Ultrasound-guided epidural anesthesia and sedation for open abdominal surgery in 20 consecutive children: a prospective case series and proof-of-concept study

Werner Schmid (✉ werner.schmid@meduniwien.ac.at)

Medical University of Vienna

Philipp Opfermann

Medical University of Vienna

Markus Zadrazil

Medical University of Vienna

Ursula Tonnhofer

Medical University of Vienna

Martin Metzelder

Medical University of Vienna

Peter Marhofer

Medical University of Vienna

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Abstract

General anesthesia (GA) in children is associated with respiratory events and a potential for drug-induced neurotoxicity. Aiming to reduce airway manipulation and the use of GA drugs, we designed a study of abdominal surgery under epidural anesthesia in sedated, spontaneously breathing children. We enrolled 20 children (3 – 83 months, 6.3 – 25.0 kg) scheduled for open abdominal surgery with Pfannenstiel incision. Sedation was followed by ultrasound-guided epidural anesthesia. Increases in heart rate by > 15% and or patient movements upon skin incision were rated as block deficiencies. Intubation equipment for advanced airway management was kept on standby. The primary study endpoint was successful blockade, meaning that no sequential airway management was required during surgery. Secondary endpoints included any use of fentanyl/propofol intraoperatively and of postoperative analgesics in the recovery room. All 20 blocks were successful, with no block deficiencies upon skin incision, no need for sequential airway management, and stable SpO₂ levels (97–100%). Surgery took a median of 120.5 minutes (IQR: 89.3–136.5) and included one bolus of fentanyl 120 minutes into a protracted operation. No more systemic analgesia had to be provided in the recovery room. Sedation and epidural anesthesia emerged as a useful alternative to GA from our consecutive case series.

Introduction

Vesicoureteral reflux (VUR) is the most widespread disease of the urinary system in children, with an estimated prevalence of 0.4–1.8%.¹ Nonsurgical and surgical treatment modalities are available. Among the latter, the most common approaches are to perform an endoscopic injection of a bulking agent to the ureteric orifice or to reimplant the ureter into the bladder, as by open ureteroneocystostomy (Cohen or Politano-Leadbetter procedure).²

General anesthesia (GA) with tracheal intubation is the usual way of managing open abdominal surgery, and respiratory events are the most common critical incidents in connection with pediatric GA. Undersized tracheal tubes and a relatively narrow airway are major factors that have been implicated in these events.^{3–5} Even though highly controversial observational research into neurodevelopmental sequelae of GA has repeatedly confirmed such associations,^{6–9} indicating neurotoxicity of various GA drugs in infants and small children,

Epidural anesthesia, with or without sedation, can minimize the use of GA drugs and might also be suitable for open ureteroneocystostomy. Many practitioners are still concerned about the safety of epidural punctures in infants, and few studies have investigated spinal¹⁰ or caudal¹¹ anesthesia to avoid tracheal intubation and mechanical ventilation during abdominal surgery in children. While high spinal anesthesia carries a major risk of unpredictable cranial spread to the subarachnoid space followed by cardiac and respiratory failure,¹² caudal blocks might not suffice for abdominal procedures with a supraumbilical skin incision.

We have long addressed this problem by developing ultrasound techniques allowing us to directly visualize the spread of local anesthetics (LA) inside the epidural space of infants and children.^{13,14} Even though epidural anesthesia without intubation has not been extensively compared to GA and remains highly controversial in both children and adults,^{15,16} a number of surgical procedures can be managed in this way.^{11,17} In an effort to broaden this spectrum, we enrolled the first 20 consecutive cases of open ureteroneocystostomy managed without GA in a prospective observational study.

Methods

Preparations for the study

This single-center trial, designed in line with the STROBE statement, was approved by the institutional review board (Ethics Commission at Medical University of Vienna; ref. 1133/2017, date of approval 24/08/2017) and entered into the German Clinical Trial Register (DRKSID: DRKS00012683, date of approval 15/07/2019). This study was performed in accordance with relevant guidelines and regulations. Parents or legal guardians of all enrolled children gave their written informed consent, having been comprehensively informed about the nature and scope of the study and the procedures to be conducted.

Patient enrolment and exclusion criteria

Between 11/2017 and 08/2020, a total of 20 consecutive children (age: 0 to 6 years) scheduled for open ureteroneocystostomy to treat vesicoureteral reflux (VUR) were assessed for eligibility and enrolled in our center (Division of Pediatric Surgery, Medical University of Vienna, Austria). Exclusion criteria were contraindications to epidural anesthesia, midazolam, or amino-amide local anesthetics; any presence of allergies, neurological disorders, coagulation disorders, thrombocytopenia, local infection at the intended injection site, or spine malformations; as well as participation in another clinical study ≤ 4 weeks before surgery, clinically relevant ECG abnormalities such as AV block or bradycardia, or inability to understand the study protocol and/or all procedures associated with the study. No surgical exclusion criteria were defined.

Patient preparation and premedication

Preoperative fasting conformed to our departmental standard of care (6 hours for solid food, 4 hours for breast milk, 2 hours for clear fluids). One hour before anesthesia induction, lidocaine 2.5% mixed with prilocaine 2.5% (EMLA 5% Cream; Astra Zeneca, Vienna, Austria) was applied to establish an intravenous access and depending on the expected neuroaxial procedure (see below) over the caudal window or over the thoraco-lumbar spinal junction, to reduce puncture pain. Premedication was performed via the rectal or oral route with 1 mg kg⁻¹ midazolam (Dormicum™; Roche, Vienna, Austria) (maximum dose 15 mg) thirty minutes prior induction of anesthesia; children less than 6 month of age were not premedicated.

Pre-epidural steps in the operating theatre

Cardiorespiratory monitoring (ECG, noninvasive arterial pressure, SpO₂) was started with the child placed on a forced-air warming blanket (Bair Hugger; Arizant, Eden Prairie, MN, USA). Then sedation was initiated

with a facemask and sevoflurane at 8 vol%, or if a vascular access had been established with propofol a bolus $\leq 2 \text{ mg kg}^{-1}$. Since spontaneous breathing was maintained in all cases to minimize airway manipulation, we preferred sevoflurane sedation, especially in small children (≤ 24 months). Depending on age, the children received an infusion of either $5 \text{ ml kg}^{-1} \text{ h}^{-1}$ Elo-Mel isotone or $10 \text{ ml kg}^{-1} \text{ h}^{-1}$ Elo-Paed balanced (Fresenius Kabi, Graz, Austria) plus glucose 1%. For the subsequent epidural block, they were turned to a left lateral position with the hips and knees flexed. Depending on the expected surgical duration, complexity, and postoperative course a decision was made between single-shot caudal blockade and a catheter technique with the option to give additional boluses of LA, no epidural infusions were administered. Sevoflurane administration was stopped immediately after performing and finishing the epidural block.

Epidural anesthesia by single injection

The first step for these caudal blocks was to palpate the sacral hiatus (the equilaterally triangular aperture at the base of the sacrum) and sacrococcygeal membrane. Sterile preparation was followed by an initial ultrasound scan of the puncture area and the dura mater, using a portable ultrasound device (M-Turbo; SonoSite, Bothell, WA, USA) with a linear transducer (50 mm, 6 – 15 MHz) and the probe prepared with a sterile cover (Safersonic, Ybbs, Austria). For the caudal puncture, we used an ‘immobile needle technique’ with a needle featuring a shortbevel facet (50 mm, 22 G) and a prefilled 30 cm injection line (Pajunk, Geisingen, Germany). In accordance with our clinical standards, 1.0 ml kg^{-1} ropivacaine 3.8 mg ml^{-1} was injected into the caudal space.

Epidural anesthesia through a catheter

For the more proximal route of epidural anesthesia, the puncture was placed at the level of the thoracolumbar transition, directly visualizing the neuraxial structures with the same ultrasound device from a paramedian angle. On identifying the dura mater and epidural space, the puncture was performed with a 20G or 19G 50 mm Tuohy needle and an 8 ml loss-of-resistance syringe (Smiths Medical, Hranice, Czech Republic) via a median approach. Inside the epidural space, 0.25 ml kg^{-1} ropivacaine 3.8 mg ml^{-1} was injected, the correct site of administration being sonographically verified by anterior movement of the dura mater. Then an epidural catheter was introduced, advanced 1.5 to 3 cm into the epidural space (depending on ultrasound image, size and age of the child), another 0.25 ml kg^{-1} ropivacaine 3.8 mg ml^{-1} injected through it, attached using a sterile transparent adhesive dressing, and the child turned to the supine position. In accordance with our clinical standards, the epidural catheter was removed no later than the fourth postoperative day.

Post-epidural preparations and surgical technique

The usual onset time of surgical analgesia was 10 to 15 minutes. During this interval, the child was correctly positioned and the surgical area prepared. Frequently cystoscopy was performed prior to the surgical intervention. Procedures lasting < 45 minutes did not require additional sedation, while propofol $5 \text{ mg kg}^{-1} \text{ h}^{-1}$ was used during longer procedures, following gentle aspiration of gastric juice via a gastric tube. Spontaneous breathing was continuously verified by an end-tidal CO_2 line fitted to a facemask,

through which oxygen-enriched air (FiO_2 : 0.40) was administered (Fig. 2). Fifteen minutes after performing the block, cystoscopy was started or the skin was incised (standard Pfannenstiel technique) for open ureteroneocystostomy (Cohen's cross-trigonal reimplantation or Politano-Leadbetter technique). All current techniques of surgical VUR treatment offer excellent results with few complications and high success rates of 92–98%.¹⁸

Evaluation of anesthesia and emergency management

Blockade was considered successful if no movement or hemodynamic instability was noted upon skin incision. Any increase in heart rate by $> 15\%$ from before the epidural, or other indications of pain like tachypnea or movement, were defined as requiring a bolus of fentanyl and, if needed, propofol. Equipment for advanced airway management was on standby and respiratory failure necessitating its use defined as paradox ventilation, disappearance of the end-tidal CO_2 curve, or drop in SpO_2 to $< 92\%$. The protocol for sequential airway management to re-establish adequate oxygenation included careful facemask ventilation with < 10 mmHg of inspiratory pressure and rapid-sequence intubation with propofol 5.0 mg kg^{-1} and rocuronium 1 mg kg^{-1} .

Postoperative management in the recovery room

Pain was monitored either based on the 'objective pain scale' (OPS) or by patient self-reporting using the 'revised faces pain scale' (FPS-R) normally usable in children 4 years and over. Pain scores were obtained on admission to the recovery room and every 30 minutes during the first 2 postoperative hours, typically after 2 h in the recovery room patients were transferred to the ward. Given a maximum total score of 10 with both scales, any two consecutive scores of ≥ 4 were followed up by i.v. administration of metamizol 10 mg kg^{-1} or piritramide 0.05 mg kg^{-1} or nalbuphine 0.1 mg kg^{-1} depending on age and score. A clinical examination for local infection as well as for lower-limb sensory and motor function was performed 24 hours after surgery.

Study endpoints and data analysis

The primary study endpoint was successful blockade, meaning that no sequential airway management was required during surgery. Secondary endpoints included any use of fentanyl/propofol intraoperatively and of postoperative analgesics in the recovery room. All recorded data were analyzed in spreadsheets (Excel 2016; Microsoft, Redmond, WA, USA) and statistical software (Prism 8.3.0; Graph Pad Software Inc., San Diego, CA, USA) with negative D'Agostino-Pearson testing for normal distribution.

Results

As apparent from Fig. 1, all children who had been included—and whose pertinent demographic data are summarized in Table 1—completed the study and could be evaluated. They underwent surgery for a median of 120.5 (IQR: 89.3–136.5) minutes in total, with previous cystoscopy in 13 cases.

Table 1
Pertinent patient data. All findings other than for sex distribution are expressed as median values and interquartile ranges (IQR).

Patient data	
Sex (m/f)	9/11
Age (months)	23 (14–41.8)
Weight (kg)	12.5 (10.2–15.4)
Height (cm)	85 (76.5–102.8)
Duration of surgery (min)	120.5 (89.3–136.5)

Block deficiencies requiring airway management

The primary endpoint of successful blockade was invariably achieved, as anesthesia management, including sedation and the ultrasound-guided epidural, yielded the expected results in all patients (Table 2), none of whom experienced any kind of respiratory failure, eliminating any need for sequential airway management as described in the methods section. Oxygen saturation invariably remained within a stable range of 97–100% throughout the anesthetic and surgical treatment.

Table 2

Overview of anesthesia management, including sedation details and volumes of local anesthetic administered. Results are expressed as mean values (min–max).

Neuraxial procedure (n)	CB = 9	EC = 11
Volume of LA (ml)	14.7 (9–20)	12.5 (6–22)
Total volume of LA (ml)	13.5 (6–22)	
Second bolus of LA (n)	0	1
Second bolus of LA (ml)	0	6
Opioid-free (n)	8	11
Total i.v. fentanyl (µg)	10 (one patient)	0
Clonidine (n)	6	0
Clonidine (µg)	12.5 (15–40)	0
Metamizol (mg)	0	0
Nalbuphine (mg)	0	0
Piritramid (mg)	0	0
CB = caudal blockade; EC = epidural catheter; LA = local anesthetic		

Block deficiencies, anesthesia management and medication

Regarding the secondary endpoints, none of the children exhibited block deficiencies during skin incision. As depicted in Table 2, one child with a single-injection caudal epidural (without clonidine) required a bolus of fentanyl ($1 \mu\text{g kg}^{-1}$) 120 minutes after the skin incision to cover a protracted (155 minutes) surgical procedure. A total of six of out of nine caudal blocks received clonidine $12.5 \mu\text{g}$ (15–40 µg; min-max) additional to the LA, none of the patients with the catheter technique; only one child with an epidural catheter needed an additional bolus of 6 ml of ropivacaine. Comparing propofol consumption between the children with caudal block or epidural catheter, no differences in propofol administration via continuous-infusion or bolus were detected. As expected, the heart rates decreased by a median of 15% (3–25%) following administration of ropivacaine 3.8 mg ml^{-1} and then remained stable throughout the surgical procedures, without a difference between single-shot and catheter-based blocks (data not shown).

Pain scores and final examinations

All pain scores, whether OPS or FPS-R, remained below five, so that additional systemic analgesics in the recovery room were not required. All examinations for local infection and lower-limb sensory/motor

function led to normal findings 24 hours after surgery.

Discussion

Airway manipulation and mechanical ventilation could be completely avoided in this prospective study of sedation plus epidural blockade for open abdominal surgery, and opioid-free anesthesia was achieved in 95% of the 20 children. The only intraoperative requirement for fentanyl (bolus of 10 µg 2 hours after skin incision) arose when a caudal block with a single bolus of ropivacaine (without clonidine) failed to last over 155 minutes of surgery, the third longest of all 20 operations. That said, while the longest operation of 164 minutes involved an epidural catheter, four of the eight longest procedures (127–137 minutes) proceeded without a problem under a single-injection caudal epidural with addition of clonidine 1 µg/kg.

GA is the standard way of managing major open abdominal surgery in both children and adults. While severe aspiration is rare in pediatric patients,¹⁹ most anesthetists would agree that, in infants, the tracheal intubation associated with GA carries a high risk of hypoxia and critical respiratory events, thus requiring special hand skills and experience. Respiratory events have repeatedly proven to cause the majority (46.5–77.4%^{4,5,20,21}) of critical incidents, and their high incidence in pediatric anesthesia has been attributed to undersized tracheal tubes, narrow airways, and difficult-airway syndromes.³ Our group has shown that epidural anesthesia with spontaneous breathing and minimized airway manipulation can be a safe alternative for various surgical procedures.^{15,22,23}

Abdominal surgery under sedation and neuraxial anesthesia, in the absence of GA and intubation, is highly controversial in both children and adults.^{16,24} Clearly, intubation should not be avoided “at all costs” and epidurals in newborns be performed exclusively by experienced pediatric anesthetists well versed with neuraxial regional techniques. The real question is whether we should deny our patients less postoperative pain, shorter exposure to anesthetics, earlier breast feeding, or better respiratory outcomes for lack of data from large prospective trials and on the precise incidence of complications, even though centers with high case loads and staff experienced in pediatric anesthesiology may be easily capable of safely performing a wide range of surgical (including laparoscopic) procedures on spontaneously breathing patients under neuraxial anesthesia.

Given a number of large prospective multi-regional audits^{25–27} demonstrating the safety of regional (including epidural) anesthesia in children, there is actually a simple answer to the question whether neuraxial anesthesia under sedation is an improvement or may, on the contrary, increase the risk-benefit ratio from standard GA. For caudal blocks as the most widely used regional technique (27–40% of all audited blocks), large series have yielded high success rates and a very low incidence of serious complications notably in younger children.^{26,28} Epidural catheterization at the segmental level (which can be more reliable in older children depending on the incision height) has proven to be safe with appropriately sized equipment in experienced hands.²⁷ It has been shown that regional anesthesia/analgesia can be applied as safely under awake sedation as under GA in children.²⁸ Overall

complication rates of 0.09%²⁹ to 0.2% (n = 14,917 blocks)²⁶ have been reported for regional pediatric analgesia, with higher rates in younger (≤ 12 months: 0.3%) than older (> 12 months: 0.07%) children, mostly as a result of dosing errors.²⁷

From our perspective, it is obvious that regional anesthesia in general, and epidural blockade in particular, should offer distinct advantages over GA (perioperative pain management, cardiorespiratory performance) notably in children (effective analgesia without opioid-related respiratory effects, less postoperative ventilation, stable hemodynamics, improved gastrointestinal function, reduced neurohumoral stress response). Although not yet confirmed by large-scale comparative clinical trials, a case can be made that these benefits by various techniques of regional anesthesia are real by reducing the requirements for systemic sedation and analgesic drugs in children.¹⁵ It is also worth considering the controversial data available on associations between GA exposure and pediatric CNS development. Studies to this effect^{6–9, 30} suggest neurotoxic sequelae of various GA drugs in infants and small children, including learning disabilities, attention-deficit hyperactivity disorder (ADHD), memory problems, and poor scoring in standardized achievement tests. In a 1976-to-1982 birth cohort, multiple (but not single) exposures to anesthesia before 3 years of age were associated with subsequent ADHD diagnoses and learning disabilities, with the incidence of the latter actually doubling.^{7,30}

That said, a randomized controlled trial, which compared neurocognitive outcomes in 722 infants (postmenstrual age: < 60 weeks) following either sevoflurane-based GA or awake spinal or epidural anesthesia for inguinal hernia repair, did not reveal statistically significant differences neither in cognitive scores nor in other domains like language, motor, social, emotional, and adaptive behavior at 2 and 5 years of age.^{31,32} While these findings offer some evidence that a single brief exposure to GA at a young age may be safe without detectable neurodevelopmental sequelae, a conclusive judgment on this issue cannot be given at this time. Also, emergence delirium is a neurocognitive complication often seen in the immediate postoperative course of children managed by GA and has been shown to occur less frequently on switching from mainly volatile to propofol-based, completely intravenous anesthesia.³³ Given that postoperative pain as such has also been implicated in emergence delirium,³⁴ there are actually two separate pathways by which non-GA sedation plus epidural anesthesia may enable this documented short-term neurological benefit.

Over the past 15 years, our study group has accumulated substantial experience with central nerve blocks under ultrasound guidance in children.^{35,36} Based on this experience and the aforementioned findings, we considered that ultrasound-guided epidural blocks with sedation might be a useful alternative to other techniques, which is confirmed by this first consecutive series of children undergoing open ureteroneocystostomy. Once the epidural space was located by direct visualization and loss of resistance, the spread of LA could be directly monitored and was found to move in a cranial direction without changes in ventilation. While the concentration (0.38%) and volume ($0.75\text{--}1.0\text{ ml kg}^{-1}$) of ropivacaine we administered may seem high, the pharmacokinetics of epidural ropivacaine is not well documented in infants. Compared to animal studies, however, we have previously found safe plasma levels—with a

mean Cmax of 1.16 ± 0.49 (and up to 2.61) $\mu\text{g ml}^{-1}$ —in children and adolescents weighing 30–50 kg at the same concentration and volume of caudally injected ropivacaine.^{36,37}

Another finding suggesting a favorable safety profile is that ropivacaine gets resorbed more slowly from the epidural space than bupivacaine in infants.³⁸ Lacking CNS data, we are unable to close the case of direct effects of ropivacaine on the CNS. Further studies should explore lower concentrations of epidural ropivacaine in the treatment of vesicoureteral reflux. While it is important to understand the special training and hand skills for the technique here reported, today's degree of specialization really implies that *all* procedures in children should be conducted by dedicated pediatric anesthesiologists and surgeons.

Ultrasound-guided epidural anesthesia may be considered a safe technique in experienced hands.³⁹ No less important to the safety and success of such management is careful attention to miscellaneous factors, maintenance of spontaneous breathing during sedation or suctioning of the stomach being two examples.

Nevertheless, some colleagues will not foresee that our approach will be a widely implemented technique. It requires specialists with expertise and not many anesthesiologists, pediatric anesthesiologists included, will feel comfortable with this technique. Acknowledging these considerations and the required hand skills for the placement of a pediatric epidural catheter, we began to adapt our approach and increasingly used caudal anesthesia solely, which is much easier to perform and should be in the armamentarium of every anesthesiologist. Considering the fact that only one child with an epidural catheter needed one additional bolus of LA and the only patient who needed fentanyl was a child with caudal anesthesia without clonidine, we are now performing just caudal blocks and all with additional clonidine for these kind of surgical procedures. Further studies will have to show whether this will pave the way for opioid-free anesthesia in this type of procedure.

Additionally, open abdominal surgery under epidural anesthesia solely, also has a potential of substantially reducing operation-theatre occupancy, as spontaneous breathing is never interrupted. This “skipping” of the recovery phase not only eliminates the risks of emergence from GA but also saves time and money. Our study group has calculated cost savings of almost € 15 per OT minute.⁴⁰ Time savings are likewise on record for spinal anesthesia versus GA in the management of open pyloromyotomy.¹⁰ Consecutive case series have obvious limitations but are useful in demonstrating the feasibility of new anesthetic techniques for specific surgical procedures, setting a point of departure for further studies and supporting hypothesis-driven science. As a case in point, the consecutive cases here presented demonstrate that sedation and epidural anesthesia without GA has performed well, without hemodynamic or respiratory complications, in a series of 20 children with vesicoureteral reflux treated by open abdominal surgery with Pfannenstiel incision.

Declarations

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Individual contributions

WS, PM, PO, and MZ contributed equally to analysing and interpreting the data and WS, PM, and WK equally to drafting the manuscript. WS was in charge of communication and administrative tasks related to ethics committee approval, the Austrian Agency for Health and Food Safety, and trial registration. WS, MM and PM contributed to designing and analysing the study and WS, PM, UT and MM to the clinical patient management.

Competing interests

The authors declare that they have no competing interest.

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Figures

Figure 1

Flow chart of the study.

Figure 2

Intraoperative setting illustrating a sedated, spontaneously breathing patient with oxygen supplied through a facemask.