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On-table extubation in neonates undergoing anoplasty: an experience of anesthetic management on the concept of fast-tracking anesthesia

A pilot study

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Abstract

Fast-track anesthesia (FTA) is difficult to achieve in neonates due to immature organ function and high rates of perioperative events. As a high-risk population, neonates require prolonged postoperative mechanical ventilation, which may lead to contradictions in cases where neonatal intensive care unit resources and ventilator facilities are limited. The choice of anesthesia strategy and anesthetic can help achieve rapid postoperative rehabilitation and save hospitalization costs. The authors describe their experience with maintaining spontaneous breathing in neonates undergoing anoplasty without opioids or muscle relaxants.

This retrospective chart review included neonates who underwent anoplasty in the authors' institution. Twelve neonates who underwent the procedure with atomized 5% lidocaine topical anesthesia around the glottis, combined with sevoflurane sedation and caudal anesthesia facilitating tracheal intubation without opioid and muscle relaxant comprised the FTA group. Ten neonates who underwent the intervention with routine anesthesia techniques in the same period comprised the control group (group C).

The surgical success rate in the FTA group was 91.7%. There were no severe complications related to lidocaine administered around the glottis. Extubation time was significantly shorter in the FTA group than in group C (4 [2.5, 5.2] vs 81.5 [60.6, 96.8], respectively; $P < .01$). The duration of stay in the surgical intensive care unit (SICU) was longer in group C than in the FTA group (2 [2.0, 2.6] vs 1 [0.9, 2.0], respectively; $P = .006$,). A statistically significant lower rate of extubation-cough was noted after endotracheal tube removal in the FTA group compared with group C (18% vs 90%, respectively; $P < .001$). There was no difference in the duration of anesthesia or hospitalization costs between the 2 groups. No neonates required re-intubation after extubation.

On-table extubation via 5% atomized lidocaine topical anesthesia around the glottis for tracheal intubation combined with sevoflurane sedation and caudal anesthesia without opioid and muscle relaxant was feasible in neonates undergoing anoplasty. This reduced time to extubation, length of SICU stay and saved resources. A similar trend in cost savings was also found; nevertheless, more studies are needed to confirm these results.

Abbreviations: CNS = central nervous system, ECG = electrocardiograph, ETCO2 = end tidal carbon dioxide, FTA = fast-track anesthesia, IV = intravenous, SICU = surgical intensive care unit.

Keywords: anoplasty, caudal anesthesia, fast-track anesthesia, lidocaine topical anesthesia, neonates, sevoflurane sedation

1. Introduction

Anorectal malformation has an incidence 1/5000[1] and is a common congenital digestive tract malformation that always requires surgical intervention involving general anesthesia. Anesthesiologists have encountered several challenges in anesthesia management for neonates who undergo surgery under general anesthesia due to the immaturity of various organs, poor tolerance to anesthetic agents, and low oxygen reserve. In routine work on neonates, general anesthesia with multiple drugs has always been used during surgical repair, leading to long extubation times and high medical expenses. As a high-risk population, neonates often require prolonged postoperative mechanical ventilation, which may lead to contradictions in cases where neonatal intensive care unit resources and ventilator facilities are limited. Furthermore, prolonged exposure to inhalation anesthetics has been shown to be toxic in research involving neonatal rodents.[2] Nevertheless, it is unacceptable to perform surgery in neonates without the use of anesthetics. The notion that newborns cannot feel pain has long been abandoned. Further research demonstrated that repeated pain stimulation in neonates led to behavioral difficulties later in life.[3] Intravenous

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(IV) opioids have been a good choice to maintain adequate intra- or postoperative analgesia. However, due to immature liver and kidney function, opioid clearance rates are decreased, resulting in a delay to awakening and respiratory depression, which are not safe for neonates.[4]

The purpose of fast-track anesthesia (FTA) is to remove the endotracheal tube early, decrease respiratory complications, shorten the length of hospital stay, reduce mortality and costs, and return to productivity early. The appropriate choice of anesthesia maneuvers and anesthetics can facilitate rapid postoperative rehabilitation. Some clinical evidence indicated that rapid recovery after surgery was closely related to anesthesia.[5,6] However, FTA was difficult to achieve in neonates because of physical differences from adults. Therefore, it is worth exploring methods to minimize intra-operative anesthetic exposure, remove the endotracheal tube early, accelerate recovery, and decrease medical costs in neonates with lower resources.

There is no definitive evidence supporting the best maneuver for anesthesia in neonates. In our institution, different approaches are chosen by different anesthesiologists. Caudal anesthesia is a well-established and valuable adjunct to general anesthesia in pediatric patients undergoing perineal surgical intervention. We describe our experience with maintaining spontaneous breathing via 5% atomized lidocaine topical anesthesia around glottis in tracheal intubation, combined with sevoflurane sedation and caudal block without opioid and muscle relaxant, in neonates undergoing anoplasty.

2. Methods

This retrospective chart review was approved by the Ethics Committee of Chengdu Women's and Children's Central Hospital (Chengdu, China). Given the retrospective nature of the study and the use of anonymized patient data, requirements for informed consent were waived. This study enrolled neonates with anorectal malformation who were scheduled for anoplasty, either elective or emergency. Neonatal surgical procedures in the FTA group were performed under combined general and caudal anesthesia in a referral hospital during the period from May 2016 to May 2017. The airway was locally anesthetized with 5% atomized lidocaine to facilitate intubation and maintain spontaneous breathing. In addition to the FTA group, neonates who were diagnosed with anorectal malformations and underwent surgical intervention (ie, anoplasty) in the same period were designated as a control group (C group). The perioperative management remained unchanged over the same time period.

Eligibility criteria included neonates with a gestational age >35 weeks and scheduled for either elective or emergency anoplasty. Neonates with assisted ventilation, central nervous system (CNS) disorders, coexisting spinal issues, congenital heart diseases, or coagulation disorders were excluded. All cases were performed by attending anesthetists with ≥5 years' experience in pediatric anesthesia. As a rule in the authors' institution, only anesthetists ≥5 year' experience attending in pediatric anesthesia can perform anesthesia in neonates.

The protocol for the management of the FTA group was as follows. IV access and naso-gastric tube were established in the neonatal ward. In the operation room, electrocardiograph (ECG), non-invasive blood pressure, end-tidal carbon dioxide ($ETCO_2$) and pulse oximetry were monitored. Anesthesia was induced using 4% sevoflurane in 100% oxygen (2 L/min) initially via mask. Spontaneous breathing was closely monitored. If the respiratory rate decreased to <20 breaths/min, the concentration of sevoflurane was rapidly reduced to ≤3%. Eight minutes later, topical anesthesia with 5% atomized lidocaine (Lidocaine Aerosol, China) (4.5 mg [1 spray]) was performed under laryngoscope guidance around glottis, followed by continuous inhalation of 4% sevoflurane for 2 min. No opioid or muscle relaxant was administered. Subsequently, a tube was inserted into the glottis. All of the caudal blocks were performed after induction of anesthesia. In the FTA group, the caudal epidural space was identified using a 22-gauge hypodermic needle under ultrasound guidance in the left lateral position (Fig. 1). Lidocaine (1 mL/kg [0.5%]) was injected after confirmation in epidural space via ultrasonography. All caudal blocks were performed by the attending anesthetist. Anesthesia was maintained with

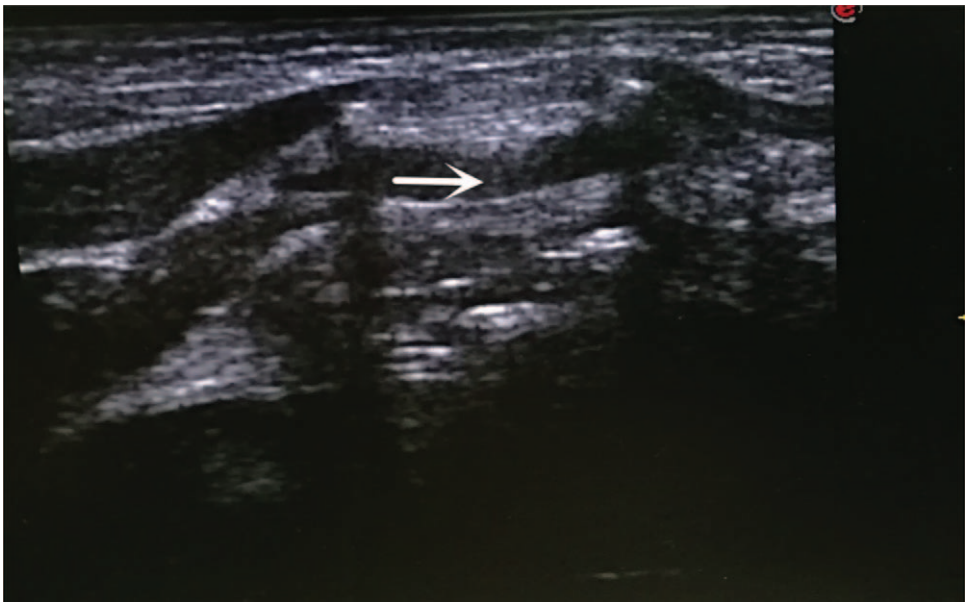

Figure 1. Caudal block under the guide of ultrasound in transverse view. Arrow: needle point in sacral hiatus.

sevoflurane and was discontinued 3 min before the conclusion of surgery.

Procedures in group C were performed using traditional general anesthesia with or without caudal block. For safety and to improve the efficiency of the operation, removal endotracheal tube was performed in SICU.

Patients in both groups received postoperative ventilatory support until fully awake.

Primary outcomes included extubation time, length of SICU stay, and hospitalization costs. Secondary outcomes included duration of anesthesia, surgical success rate, and perioperative complications. Extubation time was defined as the end of the skin suture to tracheal tube removal. Indicators of extubation in neonates included fully awake with limb movement, with regular breathing and tidal volume 5–7 mL/kg. Perioperative data were retrieved from the neonate database. Duration of anesthesia was defined as the time from the first carbon dioxide reading to the neonates' leaving the operation room. Surgical success rate was defined as the proportion of neonates who had completed the surgery without additional anesthetics or anesthetic techniques. Perioperative complications included: bradycardia or tachycardia (heart rate <100 beats/min or >180 beats/min); hypotension or hypertension (blood pressure <20% or >20% baseline value); respiratory depression (respiratory rate <20 breaths/min); re-intubation: neonates requiring re-endotracheal intubation in the first 24 h postoperatively; respiratory-related events, such as peri-anesthesia cough, laryngospasm, or bronchospasm. All the events were recorded in detail and managed appropriately.

All data were analyzed using SPSS version 13.0 (IBM Corporation, Chicago, IL). The student *t* test was used to compare normally distributed data. The chi-squared test was used for categorical data. $P < .05$ was considered to be statistically significant.

3. Results

A total of 22 neonates were enrolled in the present retrospective pilot study, including 12 who underwent the new anesthesia technique (FTA group) and 10 in the control group (group C). In the FTA group, 11 neonates successfully completed the surgery using this new technique alone, and only 1 neonate required additional fentanyl (5 μg/kg) during the surgery due to a change in the surgical technique. Overall, the surgical success rate using the new technique alone was 91.7%.

Demographic characteristics were comparable between 2 groups (Table 1), including gestational weeks, duration of surgery, and the number of neonates who were diagnosed with lung disease before surgery. In the FTA group, all neonates who received 5% atomized lidocaine around the glottis underwent general anesthesia combined with caudal block, whereas 4 patients in group C received general anesthesia alone.

Table 1

Characteristics and operative data. Values are presented as mean (SD), median (IQR) or number (proportion).

	FTA group	C group	*P*
Male gender (%)	7 (64)	6 (60)	.61
Body weigh (kg)	2.9 (0.5)	2.8 (0.3)	.57
Gestational weeks	36.9 (1.4)	36.9 (1.3)	.99
Age at the time of surgery (days)	1.8 (0.6)	2.1 (0.6)	.29
The number of neonates diagnosed lung disease before surgery (%)	6 (55)	5 (50)	.59
Duration of surgery (minutes)	65 (58–72)	66.5 (58–75)	.49

Table 2

Comparation of extubation time, length of SICU stay, hospitalized cost and duration of anesthesia for neonates either in FTA or C group. Values are presented as mean (SD), median (IQR)or number (proportion).

	FTA group	C group	*P*
Extubation time (minutes)	4 (2.5–5.2)	81.5 (53–101)	.000
Length of SICU stay (days)	1 (0.9–2.0)	2 (2.0–2.6)	.01
Hospitalizing cost (ten- thousand-yuan)	2.3 (0.5)	2.6 (0.4)	.13
Duration of anesthesia (minutes)	100 (98–115)	104 (100–115)	.92
Extubation-cough (%)	2 (18)	9 (90)	.000

There were no severe complications related to the 5% atomized lidocaine administered around glottis. The extubation time was significantly shorter in the FTA group than in group C (4 [2.5, 5.2] vs 81.5 [53,101]; $P < .01$). The neonates in C group had longer SICU stays, compared with neonates in the FTA group (2 days [2.0, 2.6] vs 1 day [0.9, 2.0], $P = .006$). A statistically significant difference in the incidence of extubation-cough was apparent after endotracheal tube removal, with a lower rate in the FTA group compared with group C (18% vs 90%, respectively; $P < .001$). There was no difference in duration of anesthesia (100 min [98, 115] vs 104 min [100,115]; $P = .91$) and hospital cost (2.3 ± 0.5 vs 2.6 ± 0.4, $P = .13$) between the 2 groups (Table 2).

One common side effect of sevoflurane in the neonates was respiratory inhibition, especially in high concentrations. Therefore, induction using 4% of sevoflurane with 5% atomized lidocaine around the glottis resulted in no respiratory inhibition and intubation-cough in the spontaneous breathing group. Because the choice of anesthetic had a significant influence on the incidence of intubation-cough and respiratory inhibition, we focused on the spontaneous breathing group only. No patient developed significant abnormal heart rate or blood pressure, except 1 neonate who experienced transient hypotension after caudal block and recovered after of IV fluid administration (10 mL/kg). No neonates required re-intubation after being extubated.

4. Discussion

In our study, 5% atomized lidocaine topical anesthesia administered around glottis for tracheal intubation, combined with sevoflurane sedation and caudal block without opioid or muscle relaxant in neonates, failed to reduce hospitalization costs or the duration of anesthesia. However, the technique reduced extubation time, length of SICU stay, and the incidence of extubation-cough, without severe complications. We described an alternative anesthesia technique demonstrating that on-table extubation in neonates was fast, feasible and safe in a low-resource setting.

Sevoflurane induction, which can be performed easily and safely, was tolerated by the majority of children; however, it produced dose-related respiratory depression. Some studies have reported that sevoflurane achieved satisfactory intubation conditions without adjuvants [7,8]. However, other clinical studies reported that high concentrations of sevoflurane could lead epileptiform electroencephalogram activity and bradycardia.[9,10] There has been no evidence to demonstrate that low concentrations sevoflurane are unsafe; however, excessively low levels are insufficient to satisfy intubation or surgical conditions. Substituting opioids and neuromuscular relaxants are required to

facilitate tracheal intubation and to avoid high inspired concentrations of sevoflurane.

Fentanyl is the most frequently used opioid analgesic in infants and children, and helps patients maintain stable hemodynamics and avoid stress responses.[11] The required dose of fentanyl in anesthesia is, however, highly variable, with a half-life ranging from 317 min to 1062 min.[12] The half-life is prolonged by a factor of 1.5 to 3 times in neonates with increased intra-abdominal pressure. Fentanyl has a high hepatic extraction ratio, and clearance relies, in large part, on hepatic blood flow. In addition, hepatic perfusion was diminished in neonates with anal atresia due to increased intra-abdominal pressure, which could slow fentanyl clearance.[12] Increases in plasma fentanyl levels have been associated with significantly prolonged ventilation support,[12] which was similar to what was observed in our study. In a previous study, Silva et al[13] reported that fentanyl was associated with respiratory depression requiring a rescue intervention in adults. In our routine practice, breathing support after surgery in neonates is required until complete anesthetic clearance. On the other hand, short-term exposure to morphine has been reported to promote neuronal apoptosis,[14] and may impair cognitive functioning in adult rodents.[15] To date, however, no clinical study has confirmed that single-short term exposure to fentanyl leads to neurotoxicity and learning deficits in neonates; nevertheless, surgeons and clinicians should remain aware of this problem.

Infants are more sensitive to muscle relaxants, to which their responses vary to a greater degree.[16] In pediatric anesthesia, muscle relaxants have most commonly been used to facilitate intubation and improve surgical conditions. For these purposes, an unnecessary high dose of muscle relaxant may be administered to achieve satisfactory conditions, which may lead to a prolonged effect and influence the reversal time.[17] The extension of muscle relaxant reversal time results in prolonged mechanical ventilation time, which undoubtedly results in a waste of financial and human resources.

Considering these issues, we were prompted to find an alternative safe and fast anesthesia technique for neonates undergoing anoplasty, which would facilitate early extubation, reduce length of SICU stay, and save hospitalization costs. The concept of an anesthesia technique for neonates undergoing anoplasty should address rapid wake-up while satisfying analgesic requirements. Topical lidocaine anesthesia administered around the glottis in tracheal intubation, combined with sevoflurane sedation and caudal block without opioid and muscle relaxant, may be the best choice. Spontaneous breathing should last the entire procedure, and intubation was an option and remedy in the event of an accident in neonates.

Intratracheal application of topical lidocaine anesthesia has been widely used in children to facilitate intubation or attenuate intubation stress responses,[18] which was an adequate solution to the problem of intubation analgesia. A previous study reported that 6.5% topical lidocaine spray in neonatal intubation did not induce any considerable side effects.[19] Current evidence supports the local application of lidocaine <4 mg/kg to be safe in pediatric patients.[20] Atomized lidocaine has several advantages over non-atomized liquid, including higher plasma concentration and an increased surface area because of the smaller atomized particles when compared with conventional lidocaine spray.[21] Hence, it was necessary to use atomized lidocaine around the glottis to inhibit the intubation response while reducing the dosage of lidocaine as much as possible. In our study, we demonstrated that administering 5% topical lidocaine anesthesia around glottis with sevoflurane sedation could facilitate complete tracheal intubation without any side effects.

A previous study reported that precise caudal block with real-time ultrasound guidance, which reduced opioid consumption, was used as a supplement to general anesthesia for neonates.[22] The duration of anoplasty in our institution is approximately 1 h; therefore, a single injection of lidocaine-maintained analgesia, except for 1 case in which the surgery changed and additional fentanyl was administered.

Most neonates have no health-insurance or have health-insurance that does not cover inpatient care of newborns in developing countries.[23] Postoperative continuous mechanical ventilation and high-level neonatal care service in the SICU comprise the major portion of hospitalization costs. Daily intensive care unit consumption in Indian private hospitals is similar to that in North America.[24] Although there were no data from China, the costs should also be similarly exorbitant. The burden of medical expenses, which may lead to catastrophic bankruptcy, can be only borne by the family. In developing countries, insufficient medical resources, lack of medical workers, and the shortage of equipped facilities required us to improve the efficiency of treating more patients. Efficiency improvement could be achieved by decreasing operation room turnover time, and increasing operation room productivity and utilization rate of SICU. In a previous cardiac surgery study, on-table extubation helped curtail costs and shorten hospital length of stay.[25] In our study, we identified a significant reduction of SICU stay by early extubation. This result was similar to the observation from a previous study by Beamer.[25] In addition, we also noted a decrease in hospitalization costs, but the difference was not significant because of our limited sample size.

The study has some limitations. To date, the safety and efficacy of this technique in neonates undergoing anoplasty has been demonstrated in our institution. However, the sample size was too small to generalize our results across all facilities. We are currently planning to conduct a randomized controlled trial, which has been registered in a Chinese Clinical Trial Registry (ChiCTR-INR-17012576), in which we compare 5% atomized lidocaine trachea anesthesia combined with sevoflurane sedation and caudal block and routine general anesthesia with caudal block to provide more convincing evidence confirming the advantages as well as long-term prognosis. To optimize postoperative pain management, ropivacaine will be used as the local anesthetic for its long duration of sensory analgesia. When the study is completed, the raw data will be uploaded to a repository via the website http://www.chictr.org.cn/index.aspx within 6 months.

Author contributions

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Investigation: Yu Cui, Rong Cao, and Kai Liu.
Methodology: Yu Cui, Yu Wang, Qing-hua Huang, and Bin Liu.
Project administration: Yu Cui and Bin Liu.
Resources: Yu Cui and Bin Liu.
Software: Yu Cui.
Supervision: Yu Cui and Bin Liu.
Validation: Yu Cui, Bin Liu.
Visualization: Yu Cui.
Writing – original draft: Yu Cui and Yu Wang

Writing – review & editing: Bin Liu, Yu Cui, Yu Wang, and Rong Cao

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