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Research Article

Regional Analgesia in Complete Primary Repair of Bladder Exstrophy: Single Centre Experience

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Abstract

Introduction: Complete primary repair of exstrophy (CPRE) combines bladder closure, bladder neck reconstruction, epispadias repair and bilateral anterior oblique osteotomy. The single-step repair incorporates in one operative session several very painful procedures, so pain control is a crucial aspect of perioperative care in patients undergoing CPRE.

Purpose of the Study: The purpose of this study is to verify the safeness and efficacy of epidural analgesia even in the complex and painful setting of CPRE patients.

Patients and Methods: Since 2009 in our Institution all bladder exstrophy patients have been operated on with the CPRE technique including anterior oblique osteotomy and subsequent immobilization. Intra- and post-operative analgesia follows a protocol which protocol that includes a single bolus of ropivacaine (2mg/kg), followed by a continuous infusion of it at 0.2% concentration (Naropin©, Astra Zeneca) (0.1 - 0.2 mg/kg/h) via the epidural catheter. Postoperatively, patients are kept paralyzed and sedated in the NICU for 3 to 7 days. Post-operative pain is controlled by infusion of epidural ropivacaine 0.125%; paracetamol is added to baseline therapy when needed.

Results: In 24 months 11 patients underwent CPRE. Epidural catheter was maintained for an average of 13 days (range 1 - 21). Two patients required removal of the epidural catheter prior to the intended date, due to accidental dislocation. Overall, 14 extra-doses of paracetamol were required in 7 patients in association to epidural analgesia in order to achieve a better pain control.

Conclusion: Even in the complex and painful setting of CPRE patients, epidural analgesia seems to be safe and effective in controlling intra- and post-operative pain, facilitating immobilization which that is crucial for success.

Level of Evidence: Level IV.

Keywords: *Neonate; NICU; Bladder Exstrophy; Regional Analgesia; Acute Pain*

Introduction

Bladder exstrophy is a rare congenital malformation that affects the genitourinary tract in a proportion of $2{:}10^{-6}$ live births [1]. It is an embryologic malformation that results in a complex deficiency of the anterior midline, with urogenital and skeletal manifestations. Urogenital reconstruction is a challenging surgical treatment that can be completed in a single stage or multiyear staged approach. Complete primary repair of exstrophy was developed in the late 1990's and combines bladder closure, bladder neck reconstruction, epispadias repair and bilateral anterior oblique osteotomy [2]. The single-step repair incorporates in one operative session several very painful procedures, so pain control is a crucial aspect of perioperative care in patients undergoing CPRE. Poor post-operative pain control increases the baby's stress, crying, and spontaneous movements, all aspects that could contribute to wound dehiscence and bladder prolapse, which in turn worsens the probability of attaining continence in the future [3].

Although pain control represents a crucial factor in the successful treatment of bladder exstrophy, it has received minor attention in the medical literature, with few reports on peri-operative pain management, most exclusively based on staged repair techniques, and only in recent years [4-6].

Aim of the Study

The aim of the present study is to report our experience with loco-regional analgesia in a cohort of patients treated for bladder extrophy with CPRE.

Methods

We retrospectively reviewed the medical records of all consecutive patients treated with CPRE for bladder exstrophy in 24 months in our department with particular attention to peri- and post-operative pain management. All patients were dealt with a dedicated "exstrophy team" including neonatal surgeon, urologist, orthopedic surgeon, anesthesiologist, neonatologist and clinical nurse specialist.

Surgery was performed under combined general and epidural anesthesia. A complete spine radiography excluded the presence of malformations before the epidural catheter insertion. After induction of general anesthesia with propofol 3 mg/kg, rocuronio 0.6 mg/kg and fentanyl 2 mcg/kg, patient was intubated and an epidural catheter (Perifix® ONE Paed Set 20 B. Braun) was inserted under sterile conditions at the L1/L2 inter-vertebral space and subcutaneously tunneled approximately 2.5 cm above the insertion site [5]. Once the epidural space was identified a single bolus of ropivacaine (Naropin©, AstraZeneca) 2 mg/kg 0.2% was injected slowly (90 sec). The anesthesia was maintained with O_2/Air/sevoflurane 2% and continuous epidural infusion of ropivacaine 0.125% (0.1 mg/kg/h) via the epidural catheter. During the operation the conditions of the infant were monitored and in case of inadequate analgesia, the infusion of ropivacaine was increased up to the maximum dosage (0.2 mg/kg/h).

Postoperatively the infants were placed in a previously designed spica-cast and transferred to the NICU where conventionally the infant remained intubated, paralyzed (rocuronio 0,3 mg/kg/h), for a maximum of three days and sedated (midazolam 0.1 mcg/kg/min) up to seven days, in order to avoid disruption of the surgical pubis synostosis and abdominal wall closure. The patients were extubated when pain control and sedation were adequately balanced to keep the voluntary motion to a minimum. Once extubated the infants were transferred to an intermediate care ward with continuous monitoring of cardio-respiratory parameters. For one further week, patients' movements were limited as much as possible with continuous administration of midazolam 4 mcg/kg/min. Post-operative pain was managed with continuous epidural infusion of ropivacaine 0.125% (0.1 - 0.2 mg/kg/h) that was left in situ for a maximum of three weeks.

The pain was measured by the appropriate CRIES scale (Crying, Requires increased O_2 administration, Increased vital signs, Expression, Sleepiness) [7] and FLAAC scale while intubated. Paracetamol (10 mg/kg^{-1} e.v. max tid) was added if pain score recorded was high. Pain control was considered effective when no additional subministration of medication was needed. All the patients received preoperative antibiotics that were continued intravenously for two weeks.

The following aspects of the post-operative care were recorded regularly: time to pass first stools, time to full enteral feeding, catheter-related complications, duration of mechanical ventilation and NICU stay. Results are expressed as medians and percentage.

Results

In 24 months 11 consecutive patients (8 male and 3 female) underwent CPRE in our Department. Eight patients had isolated bladder exstrophy; one female patient had a cloacal exstrophy. Two male patients had associated anomalies, one a congenital diaphragmatic hernia and one an omphalocele. This one was premature (36 weeks). All these patients were out-born with a prenatal diagnosis.

Post-conceptual age at birth was 39 weeks (range 36 - 41), age and weight at surgery were 48 days (range 8 - 60) and 4462 gr (range gr.2250 - 6050), respectively. The epidural catheter was kept in place for 13 days (range 1 - 19). Two patients had accidental dislocation of the epidural catheter, the first 11 hours and the second 36 hours post-operatively. No child developed signs of local inflammation at the epidural insertion site and none developed complications from this procedure.

Duration of mechanical ventilation was 9 days (range 3 - 17). All the children were breathing spontaneously before the surgery except for the premature patient. Two children remained intubated longer: the first one developed an infection 48 hours after surgery, the second one was born premature with an omphalocele.

Overall extra doses of paracetamol were required in 7 patients (63.3% of the patients). The two patients who had early catheter dislodgement required intravenous fentanyl administration, up to 2 mcg/kg/h, as well as more paracetamol administration in the post-extubation period compared to the ones who had ropivacaine in infusion for a longer period. Time to pass first stools was 5.2 days (range 2 - 21) days. In particular, in the two patients with catheter dislocation it was 15 and 21 days, respectively. Time to full feed was longer in these two patients, 25 and 45 days, compared with the result in the whole population,16 days (range 7 - 46). Length of hospital stay was 48 days (range 19 - 120).

Discussion

Complete primary repair of bladder exstrophy is a complex surgical procedure described in the early 1990s by Grady and Mitchell [8]. Experience with this condition, a multi-disciplinary team and an appropriate and effective postoperative immobilization of the patient are essential for good result.

As emphasized by different authors [9-12], the key point for success in CPRE is the excellent post-operative care with pain control and appropriate patient and pelvic care. In particular the CPRE procedure combines bladder closure, bladder neck reconstruction, epispadias repair as a single stage approach. Osteotomies and the difficult sequences of the surgery makes CPRE more painful not only than staged approach but also than other major surgery in newborns.

Although a large number of papers have been published over the years regarding bladder exstrophy management, only a few have addressed the question of analgesia in this complex surgery. The first paper was the one from Messeri in 1995, who reported the use of an epidural technique for postoperative analgesia. In this paper the Author refers to a multistaged approach without pelvic osteotomy [13]. Aram L, in his large series of 25 patients, described the management of seven newborn/infants operated on for bladder exstrophy, in which tunneled epidural catheters were used for analgesia. The tunneled epidural catheter is described as safe and effective and in these cases the catheter insertion was made by a caudal approach; medications used where fentanyl associated with lidocaine while in one case bupivacaine and hydromorphone. In this paper a substantial reduction in pain and in the need for supplemental opioids was demonstrated but there is no description of the surgical technique used to repair the bladder exstrophy, furthermore all those patients were older than the ones in our group [14]. Kost-Byerly in 2008 reported [5] their experience with a series of 23 newborn/infants under-

going staged surgery for bladder exstrophy under a combined epidural and general anesthetic technique. In these cases all the children had a tunneled caudal epidural for bupivacaine 0.25% and epinephrine 1:200.000 in infusion; postoperatively the patients were treated with lidocaine 0.1% and they received acetaminophen and diazepam on a needed basis. In this paper the authors describe the efficacy of epidural analgesia in their newborns patients with no complications; the catheters were maintained for a maximum of 3 weeks. A horizontal and pelvic osteotomy was performed only in two of these newborn babies. The same group later on published a larger series of 65 newborns undergoing staged repair of bladder exstrophy [6]. In this population 93.8% patients had a tunneled epidural or tunneled caudal catheter but only in 29.2% of these neonates an osteotomy was performed. As with the previously mentioned report the effectiveness of pain control and need of supplemental analgesics is not described in detail, which could limit the interpretation of effectiveness of the regional analgesia in these cases. Massonyi., *et al*. gave a general description of the surgical technique and arising problem; again, only patients with staged approach were comprised in this paper [15].

More recently post-operative management of bladder exstrophy was compared in two groups of patients: those managed in the surgical ward using epidural analgesia and those undergoing muscle paralysis and ventilation in ICU. All the patient population consisted of 74 babies operated on by staged approach [16].

Differently from the above reports, all patients in our series underwent a one-stage procedure which included anterior oblique osteotomy that needs a far great operation time than the staged one. This, in turn, may lead to a greater surgical stress, induced not only by anterior osteotomy but also by the radical dissection of the bladder neck, which is crucial for a correct repositioning into the pelvis. In order to control this pain we went on with epidural administration of ropivacaine for three weeks when possible and e.v. paracetamol was added according to the registered pain score. To our knowledge none of the previous description on CPRE surgery focused on perioperative analgesic management even though, as pointed out by Grady [10] adequate postoperative pain management is crucial for successful repair of bladder exstrophy, and this is particularly true in the case of single-stage CPRE.

Our most significant result is that in our series intense pain produced by this complex surgery was effectively controlled by continuous administration of epidural ropivacaine, combined with mild systemic analgesic. This combination allowed us to control pain and prevented the use of oral and e.v. narcotics. We also reached the goal to keep infants content and immobilized in the Spica cast allowing minimum spontaneous mobility without keeping them paralyzed. The second achievement was the low frequency of complications: an effective stabilization of the epidural catheter prevented its accidental dislocation. Our technique actually provides a sandwich type mechanism with the catheter contained between two steril-strips that reach the shoulder contralateral to CVC insertion site**.** Nevertheless two of our patients had the catheter dislodged. This fact could be explained by limited nursing experience in handling this catheter, especially at the beginning of our experience. Over the years the management of the catheter has progressively reached a standardized management in our hospital. As previously mentioned, we used a subcutaneous tunneled epidural catheter in order to decrease the chance of its accidental dislodgment and to provide an additional protection against colonization. The bacterial colonization of an epidural catheter normally occurs after 48-72 hours and the tunneling decreases the risk of infection [17]. Among our cases, there was no local or systemic catheter-related infection.

A further advantage of using an epidural catheter combined very low dosage of non-opioid systemic analgesia is the reduced need of systemic opioids and muscle blockade, thereby avoiding their well-known side effects. Now the epidural analgesia with its block of the sensitive afferents and therefore of the pain, allows the small patient to remain immobile, without using a prolonged muscle blockade and an excessive use of opioid, morphine in particular that could cause apneas, difficulty in extubation and bowel motility reduction. This kind of analgesia helps us to reduce the admission time in ICU, to get a faster return to feeding and ultimately a shorter hospital stay. This result is consistent with our previous results on patients undergoing thoracotomy and in patients with ARM. We confirmed the safety and effectiveness of regional block and we described a reduced intensity of postoperative care in these patients than in the one undergoing

systemic analgesia [18,19]. In our experience with CPRE, ropivacaine 0.125% in continuous infusion through the catheter even over three weeks did not produce appreciable detrimental effects. The concentration of ropivacaine we used is lower than the one used by Sabin Kost-Byerly [5], but even with this dosage we reached an effective pain control without side effects [20]. Our case series supports the idea that combined epidural and non-opioid systemic analgesia is safe and effective also in infants undergoing CPRE, a painful surgery in which post-operative pain control and immobilization are crucial to the short and long-term outcomes of the procedure. However, a prospective randomized study would be necessary to compare different concentrations of ropivacaine in reaching an ever more accurate pain control and a further reduction of post-operative and hospital stay thus reducing risk of toxicity.

Conclusion

Even in the complex and painful surgical setting of the neonatal CPRE, combined epidural and non-opioid systemic analgesia may prove safe and effective for the entire process of perioperative pain management. Such techniques should be carried out by a dedicated anesthesiologist within an "exstrophy team "which should be created in each referral center designated to deal with such complex malformation. A multicenter study is recommended to compare such strategies with those adopted with alternative surgical techniques.

Bibliography

1. Nelson C P., *et al*. "Contemporary epidemiology of bladder extrophy in the United States". *The Journal of Urology* 173 (2005): 1728.

2. Grady RW., *et al*. "Complete primary closure of bladder exstrophy. Epispadias and bladder exstrophy repair". *Urologic Clinics of North America* 26.1 (1999): 95-109.

3. Husmann DA. "Surgery insight: advantages and pitfalls of surgical technique for the correction of the bladder exstrophy". *Nature Clinical Practice Urology* 3.2 (2006): 95-100.

4. Baradaran N., *et al*. "Delay primary closure of bladder exstrophy: immediate postoperative management leading to successfull outcomes". *Urology* (2012): 415-419.

5. Kost Byerly S., *et al*. "Perioperative anesthetic and analgesic management of newborn bladder exstrophy repair". *The Journal of Pediatric Urology* 4.4 (2008): 280-285.

6. Stec AA., *et al*. "The modern staged repair of classic bladder exstrophy. A detailed postoperative management strategy for primary bladder closure". *The Journal of Pediatric Urology* 8 (2012): 549-555.

7. Krechel SW and Bildner J. "CRIES: a new neonatal postoperative pain measurement score. Initial testing of validity and reliability". *Paediatric Anaesthesia* 5.1 (1995): 53-61.

8. Grady RW and Mitchel ME. "Complete primary repair of exstrophy". *The Journal of Urology* 162.4 (1999): 1415-1420.

9. Kozlowski Lori J. "The acute pain service nurse practitioner: a case study in the postoperative care of the child with bladder exstrophy". *Journal of Pediatric Health Care* 22.6 (2008): 351-359.

10. Husmann DA., *et al*. "Closure of the extrophic bladder: an evaluation of the factors leading to its success and its important on urinary continence". *The Journal of Urology* 142.2-2 (1989): 522-524.

11. Meldrum KK., *et al*. "Pelvic and extremity immobilization after bladder exstrophy closure: complications and impact on success". *Urology* 62.6 (2003): 1109-1113.

12. Mitchell ME. "Bladder exstrophy repair: complete primary repair of exstrophy". *Urology* 65.1 (2005): 5-8.

13. Messeri A., *et al*. "Continuous epidural block for pain control in bladder exstrophy: report of a case and description of technique". *Paediatric Anaesthesia* 5.4 (1995): 229-232.

14. Aram L., *et al*. "Tunneled epidural catheters for prolonged analgesia in pediatric patients". *Anesthesia and Analgesia* 92.6 (2001): 1432-1438.

15. Massanyi EZ., *et al*. "Perioperative management of classic bladder exstrophy". *Research and Reports in Urology* 5 (2013): 67-75.

16. Mushtaq I., *et al*. "Primary bladder exstrophy closure in neonates: challenging the traditions". *The Journal of Urology* 191.1 (2014): 193-197.

17. Kost-Byerly S., *et al*. "Bacterial colonization and infection rate of continuous epidural catheters in children". *Anesthesia and Analgesia* 86.4 (1998): 712-716.

18. Di Pede A., *et al*. "Comparison of regional vs. systemic analgesia for post-thoracotomy care in infants". *Paediatric Anaesthesia 24*.6 (2014): 569-573.

19. P Bozza., *et al*. "Stress and ano-colorectal surgery in newborn/infant: role of anesthesia". *Pediatric Surgery International* 28 (2012): 821-824.

20. Bosenberg AT., *et al*. "Pharmacokinetics and efficacy of ropivacaina for continuous epidural infusion in neonates and infants". *Paediatric Anaesthesia* 15.9 (2005): 739-749.

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