Original Article | http://dx.doi.org/10.3349/ymj.2012.53.5.1014 pISSN: 0513-5796, eISSN: 1976-2437 | Yonsei Med J 53(5):1014-1021, 2012 | YMJ

# Remifentanil Use in Pediatric Scoliosis Surgery-An Effective Alternative to Morphine (A Retrospective Study)

Ibrahim Abu-Kishk,[1]* Roei Hod-Feins,[2]* Yoram Anekstein,[2] Yigal Mirovsky,[2] Josi Barr,[1] Eli Lahat,[3] and Gideon Eshel[1]

[1]Pediatric Intensive Care Unit, [2]Spine Unit, Department of Orthopedics, and [3]Pediatric Neurology Department, Assaf Harofeh Medical Center, Zerifin, Israel, affiliated to The Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

Received: July 7, 2011
Revised: October 31, 2011
Accepted: November 1, 2011
Corresponding author: Dr. Ibrahim Abu-Kishk, Pediatric Intensive Care Unit, Assaf Harofeh Medical Center, Zerifin 70300, Israel.
Tel: 972-8-977-9105, Fax: 972-8-977-9109
E-mail: fredricag@asaf.health.gov.il

*Ibrahim Abu-Kishk and Roei Hod-Feins contributed equally to this work.

· The authors have no financial conflicts of interest.

**Purpose:** The unique properties of remifentanil make it ideal for pediatric use despite a lack of wide randomized clinical trials and fear of adverse events due to its high potency. We aimed to consolidate preliminary conclusions regarding the efficacy of remifentanil use in pediatric scoliosis surgery. **Materials and Methods:** The medical charts of children with idiopathic scoliosis who underwent primary spinal fusion between 1998 and 2007 at a large tertiary university-affiliated hospital were retrospectively reviewed and divided into two groups according to anesthetic regime (remifentanil vs. morphine). Demographic, surgery-related details and immediate postoperative course were recorded and compared. **Results:** All 36 remifentanil children were extubated shortly after termination of surgery, compared to 2 of the 84 patients in the morphine group. The remaining patients in the morphine group were extubated hours after surgery [5.4 hours; standard deviation (SD) 1.7 hours]. Six remifentanil children were spared routine intensive care hospitalization (vs. 2 morphine children-significant difference). Shorter surgeries [5.6 hours (SD 1.82 hours) vs. 7.14 hours (SD 2.15 hours); $p$=0.0004] were logged for the remifentanil group. To achieve controlled hypotension during surgery, vasodilator agents were used in the morphine group only. A comparison of early postoperative major or minor complication rates (including neurological and pulmonary complications) between the two groups yielded no significant differences. **Conclusion:** Remifentanil use can shorten operating time and facilitate earlier spontaneous ventilation and extubation, with less of a need for intensive care hospitalization and no increase in significant complications.

**Key Words:** Remifentanil, morphine, idiopathic scoliosis, ICU, postoperative complications and ventilation



## INTRODUCTION

Remifentanil is an ultra-short acting mu-opioid receptor agonist that allows for shorter mechanical ventilation in Intensive Care Units and may also reduce duration of surgery and anesthesia.[1,2]

It is useful for spinal procedures, where rapid recovery, immediate neurological examination and hemodynamic stability, as well as a minimal effect on electrical evoked potential monitoring are desirable.[3-5]

A study of anesthetic techniques during spinal fusion surgery revealed earlier spontaneous ventilation and earlier movement of the hands and feet when remifentanil was used in comparison to alfentanil-propofol.[6]

Our Medical Center serves as a tertiary spine center that attracts the majority of pediatric spine disorders in Israel, pediatric idiopathic scoliosis (IS) being the most common entity.

In 2003, the anesthesiologists at our medical center started using remifentanil.

In 2005, we replaced morphine with remifentanil infusion during anesthesia for scoliosis surgery.

Our aim was to evaluate the efficacy of remifentanil-based anesthesia by comparing remifentanil and morphine-based groups.

## MATERIALS AND METHODS

This study retrospectively reviewed the records of children with pediatric scoliosis who underwent primary spinal fusion, by instrumentation of the thoracic-lumbar spine, at our Medical Center between the years of 1998 and 2007. During this period, the surgeons and chief anesthesiologists who performed the procedures remained unchanged. The study was approved by the hospital's Ethics Committee.

The study included patients with scoliosis of idiopathic etiology only (excluding children of other etiological groups, such as neuromuscular, neurofibromatosis, congenital scoliosis, etc., due to a small number of observations). A scoliosis curve of >50° in adolescent patients was the main indication for surgery.

Echocardiography, chest X-ray and spirometry were performed for all the participants before the surgical procedure was carried out.

A combination of screws, hooks and two titanium rods was used in all patients.

The children who were included were divided into two groups according to the anesthetic regimen administered. In both groups, large-bore intravenous access with a fluid warmer and an intra-arterial line for monitoring was routinely applied. Routine pre-medication included oral midazolam 0.15-0.2 mg/kg (mean dose 8 mg) and intramuscular or intravenous morphine (0.1-0.15 mg/kg) in combination with oral atropine (0.5 mg). For muscle relaxation, IV pancuronium bromide 0.05-0.1 mg/kg was administered, while succinylcholine (1 mg/kg) was administered in cases of suspected difficult intubation. In both groups, anesthesia was induced with a dose of 2 to 2.5 mg/kg propofol. For the maintenance of anesthesia, inhaled isoflurane was used. The minimal alveolar concentration of isoflurane was maintained at a level of 0.5 to 1.5.

Controlled hypotension was induced in order to limit intraoperative blood loss. Since all the patients in the current study were teenagers, adult blood pressure limits with a reduction of systolic blood pressure to 80-90 mm Hg and a reduction of mean arterial pressure to 50-60 mm Hg were used. The use of vasodilator agents such as nitroglycerin 0.5-2 mcg/kg/min or nitroprussid 0.5-2 mcg/kg/min was added as needed during surgery.

Somatosensory and motor evoked potentials were routinely recorded, combined with Stagnara's wake-up test whenever indicated.

Routine complete blood count (CBC), electrolytes and clotting studies were performed during surgery.

Normal saline, Cell Saver® autologous blood recovery (Haemonetics Corp., Braintree, MA, USA), packed red blood cells (PRBC), fresh frozen plasma (FFP), platelets and cryoplasma units were given according to estimated blood loss, intraoperative blood test results and hemodynamic status.

In the first group, analgesia was induced by an IV morphine bolus (1-1.5 mg/kg), and fentanyl (2 to 3 mcg/kg) was administered according to hemodynamic responses (a change in heart rate or blood pressure ≥20% from baseline) during surgery (operations performed before mid 2005).

In the second group, analgesia was induced by an infusion of IV remifentanil (from mid 2005 and thereafter). Remifentanil infusion was begun at a rate of 0.2 mcg/kg/min and subsequently titrated in increments of 0.05 mcg/kg/min according to hemodynamic responses (a change in heart rate or blood pressure ≥20% from baseline). IV morphine (0.1-0.3 mg/kg) was administered 30 minutes before the end of surgery for analgesia control.

At the end of surgery, an attempt at extubation was performed in the recovery room. Extubation criteria were: patient awake, calm and cooperative; hemodynamic stability; negative inspiratory force >20 cm $H_2O$; respiratory rate <30/min, $PaCo_2$ <50 mm Hg; and $PaO_2$ >70 mm Hg with $FiO_2$ <0.4. Patients who were extubated and stable for at least 2 hours were transferred to the Pediatric Orthopedic

**Table 1.** Classification of Major and Minor Complications

| Type of complication | Major | Minor |
|---|---|---|
| Neurological | Convulsions, motor or sensor deficiencies | Temperature difference between legs |
| Pulmonary | Respiratory distress of any cause (significantly low oxygen saturation requiring oxygen supplementation or prolonged intubation), pneumonia, significant atelectasis (requiring prolonged chest tube) | Asymptomatic pleural effusion, pneumothorax, atelectasis or lung contusion |
| Hematological & biochemical | Continuous bleeding from incisions, venous thrombosis | Asymptomatic coagulopathy or thrombocytopenia, asymptomatic electrolytic abnormalities, anemia, hypoalbuminemia |
| Gastrointestinal tract | Recurrent gastrointestinal bleeding | Constipation, elevated liver enzymes or bilirubin, nausea or vomiting |
| Cardiovascular | Hemodynamic instability (this was defined as systolic pressure below 90 mm Hg/mean arterial pressure below 50 mm Hg combined with clinical parameters of low peripheral perfusion) | Low blood pressure at arrival to the ICU, temporary oliguria |
| Infectious | None in this series | Urinary tract infection |
| Miscellaneous | Multiple decubitus ulcers | Fever up to 39 degrees, decubitus ulcer |

ICU, intensive care unit.

Ward. Those who did not meet the extubation criteria or who, according to the anesthesiologist's judgment, needed stricter follow-up were transferred to the Pediatric Intensive Care Unit (PICU). Antibiotics were routinely administered before beginning the surgery, and appropriate antibiotic coverage was used until drain removal. Whenever fever of a suspected infectious etiology appeared, antibiotic cover was adapted according to culture results or current guidelines. Follow-up included daily physical examinations (including attentive neurological assessment), vital signs monitoring, routine blood tests, chest X-rays and other ancillary tests as required. The same extubation criteria were implemented in the PICU. Patients who remained stable for at least 24 hours after extubation and had no active bleeding from the operation site or drains were transferred to the Pediatric Orthopedic Ward. The attending physicians recorded any complications and events during the early postoperative period, which was defined as the hospitalization period until discharge to orthopedic rehabilitation.

Postoperative pain control was administered in both groups using a combination of morphine (0.1 mg/kg/dose) every 4 hours and ibuprofen [a non-steroidal anti-inflammatory agent (NSAID)], (10 mg/kg/dose) every 6 hours. A numerical pain scale with a range of 0 to 10 was used to gauge a patient's pain, where zero indicated no pain and 10 indicated the worst pain. Mild to moderate pain (2-6 on the scale) was treated with NSAIDs and severe pain was treated with narcotics.

Demographic data and a list of surgery-related details were collected and compared between the groups (see below). Early postoperative complications, the rate of postoperative blood product administration and the length of hospitalization in the Pediatric Intensive Care Unit were also recorded and compared.

The classification of major and minor complications was based on previous studies published on the subject (Table 1).[7]

**Demographic and surgery-related data**

Demographic and surgery-related data for each patient were collected including: 1) gender distribution 2) age at diagnosis; 3) age at surgery; 4) weight percentile; 5) preoperative forced expiratory volume in 1 second (FEV1); 6) preoperative Cobb angle (coronal deformity angle); 7) fusion approach; 8) fusion extent; 9) the addition of thoracoplasty; 10) use of medications and blood product transfusion; as well as 11) length of surgery transfusion;

Weight percentile was used instead of BMI, since height measurements in deformed scoliotic children do not represent true body size.

**Statistical analysis**

Logarithmic transformation was applied for Cell Saver, PRBC and FFP amounts, since these parameters did not exhibit normal distributions.

t-tests were used in order to assess differences between continuous parameters of the two groups. Correlations between categorical parameters were carried out using Fisher's exact test and the chi-square test.

Statistical analysis was performed with SPSS software

version 12.0. Averages and rates are presented, with ranges and SDs when appropriate. A *p*-value of less than 0.05 was considered significant.

## RESULTS

### The database

Data mining revealed 120 IS children who were operated on between the years 1998 and 2007. Among these, we assigned 36 children to the remifentanil group and 84 to the morphine group.

Echocardiography, chest X-ray and spirometry revealed no significant cardiac or respiratory abnormalities.

During surgery, the mean calculated dosages of morphine, fentanyl and remifentanil were 0.39 mg/kg/hour, 0.67 mcg/kg/hour, and 0.4 mcg/kg/hour, respectively. The morphine group required vasodilator agents (nitroglycerin for 73 patients, nitroprussid for 13 patients). Administration of vasodilator agents was not required in the remifentanil group. The wake-up test was performed in 3 patients, 2 of them in the morphine group. The wake-up test required a waiting time during surgery, 27 minutes and 32 minutes in the morphine group and 4 minutes for the single case in the remifentanil group. The mean requirement of morphine and NSAIDs (mg/kg/48 hours) for the 2 consecutive postoperative days was, respectively, 1.42 and 63 in the morphine group and 1.39 and 67 in the remifentanil group.

At the end of the operation, following extubation, 8 children were hospitalized directly in the Pediatric Orthopedic Department [the "bypass group"-2 children who were given morphine, in comparison to 6 who were given remifentanil ($p<0.01$)]. In all these cases, the decision to hospitalize in the Pediatric Orthopedic Department was based on the anesthesiologist's clinical judgment (absolute respiratory and hemodynamic stability) and not on the space or equipment available in the PICU, since all these operations were performed on an elective basis. All these children were excluded from the length of PICU hospitalization analysis. When extubation was carried out, no episodes of apnea were recorded in any of the participants.

### Comparison of demographic and surgery-related parameters between the groups (detailed analysis is presented in Table 2)

Comparisons of gender distribution, age at diagnosis and surgery, weight percentile, preoperative FEV1, Cobb angle, fusion approach and extent, and the addition of thoracoplasty, yielded no significant difference between the two groups.

However, two significant parameters were found. First, the use of vasodilator agents for induced hypotension was needed in the morphine group only. Hypotension was better achieved in the remifentanil group. Our analysis also revealed shorter surgeries in the remifentanil group [average length of surgery 5.6 hours (SD 1.82 hours) vs. 7.15 hours (SD 2.15 hours); $p=0.0004$].

**Table 2.** Comparison of Demographic and Surgery-Related Parameters between the Groups

| Parameters | Remifentanil | Morphine | Statistical significance |
|---|---|---|---|
| Gender (M/F) | 7/29 (19%/81%) | 8/76 (10%/90%) | $p=0.143$ |
| Age at diagnosis (yrs) | 11.2 (SD 3.7) | 12 (SD 3) | $p=0.305$ |
| Age at surgery (yrs) | 14.9 (SD 2.2) | 14.4 (SD 2.3) | $p=0.313$ |
| Weight percentile | 43.7% (SD 24.4%) | 42.2% (SD 27.2%) | $p=0.806$ |
| FEV1 (observed/predicted) | 79.4% (SD 14.7%) | 80.3% (SD 20.3%) | $p=0.848$ |
| Cobb angle | 63.7° (SD 15°) | 58.7° (SD 13.7°) | $p=0.112$ |
| Fusion app. (Ant/Post/Comb.) | 5/28/3 (14%/78%/8%) | 10/67/7 (12%/80%/8%) | $p=0.955$ |
| Fusion extent (number of vertebrae) | 11.2 (SD 2.8) | 11.2 (SD 2.8) | $p=0.630$ |
| Thoracoplasty (applied/spared) | 28/6 (78%/22%) | 61/19 (76%/24%) | $p=1.000$ |
| Cell Saver (applied/spared) | 27/9 (75%/25%) | 50/33 (60%/40%) | $p=0.147$ |
| Cell Saver amount (mL) | 472 (SD 331) | 503 (SD 318) | $p=0.546$ |
| PRBC (applied/spared) | 21/15 (58%/42%) | 49/34 (59%/41%) | $p=1.000$ |
| PRBC amount (units) | 1.8 (SD 0.6) | 1.63 (SD 0.47) | $p=0.196$ |
| Use of vasodilatation agents | None | All | $p=0.000$* |
| Immediate post surgery extubation | All | 2/84 | 2/84 |
| Length of surgery | 5 hrs 36 min (SD 1 hr 50 min) | 7 hrs 9 min (SD 2 hrs 9 min) | $p=0.0004$* |

FEV1, forced expiratory volume in 1 second; fusion app. (Ant/Post/Comb.), fusion approach (anterior/posterior/combined anterior-posterior); PRBC, packed red blood cells; SD, standard deviation.
*Significant results.

**Table 3.** Comparison of Postoperative Parameters between the Groups

| Parameters | Remifentanil | Morphine | Statistical significance |
|---|---|---|---|
| Postoperative blood products (applied/spared)* | 13/20 (39%/61%) | 25/23 (52%/48%) | $p$=0.365 |
| Major complications (recorded/not recorded)† | 5/31 (14%/86%) | 4/80 (5%/95%) | $p$=0.126 |
| Major+minor complications (0/1/2/≥3)‡ | 11/18/3/4 (31%/50%/8%/11%) | 18/35/20/11 (21%/42%/24%/13%) | $p$=0.206 |
| ICU hospitalization length (days)§ | 3.5 (SD 2) | 3.2 (SD 1.5) | $p$=0.410 |
| "Bypass group"‖ | 6 children | 2 children | $p$<0.01¶ |

ICU, intensive care unit; SD, standard deviation.
*Postoperative blood products represent infusion of any kind of blood product (usually packed red blood cells or fresh frozen plasma).
†Represents presence of any major complication in the immediate postoperative period (see Table 1 for classification of recorded complications).
‡Represents presence of any major or minor complication in the immediate postoperative period (see Table 1 for classification of recorded complications).
§ICU hospitalization length analysis excluded the 8 children directly hospitalized in the Pediatric Orthopedic Department following surgery.
‖"Bypass group" -children hospitalized directly in the Pediatric Orthopedic Department following extubation at the end of the operation.
¶Significant results.

**Comparison of postoperative parameters between the groups (a detailed analysis is presented in Table 3)**

All the children in the remifentanil group were extubated shortly after termination of surgery (within 6-11 minutes), in comparison to 2 patients from the morphine group. The remaining patients in the morphine group were extubated hours after surgery (5.4 hours; SD 1.7 hours) and 3 of them needed mechanical ventilation for more than 24 hours following surgery.

Nine major complications were recorded among the whole study cohort with no statistical difference between the two groups. In the remifentanil group, four children had major pulmonary complications (significant pneumothorax that led to desaturation and dyspnea) and one had a cardiovascular complication (hemodynamic instability with systolic pressure <90 mm Hg/mean arterial pressure <50 mm Hg due to continuous bleeding and coagulopathy). In the morphine group, four major complications, all of them pulmonary, were recorded (2 cases of significant lung contusions, one case of severe pneumonia and one case of significant pneumothorax). All major complications were successfully treated with conventional tools and there were no subsequent sequelae.

The rest of the minor complications included mainly hematological-biochemical complications (asymptomatic anemia, coagulopathy or hypocalcemia) and minor pulmonary complications (small insignificant pneumothorax or lung contusions with/without pleural effusions).

Overall, pulmonary complications (minor and major) were recorded in 9 children in the remifentanil group, and 19 children in the morphine group (30% and 23% of each group, respectively; difference insignificant).

No child in our study suffered any major neurological complication, but 2 (one in each group) had a minor temperature difference between both legs, which gradually resolved (considered as minor neurological complications).

No cases of ischemic optic neuropathy associated with hypotension and blood loss were observed.

Except for the case of pneumonia, there were no cases of obvious infection (urinary or wound-related). Regarding gastrointestinal complications, there were 10 cases of abdominal cramps with/without vomiting and constipation, but with no signs of gastrointestinal obstruction. Three cases were recorded in the remifentanil group and 7 in the morphine group (difference insignificant).

A comparison of the rate of postoperative blood product administration and the length of hospitalization stay in the PICU also failed to show any significant differences.

Regarding postoperative pain control, as mentioned previously, the administration of morphine combined with an NSAID was not significantly different between the groups.

Short-term follow-up (after discharge from hospital) revealed 2 children (in the remifentanil group) who developed superior mesenteric artery syndrome several days after discharge from hospital. These children were re-hospitalized and the symptoms resolved with conservative treatment.[8]

Intermediate term follow-up revealed one child in the remifentanil group who developed a deep vein thrombosis of the external iliac and femoral veins 1 month following discharge. Uneventful resolution of the condition was achieved with conservative anti-thrombotic therapy.

Long term follow-up in the morphine group revealed only one child who developed a chronic infection and was operated on for instrumentation removal 5 years later and another 2 children who were re-operated on following instrumentation dislodgement (4 months and 5 years following

the first surgery). In all these 3 cases, revision surgery was successful.

The children in the small subgroup that were hospitalized directly in the Pediatric Orthopedic Department demonstrated a rather benign immediate postoperative course-no major complications and only one child with a small pneumothorax was observed. No short-term or long-term follow-up complications were observed in any of them.

## DISCUSSION

Remifentanil was found to be an effective anesthetic agent for pediatric scoliosis repair surgery. The use of remifentanil enabled better achievement of hypotension during surgery and shorter operating times, and made reaching earlier spontaneous ventilation possible with less of a need for ICU hospitalization and no increase in significant complications.

Our database included 36 children in the remifentanil group vs. 84 children in the morphine group, all of whom were diagnosed with idiopathic scoliosis.

Comparison of demographic parameters between the groups yielded no significant differences, which is an indication of database homogeneity. Comparison of surgery-related parameters between the groups yielded three significant results: shorter surgery length, sparing of vasodilator agents for achievement of hypotension during surgery and rapid extubation at the end of surgery.

In this study, we retrospectively reviewed the charts of patients spanning nearly a decade of cases. Though the surgeons and chief anesthesiologists did not change for the period studied, other minor technical aspects of clinical care developed over the years, and these factors could have contributed to the outcomes. As the current study deals with about a decade of surgical experience, a learning curve for the surgeons could have attributed to the shorter length of surgery. The longer waiting time that was required for the wake-up test in the morphine group may have slightly contributed to the longer surgery time in this group. Although it is difficult to confirm a clear link between the length of the operation and the type of opioid used by the anesthesiologist as a single factor, we do think that this study shows easier achievement of hypotension, which probably contributed to shortening the length of the operation. This fact was reported in previous studies[2] for different orthopedic procedures in adults where the use of remifentanil allowed a reduction in time of surgery and anesthesia. The controlled hypotension induced by remifentanil is possibly related to the marked reduction in systemic vascular resistance that is not related to histamine release.[9] Vasodilatation is mainly an endothelium-dependent phenomenon, involving prostacyclin and nitric oxide release from the endothelium.[10] Remifentanil also suppresses the sympathetic nervous system[11,12] and inhibits calcium channels in human mesenteric arteriolar smooth muscle cells.[13]

In the current study, no significant difference in blood loss between the groups was noted, despite the shorter operating time in the remifentanil group.

Sedative drugs are usually used as premedication in children in order to minimize psychological trauma related to anesthesia and surgery.[14] In the current study, all the 120 participants received a similar basic premedication protocol before the induction of aesthesia; therefore, we believe that the premedication treatment in this type of surgery, which lasted from 4 to 5 hours, had minimal influence on early postoperative period complications.

Pulmonary complications (PPC) were the most often occurring complications recorded in the current study, with no significant difference between the groups. PPCs are one of the risks related to surgery and anesthesia and might exacerbate postoperative morbidity, mortality and longer hospitalization. A recent review[15] published on this topic revealed a wide range of PPC incidences (2-40%). Age, co-morbidity, the use of general anesthesia and the overall surgical insult were the highest risk factors for PPC. Since all the participants in the current study were young, healthy adolescents and had similar spirometry findings and no cardiac pathologies, we believe that PPC was more likely to be associated with surgical insult.

Six patients in the remifentanil group, in comparison to 2 patients in the morphine group, were directly hospitalized in the Pediatric Orthopedic Department following surgery. They all had a benign postoperative course ($p<0.0004$). This difference indicated a better immediate term condition for the remifentanil children who were rapidly extubated, respiratorily and hemodynamically stable, and transferred immediately to the Pediatric Orthopedic Department. Accordingly, randomized controlled trials demonstrated that remifentanil allows for earlier extubation after prolonged surgery, even when compared with other short acting opioids such as sufentanil.[16] Furthermore, while no child in the remifentanil group required postoperative mechanical ventilation, all those in the morphine group did. Three of them were extubated at more than 24 hours following surgery

(which again highlights the problem of extubation following morphine utilization).

Our database did not show a reduced length of PICU hospitalization with the use of remifentanil, although such results (including reduction of mechanical ventilation time) have been reported in the adult population.[1,2]

Had we included the 8 patients who were immediately transferred post surgery to the Pediatric Orthopedic Department in the hospitalization length analysis, our results would probably have been similar to the findings in other studies.

One of the limitations of our study was the large group of children administered a mixture of morphine and fentanyl, which are both relatively long acting opioid agents but have differing pharmacokinetics. In comparison to morphine, fentanyl is 50-100 times more potent, has a more rapid onset of action and has a lesser half-time.[17] Fentanyl was chosen by the anesthesiologist as an additive opioid to morphine, as needed during the surgical procedure in the first group, because of its properties. The therapeutic potency of remifentanil is somewhat less than that of fentanyl,[18] and a comparison of the total opioid use per hour revealed that the remifentanil group required a relatively higher dose. Achieving controlled hypotension during surgery is probably the main reason for requiring a higher dose of opioids in the remifentanil group.

Cessation of remifentanil at the end of the surgical procedure may lead to hyperalgesia. Several studies have described the possibility of developing acute opioid tolerance during infusion of remifentanil in pediatric scoliosis surgery, when compared with intermittent morphine boluses.[19,20] These studies reported significantly increased postoperative morphine consumption in the remifentanil group when a patient-controlled analgesia (PCA) device was used. Contrarily, our study showed no difference in analgesia use between the groups in the postoperative period. We believe that this finding can be partially explained by the fact that a PCA device was not used in our Pediatric Orthopedic Department at the time of the study and also by the concomitant use of NSAIDs postoperatively, especially when mild to moderate pain was revealed according to the pain scale used. Another factor possibly contributing to the reduction in hyperalgesia was the administration of morphine as premedication and at 30 minutes before the end of surgery in the remifentanil group. A combination of opioid agonists or opioid rotation has demonstrated some success in decreasing or preventing opioid-induced hyperalgesia according to some studies.[21] Theoretically, the use of a pure opioid agonist with different receptor binding characteristics and a longer duration of action than remifentanil may be beneficial when trying to prevent opioid-induced hyperalgesia.

The financial cost difference between anesthesia using remifentanil compared to morphine is also an important issue. In our hospital, the average cost of remifentanil for one operation is 200$ vs. 5$ for morphine. However, by using remifentanil, the overall time of surgery is shortened, and other vasodilator drugs, which are necessary for inducing hypotension when administering morphine anesthesia, can be spared. Furthermore, several studies have illustrated that remifentanil usage during anesthesia may allow for smaller doses of other short-acting anesthetic agents.[22,23] In addition, more patients with remifentanil anesthesia skipped PICU hospitalization in the current study. Other previous studies have also proven a reduction in PICU admission after other major surgical procedures due to remifentanil use.[24] In summation of the above, we could conclude that the cost difference might be inconsequential.

Our study is important since, for the first time, we demonstrate the immediate efficacy and possible cost effectiveness of remifentanil use in pediatric scoliosis spine surgery. Follow-up demonstrated no difference between our two groups. However, the period of follow-up in the remifentanil group was relatively short term and we still need to wait and see if long term consequences arise.

The unique properties of remifentanil (organ-independent metabolism, lack of accumulation, rapid offset of action) and the favorable performance thereof (minimal effect on electrical evoked potential monitoring, time and vasodilatatory agent economization, fast and predictable extubation and quicker ICU discharge) render it a convenient opioid.

In conclusion, remifentanil use can shorten operating time and facilitate earlier spontaneous ventilation and extubation, with less of a need for intensive care hospitalization and no increase in significant complications. Whether our findings are relevant to non-idiopathic scoliosis patients has yet to be established in a similar study on neuromuscular and cerebral palsy patients with scoliosis.

## REFERENCES

1. Muellejans B, Matthey T, Scholpp J, Schill M. Sedation in the intensive care unit with remifentanil/propofol versus midazolam/fentanyl: a randomised, open-label, pharmacoeconomic trial. Crit Care 2006;10:R91.
2. Chillemi S, Sinardi D, Marino A, Mantarro G, Campisi R. The use

of remifentanil for bloodless surgical field during vertebral disc resection. Minerva Anestesiol 2002;68:645-9.
3. Battershill AJ, Keating GM. Remifentanil: a review of its analgesic and sedative use in the intensive care unit. Drugs 2006;66:365-85.
4. Hermanns H, Lipfert P, Meier S, Jetzek-Zader M, Krauspe R, Stevens MF. Cortical somatosensory-evoked potentials during spine surgery in patients with neuromuscular and idiopathic scoliosis under propofol-remifentanil anaesthesia. Br J Anaesth 2007;98: 362-5.
5. Nathan N, Tabaraud F, Lacroix F, Mouliès D, Viviand X, Lansade A, et al. Influence of propofol concentrations on multipulse transcranial motor evoked potentials. Br J Anaesth 2003;91:493-7.
6. Imani F, Jafarian A, Hassani V, Khan ZH. Propofol-alfentanil vs propofol-remifentanil for posterior spinal fusion including wake-up test. Br J Anaesth 2006;96:583-6.
7. Grossfeld S, Winter RB, Lonstein JE, Denis F, Leonard A, Johnson L. Complications of anterior spinal surgery in children. J Pediatr Orthop 1997;17:89-95.
8. Hod-Feins R, Copeliovitch L, Abu-Kishk I, Eshel G, Lotan G, Shalmon E, et al. Superior mesenteric artery syndrome after scoliosis repair surgery: a case study and reassessment of the syndrome's pathogenesis. J Pediatr Orthop B 2007;16:345-9.
9. Sebel PS, Hoke JF, Westmoreland C, Hug CC Jr, Muir KT, Szlam F. Histamine concentrations and hemodynamic responses after remifentanil. Anesth Analg 1995;80:990-3.
10. Unlügenç H, Itegin M, Ocal I, Ozalevli M, Güler T, Isik G. Remifentanil produces vasorelaxation in isolated rat thoracic aorta strips. Acta Anaesthesiol Scand 2003;47:65-9.
11. Noseir RK, Ficke DJ, Kundu A, Arain SR, Ebert TJ. Sympathetic and vascular consequences from remifentanil in humans. Anesth Analg 2003;96:1645-50.
12. Ouattara A, Boccara G, Köckler U, Lecomte P, Leprince P, Léger P, et al. Remifentanil induces systemic arterial vasodilation in humans with a total artificial heart. Anesthesiology 2004;100:602-7.
13. Hu ZY, Lin PT, Liu J, Liao DQ. Remifentanil induces L-type Ca2+ channel inhibition in human mesenteric arterial smooth muscle cells. Can J Anaesth 2008;55:238-44.
14. Rosenbaum A, Kain ZN, Larsson P, Lönnqvist PA, Wolf AR. The place of premedication in pediatric practice. Paediatr Anaesth 2009;19:817-28.
15. Canet J, Mazo V. Postoperative pulmonary complications. Minerva Anestesiol 2010;76:138-43.
16. Gerlach K, Uhlig T, Hüppe M, Kraatz E, Saager L, Schmitz A, et al. Remifentanil-clonidine-propofol versus sufentanil-propofol anesthesia for coronary artery bypass surgery. J Cardiothorac Vasc Anesth 2002;16:703-8.
17. Peng PW, Sandler AN. A review of the use of fentanyl analgesia in the management of acute pain in adults. Anesthesiology 1999; 90:576-99.
18. Egan TD. Remifentanil pharmacokinetics and pharmacodynamics. A preliminary appraisal. Clin Pharmacokinet 1995;29:80-94.
19. Crawford MW, Hickey C, Zaarour C, Howard A, Naser B. Development of acute opioid tolerance during infusion of remifentanil for pediatric scoliosis surgery. Anesth Analg 2006;102:1662-7.
20. Engelhardt T, Zaarour C, Naser B, Pehora C, de Ruiter J, Howard A, et al. Intraoperative low-dose ketamine does not prevent a remifentanil-induced increase in morphine requirement after pediatric scoliosis surgery. Anesth Analg 2008;107:1170-5.
21. Koppert W. Opioid-induced hyperalgesia-Pathophysiology and clinical relevance. Acute Pain 2007;9:21-34.
22. Jee YS, Hong JY. Effects of remifentanil on propofol requirements for loss of consciousness in target-controlled infusion. Minerva Anestesiol 2008;74:17-22.
23. Nöst R, Thiel-Ritter A, Scholz S, Hempelmann G, Müller M. Balanced anesthesia with remifentanil and desflurane: clinical considerations for dose adjustment in adults. J Opioid Manag 2008;4: 305-9.
24. Park GR, Evans TN, Hutchins J, Borissov B, Gunning KE, Klinck JR. Reducing the demand for admission to intensive care after major abdominal surgery by a change in anaesthetic practice and the use of remifentanil. Eur J Anaesthesiol 2000;17:111-9.