. Both the anesthetist who collected the data and the patients were blinded to the treatment.

Electrocardiography, peripheral oxygen saturation, noninvasive blood pressure, and bispectral index (BIS) monitoring were performed in the operating room. General anesthesia was induced by either a mask with 8% sevoflurane in oxygen and nitrous oxide or propofol 2 to 4 mg/kg with remifentanil 1 to 1.5 μg/kg and rocuronium 0.8 mg/kg. Anesthesia was maintained with propofol 6 to 8 mg/kg and remifentanil 0.25 to 0.5 μg/kg/min. After induction, an ultrasound-guided central venous catheter in the internal jugular vein, an arterial cannula in the left radial artery, and a urinary catheter were inserted; motor-evoked potential (MEP) monitoring was also conducted.

### Surgical Technique

All operations were performed by the same surgical team. The posterior instrumentation with pedicle screws was applied to the thoracic and lumbar spine. An epidural catheter was inserted by a surgeon under direct visualization at the midpoint of the incision and advanced 5 to 6 cm cephalad to thoracic 4 to 5 before surgical closure. Intubated patients were taken to the reanimation intensive care unit after operation, and IV acetaminophen 15 mg/kg was started before extubation and repeated every 6 hours.

### Patient-Controlled Epidural Analgesia Protocols

After extubation and a neurological examination, patients in the PCIEA group received morphine 0.2 mg/mL, 0.25 mL/kg of morphine, with additional doses of 0.25 mL/kg/h with a 1-hour lockout, given by patient-controlled demand, no infusion. In Group 2, PCCEA infusion was conducted as follows: morphine 0.2 mg/mL, initial morphine loading set at 0.1 mL/kg, followed by a maintained 0.05 mL/kg/h continuous infusion, and 0.025 mL/kg bolus dose. There was a 30-minute lock-out interval, and the 4-hour limit was 4 mg.

When indicated, diphenhydramine (0.5 mg/kg) and ondansetron (0.3 mg/kg) were administered for pruritus and postoperative nausea and vomiting.

As in our routine practice, all patients were monitored in the intensive care unit for 24 hours.

### Outcome Measures

The primary outcome was morphine usage. The secondary outcomes were pain score, postoperative nausea and vomiting, pruritus, satisfaction rating, sedation scores, and motor block. The outcomes were assessed by researchers, who were blinded to the treatments received by the study groups, at postoperative 2 (T2), 4 (T4), 6 (T6), 8 (T8), 12 (T12), 18 (T18), and 24 hours (T24) in all patients.

Pain score was assessed using the VAS [choices ranging from 0 (no pain) to 10 (worst imaginable pain)]. If the VAS exceeded 5, patients in both groups received an IV rescue dose of tramadol 0.5 to 1 mg/kg. Nausea was defined as an unpleasant feeling in the stomach with or without retching, and vomiting was defined as the expulsion of gastric contents. Pruritus was assessed through self-report and was recorded as no pruritus = 0, pruritus = 1.

Patient satisfaction was evaluated using a verbal rating scale ranging from 0 to 4 (0 = not satisfied at all, 1 = dissatisfied, 2 = neutral, 3 = satisfied, 4 = very satisfied). Motor block was assessed with the Bromage scale (0 = no paralysis, 1 = unable to lift the thigh, 2 = unable to flex the knee).

### Statistical Analysis

When a 24-hour morphine consumption difference of 2.5 mg with a standard deviation of ±2.5 mg was considered, a

power analysis based on a pilot study with an alpha error of 0.05 and a beta error of 0.20 revealed that a minimum of 17 patients were required in each group for the study.

The data are presented as median with minimum and maximum values. Statistical analysis was performed using IBM SPSS statistics software 22.0. The groups were compared using Yates' corrected Chi-square test and the Mann-Whitney *U* test. Significance was defined as $P < 0.05$.

## RESULTS

Forty-seven patients were initially included in the study. However, three patients in Group 2 were excluded from the study because of problems: (1) patient experienced hypothermia and sudden bleeding during surgery, and (2) patients had uncontrolled and severe postoperative nausea, vomiting, and pruritus. Twenty-four patients in Group 1 and 20 patients in Group 2 were analyzed (Figure 1). There were no significant differences in either patient demographics or surgery duration between the two treatment groups (Table 1).

There was no difference in the distribution of gender between the groups

Both groups were provided effective pain control. There were no significant differences in the VAS between the groups (VAS pain scores are shown in Table 2).

Postoperative nausea/vomiting and pruritus were significantly decreased in Group 1 (Table 3).

Compared with Group 2, at all time points, except for $T_2$ (Table 4), morphine usage was significantly less in Group 1, and total morphine usage was significantly decreased in Group 1.

**TABLE 1. Demographical Data [Median (Min-Max) or Number]**

| | Group 1 (n = 24) | Group 2 (n = 20) |
|---|---|---|
| Age, yrs | 13,50 (9–17) | 14 (10–17) |
| Weight, kg | 41.5 (30–70) | 44 (25–60) |
| Gender, F/M | 17/7 | 14/6 |
| ASA physical status (I/II) | 14/10 | 10/10 |
| Operation time, min | 320 (270–360) | 312 (280–340) |

*ASA indicates American Society of Anethesiologists; F, female; Group 1, patient-controlled intermittent bolus epidural morphine; Group 2, patient-controlled continuous epidural morphine; M, Male.*

Transient motor block was not present in either group. There were no differences in patient satisfaction between the two groups; patient satisfaction in Group 1; 3 (2–3), and Group 2; 3 (2–3) ($P = 0.333$). Sedation scores were similar in both groups and no excessive sedation was observed.

During the postoperative 24-hour period, the rescue analgesic dose requirement doses were similar; Group 1 was 0.71 mg (0–3 mg), and Group 2 was 0.95 mg (0–6 mg) ($P = 0.66$).

## DISCUSSION

This study demonstrated that PCIEA with morphine treatment, after posterior spinal fusion surgery for idiopathic

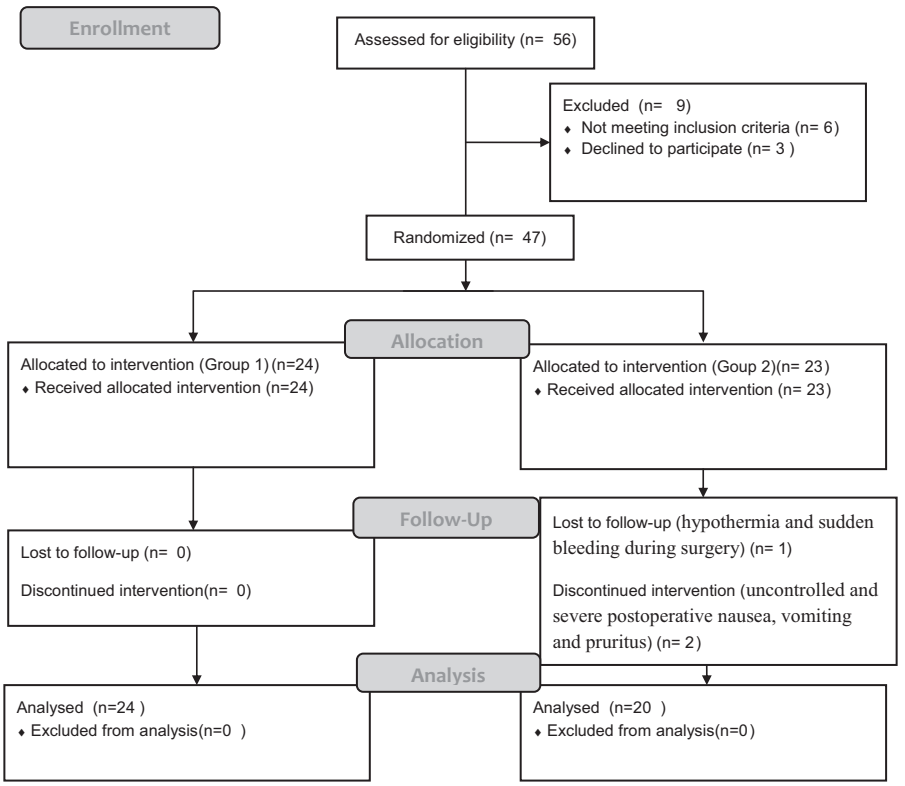


**Figure 1.** CONSORT Diagram for the trial.

**TABLE 2. Pain Score (VAS 0–10) [Median (Min-Max)]**

| | Group 1 (n = 24) | Group 2 (n = 20) | *P* |
|---|---|---|---|
| T2 | 4 (3–7) | 4 (2–7) | 0.97 |
| T4 | 4 (2–6) | 3.5 (2–5) | 0.42 |
| T6 | 3 (2–5) | 3 (1–4) | 0.20 |
| T8 | 2 (1–4) | 2 (1–4) | 0.32 |
| T12 | 2 (1–4) | 2 (1–4) | 0.12 |
| T18 | 2 (1–3) | 1 (1–3) | 0.07 |
| T24 | 1 (1–3) | 1 (1–2) | 0.06 |

*Group 1, patient-controlled intermittent bolus epidural morphine; Group 2, patient-controlled continuous epidural morphine; VAS indicates visual analog scale.*

**TABLE 4. Cumulative Morphine Consumption [mg, Median (Min-Max)]**

| | Group 1 (n = 24) | Group 2 (n = 20) | *P* |
|---|---|---|---|
| T2 | 2.25 (1.5–4) | 2.20 (1–2.80) | 0.223 |
| T4 | 2.25 (1.5–8) | 3.40 (1.40–4) | 0.008 |
| T6 | 3 (1.5–8) | 4.40 (2–5.40) | 0.047 |
| T8 | 4 (1.5–8) | 5.30 (2.40–6.90) | 0.016 |
| T12 | 5 (1.5–9) | 7 (3.40–12) | <0.0001 |
| T18 | 5 (1.5–9) | 9.90 (5–14.20) | <0.0001 |
| T24 | 5 (1.5–9) | 12.50 (6.40–16.50) | <0.0001 |

*Group 1, patient-controlled intermittent bolus epidural morphine; Group 2, patient-controlled continuous epidural morphine.*

scoliosis in adolescent patients, provided an efficacious analgesia. Compared with PCCEA infusion morphine, PCIEA with morphine was associated with less nausea/vomiting and pruritus, and lower morphine usage. To our knowledge, this is the first study to investigate the efficacy of intermittent bolus dosing of epidural analgesia to treat postoperative pain in adolescent idiopathic scoliosis patients, after scoliosis surgery.

On the basis of current data, Taenzer and Clark[1] suggested the use of an epidural catheter in adolescent scoliosis surgery, and stressed that epidural analgesia reduces postoperative nausea, VAS scores, and increases patient satisfaction. In addition, although it has been reported that the use of two catheters and a higher concentration of local anesthetic may be more useful, it is unclear whether this benefit is obtained from the use of two catheters, a higher dose of local anesthetic, or the combination of both.[1]

It has been shown that average pain scores (on a scale of 0–100) were decreased by 15 points 24 hours after treatment with epidural analgesia.[1]In other similar studies, 1 to 4 VAS points (scale of 0–10) were recorded.[6,7] In our study, similar VAS scores were reported in both groups.

Epidural analgesia is commonly administered using local anesthetics and/or treatment with opioids following scoliosis surgery.[4–6,10] In many cases, low doses of local anesthetics such as bupivacaine have been used to prevent the toxicity caused by local anesthetics. Nevertheless, convulsion, which is a sign of local anesthetic toxicity, has been reported.[11,12] Epileptic patients may have a higher risk of convulsions, and potential neural-mental problems in patients with scoliosis may also increase the risk of convulsions. In addition, high concentrations of local anesthetics can cause motor block, which prevents early mobilization and may complicate the diagnosis of neurological deficits related to surgery.

**TABLE 3. Postoperative Nausea-Vomiting and Pruritus [Number (%)]**

| | Group 1 (n = 24) | Group 2 (n = 20) | *P* |
|---|---|---|---|
| Nausea | 4 (16%) | 10 (50%) | 0.020 |
| Vomiting | 2 (8%) | 7 (35%) | 0.038 |
| Pruritus | 4 (16.7%) | 8 (40%) | 0.019 |

*Group 1, patient-controlled intermittent bolus epidural morphine; Group 2, patient-controlled continuous epidural morphine.*

Blumenthal *et al*.[10] emphasized that epidural analgesia used as a local anesthetic may be a major source of concern because it may affect neurological examination and delay a possible necessary intervention after spinal surgery. Although epidural analgesia is initiated the morning following surgery to eliminate this concern, motor block was observed in 2 of 15 patients.

Despite the fact that Saudan *et al*.[11] used lower doses of local anesthetic than Schenk *et al*.,[13] they also observed motor block. In our study, local anesthetics were not used, and motor block was not observed in the patients.

The potential side effects of intravenous opioids limit their use in surgical patients. Borgeat *et al*. reported that epidural infusion, using local anesthetics or combined adjuvants, represents a good alternative technique with lower side effects and efficient pain control in scoliosis surgery patients.[2,14] Epidural opioids have been shown to be associated with multiple side effects, such as sedation, prolonged respiratory depression, urinary retention, delayed bowel activity, nausea, vomiting, and pruritus.[3,9,15,16] In our study, the rates of nausea, vomiting, and pruritus were 56%, 40% ,and 50%, respectively, in patients who received continuous epidural morphine administration. The prevalence of these side effects was similar to that reported in studies conducted by Blumenthal *et al*.,[10,17] using IV morphine or epidural local anesthetics with morphine. In our study, the rates of nausea, vomiting, and pruritus were 21%, 13%, and 17%, respectively, in the PCIEA group. The rates were more than 50% lower than those observed with other epidural morphine applications.

Hogan[18] investigated the distribution of solution in the epidural space in a cadaveric trial, and reported that high volumes of fluid and greater injection pressure led to a more uniform distribution of the solution in the epidural space.

They emphasized that intermittent boluses of anesthetic solution may be more successful than continuous infusion to produce uniform block. It has been shown in clinical studies that the administration of bolus epidural analgesia, *versus* infusion, decreased anesthetic agent consumption, and provided greater sensory block and patient satisfaction.[19–21] In our study, patients in the PCIEA with morphine group reported VAS scores similar to previous studies, and a lower frequency of adverse effects, such as nausea, vomiting, and pruritus were reported, relative to patients who received continuous epidural morphine or morphine by IV.

There are some limitations in the present study. Catheter position should be confirmed radiographically. However, the epidural catheters inserted under direct vision of the senior surgeon were performed as previously described in other studies.[5,10,11] The two epidural analgesia techniques were not compared with other analgesia techniques. Epidural analgesia has been accepted as a procedure for this surgery, and epidural analgesia is used in the management of scoliosis in our institution.

In conclusion, we found that the two epidural analgesia techniques are safe and effective methods for postoperative pain control for posterior spinal fusion in idiopathic scoliosis. Side effects, including nausea, vomiting, and pruritus, were considerably higher in the continuous epidural infusion group. In addition, the side effects associated with epidural opioids can be avoided by an intermittent bolus with a relatively lower amount of opioid.

## ➢ Key Points

- ❑ Epidural analgesia is a safe procedure and provides good postoperative pain control in scoliosis surgery.
- ❑ The administration of bolus epidural analgesia *versus* infusion decreased anesthetic agent consumption provided greater sensory block and patient satisfaction.
- ❑ Epidural opioids are associated with multiple side effects, such as sedation, prolonged respiratory depression, urinary retention, delayed bowel activity, nausea, vomiting, and pruritus.
- ❑ Concern of the side effects associated with epidural opioid can be avoided by patient-controlled intermittent bolus epidural analgesia with a relatively lower amount of opioid.

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