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ORIGINAL ARTICLE

Intrathecal baclofen therapy for treatment of spasticity in infants and small children under 6 years of age

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Abstract

Purpose The aim of this study is to prove the efficacy and safety of intrathecal baclofen therapy in infants and children below 6 years of age by retrospective analysis of our pediatric cohort of 135 primary pump implantations.

Methods Between 2007 and 2018, 17 patients with pump implantations were below 6 years of age. Data were acquired retrospectively with a follow-up of 12 months to 11 years regarding complications.

Results The youngest infant was 11 months at implantation with a bodyweight of 6, 4 kg, and 63 cm length. Surgical complications were comparable to published literature and mainly involved the catheter (2 catheter dislocations and 1 catheter transection) and one pump infection resulting in 4 revision surgeries in 3 patients. One baclofen-related apnea during titration and an overdose after refill were treated conservatively. Using a subfascial implantation technique, we observed neither skin ulceration nor pump infection since 2007. In a growing child, catheter slides are common and related to growth, scoliosis, spine surgery, and surgical failure.

Conclusion Intrathecal baclofen therapy in infants and small children is as safe and effective as published for older pediatric patients; therefore, intrathecal baclofen can be considered in all infants as long as an 8-cm incision fits into the triangle of the anterior superior iliac spine, costal margin of the 10th rib, and navel. We suggest the utilization of subfascial surgical technique for implantation pump and catheter. Titration of intrathecal baclofen should be performed slowly to avoid bradycardia in infants. This is a retrospective study (level of evidence 4).

Keywords Intrathecal baclofen therapy · Baclofen pump implantation · Infants · Spasticity · Cerebral palsy · Dystonia · Children · Pediatrics

Introduction

Baclofen was first introduced as an anticonvulsive medication in 1962. It was abandoned as such shortly after due to adverse effects. However, the effect of baclofen on hypertonic muscle tone was clearly evaluated, and baclofen has been used ever since for the oral treatment of spasticity. Because of the blood-brain barrier, high doses of oral baclofen are needed to induce hypotonic effects, and this often results in side effects like nausea, sedation, and weakness [1]. The effect of Baclofen on the neural cells is not completely understood. It is known that baclofen interacts with the GABA-B receptors in the spinal cord. Abe et al. recently reported some evidence for pre- and postsynaptic effects of baclofen [2].

In severe spasticity, the side effects of higher doses of oral baclofen sometimes cause somnolence and even apnea. Intrathecal baclofen (ITB) therapy was first administered in 1984, and it was clearly shown that the application of baclofen directly into the intrathecal space achieved higher efficacy and lesser side effects due to direct site administration [1]. Unfortunately, it seems that the distribution range of intrathecal baclofen from the catheter tip in the cerebrospinal fluid is limited at least in pigs; in humans, it is not exactly known [3].

The first report of ITB therapy usage in pediatric patients mainly dealing with cerebral palsy was published in 1991 [4]. Although many publications thereafter covered all sorts of aspects such as surgical complications, pump infection, over

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dosage, pump failure, long-term dosing, trouble shooting, and others, most of the publications reported results in adult patients only, while few reports are available for pediatric cases [5–8]. Reports about ITB therapy in infants and small children under 6 years are rare, with only a few cases ranging from 5 to 6 years out of their cohorts, respectively [9–11]. A recent review published in 2018 quotes the lack of evidence for ITB therapy in pediatric cases [12]. We are reporting our results in infants and small children below 6 years of age, because we are convinced of the necessity to treat severely spastic infants with ITB therapy early instead postponing the therapy and forfeit crucial years of effective treatment to reduce painful spasticity, orthopedic complications like muscle tone–related fractures, contractures, and so forth.

Methods

We performed a retrospective analysis of 17 patients in whom the pump was implanted before 6 years of age out of our total collective of 135 pediatric cases of primary pump implantations for spasticity treatment between 2007 and 2018. The follow-up ranged from 12 months to 11 years. Surgical revisions and other unexpected events were recorded next to general aspects like diagnose, weight, length, and age at implantation. Daily dose at the last refill and other details like catheter tip positioning were recorded.

Implants, surgical technique, and follow-up All implanted pumps (SynchroMed II, 20 ml volume) were products by Medtronic (Medtronic GmbH Germany, Earl-Bakken-Platz, 40,670 Meerbusch, Germany). These pumps are manufactured with a thickness of 19, 5 mm, a diameter of 87, 5 mm, a volume of 20 ml, and a tissue displacement of 91 cm^3. They require an area of 8, 5–9-cm-diameter soft tissue for implantation, and the minimum incision requires 8 cm. In 2007, the 20-ml pumps were implanted subcutaneously; since 2008, the subfascial technique was utilized [13]. The implanted catheter system used from 2008 to 2011 was "Indura 1P" (model 8709) by Medtronic, which was discontinued from the market in 2011. This catheter was a single piece tube with good visibility in X-ray studies and fluoroscopy due to integrated barium. From 2011 on, we used "Ascenda" (model 8780 or 8781) by Medtronic, which is a two-piece system with reinforced tube walls to diminish the occurrence of tears in the catheter. Visibility in X-ray studies is somewhat poorer due to the lack of barium in the tube material, therefore demanding diagnostic catheter studies with contrast-enhancing test fluids to find or rule out catheter transections or disconnections.

The following details regarding surgical technique and follow-up are the authors' preferred regimen, as there is no technical defined standard, and implantation technique differs between institutions. The incision is placed preferably in the right flank which we call the "pump triangle," because many patients have gastrostomies on the left side. Nevertheless, left side implantation remains sometimes necessary because of severe scoliosis or coexisting ventriculoperitoneal shunts. The boundaries of the "pump triangle" consist of the 10th rib lower margin cranially, the navel medially, and the anterior superior iliac spine caudally. The catheters were implanted subcutaneously including a fascial anchoring system at the level of the lumbar spine from 2007 to 2011 and afterwards with placement underneath the thoraco-lumbar fascia. Vancomycin was placed at the implantation site since 2008. We ordered 3 days post-operative non-elevated patient positioning to reduce the risk of cerebrospinal fluid fistulas. All patients remained between 7 and 10 days in the hospital to carefully titrate the baclofen after pump implantation until a satisfactory tone reduction was achieved. Catheter location was documented by X-ray after mobilization. Refills were conducted in an ambulatory setting in our hospital and performed by the authors. We did not perform regular follow-up X-ray studies regarding the catheter tip position; therefore, catheter slides were not detected in all patients.

Results

The details of patient data are shown in Table 1. All suffered from bilateral spastic cerebral palsy of various etiologies, and all were level 5 according to the Gross Motor Function Classification Scale (GMFCS).

Three patients had to undergo revision surgeries within the first month after implantation. One pump had to be explanted due to pump infection after subcutaneous implantation within the first year of our program. The other revision surgeries were due to catheter events, two cases of catheter dislocations and one case of catheter transection due to opisthotonus. Of the catheter events that lead to revision surgery, two occurred in the very same dystonic patient (case #13 on Table 1) consecutively. Two more complications recorded were treated medically, an overdose during titration phase in the first week after implantation and an overdose at the first refill (pump refill with 2000 μg/ml instead of 500 μg/ml baclofen solution). Overdoses were treated by prompt dose reduction programming in the first and emergency refill with lower baclofen concentration and removal of higher concentration baclofen out of the catheter system, followed by bolus in appropriate concentration, in the second case. In the entire follow-up, we saw neither secondary pump infection nor cerebrospinal fluid fistula in this group of infants and small children, unlike others [14].

The youngest and smallest patient (case #17 in Table 1, Fig. 1) with 6, 4 kg, and 63-cm length at implantation had no complication at all and underwent uneventful implantation at 11 months of age. Nevertheless, we indicated ITB therapy already at 6 months of age in this battered child but considered

Table 1 Patients overview. Age in months, bodyweight in kilogram, length in centimeters; *FU*, follow up in months; catheter tip position regarding spinal vertebra; *C*, cervical; *T*, thoracic, in brackets the tip position in later FU if X-ray was performed, dose in μg/d at latest refill

Patient	Age at implantation	Bodyweight at implantation	Length at implantation	FU	Diagnose	Complication	Consequence	Catheter tip	Dose
1	56	13.5	87	11	Perinatal asphyxia	Apnea during titration	Daily dose reduction	C4	95
2	47	13.6	91	14	Battered child	None	–	C1	350
3	25	12.5	86	17	Battered child	Catheter dislocation	Revision	C3	400
4	64	11.7	108	87 (2nd pump)	Hypoxia drowning	Overdose at refill	Emergency refill	T1 (T5)	360
5	70	16	115	26	Perinatal asphyxia	None	–	T4 (T8) after spine surgery)	350
6	37	13	90	died	Battered child	None	–	C7	250
7	66	12.3	110	died	Prematurity dystrophic child	None	–	T3	
8	59	19	87	135 (2nd pump)	Hypoxia drowning	None	–	T6	550
9	41	17.4	97	60	M. Canavan	None	–	T6 (T8 after spine surgery)	600
10	25	8.5	81	145 (2nd pump)	Posttraumatic	None	–	T4	350
11	17	9	77	died	Hypoxia aspiration	Pump infection	Explantation	C7	250
12	65	21	103	53	Hypoxia electric shock	None	–	T4 (T7)	520
13	55	13.2	97	42	Perinatal asphyxia, dystonia	Catheter dislocation, catheter transsection	2 revisions	T2 (T4)	1200
14	50	10.2	89	126 (2nd pump)	Prematurity	None	–	T6 (T8)	800
15	49	16	105	died	Hypoxia reanimation	None	–	C4	450
16	50	15.6	99	died	Hypoxia strangulation	None	–	C3	700
17	11	6.4	63	33	Battered child	None	–	C7	500

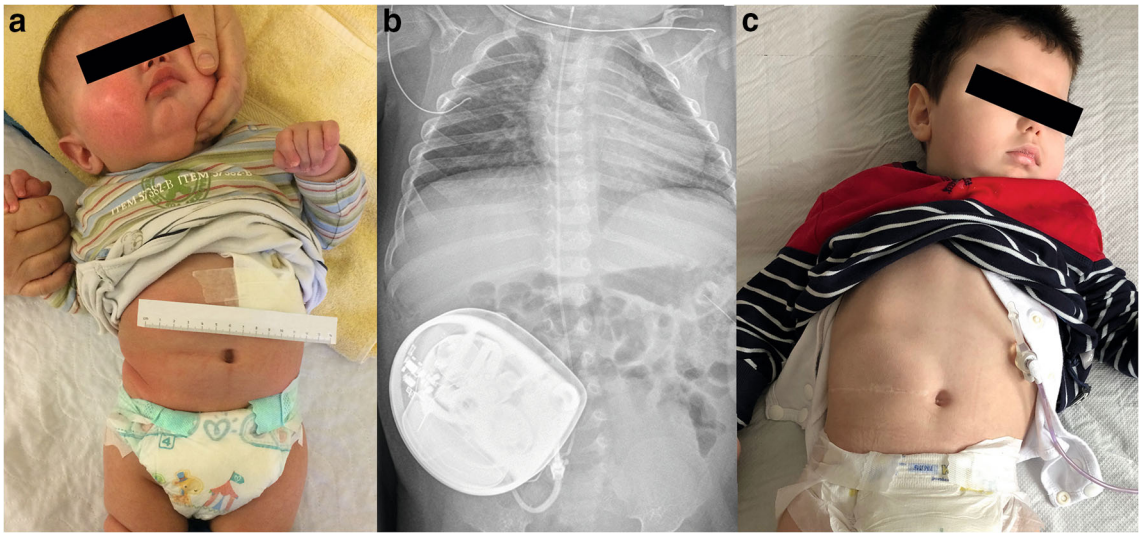

Fig. 1 Smallest infant implanted at 11 months of age, 6, 4-kg body weight, 63-cm length, using radiopaque Indura 1P catheter by Medtronic. **a** At 6 months, although already indicated for ITB therapy, there is not enough soft tissue space for implantation in the "pump triangle". **b** X-ray post-surgery at 11 months. C: 4 years post-surgery

his "pump triangle" to be too small to implant the 20-ml pump with respect to the diameter needed. In the meantime, he suffered two muscle tone–related femoral fractures at 7 and 8 months of age, before he reached the appropriate body size for pump implantation. Since implantation, there were no more tone-related fractures in this child.

Three pumps have been already exchanged due to expected battery expiry. We did not see any pump failures due to motor corrosion or other technical problems. Five children died years after pump implantation, each suffering from severe forms of epilepsy like Lennox-Gastaut or West syndrome; therefore, the causes of deaths were not related to pump implantation, but pneumonia and fatal fit in this severely handicapped patient group. The daily dose of baclofen was administered in a simple continuous fashion in all reported patients and we did not record any sudden loss of efficacy as reported by Saulino et al. [15].

In most but not all patients who underwent X-ray controls for various reasons, we saw a slide of catheter tip over the years. Significant sliding of several spinal segments was recorded after spine surgery with the correction of deformity by dorsal fusion and due to surgical failure shortly after implantation (Fig. 2). Sliding due to growth or utilization of expandable devices for scoliosis treatment like Vertical Expandable Prosthetic Titanium Ribs (VEPTR) or Magnetically Controlled Growing Rods (MCGR) mostly involved only a few spinal segments over years (Fig. 3).

Discussion

The patient group presented distributes typical aspects of patients suffering from bilateral spastic cerebral palsy due to various reasons with level 5 on GMFCS. Therefore, it constitutes a typical patient group in whom ITB therapy is often indicated. Many of the patients were diagnosed with a mixed tone disorder (spasticity and dystonia) but only one patient presented an almost pure secondary dystonia. In this patient, the dose titration phase was considerably longer and even with a transient dose of 2000 μg baclofen, tone reduction was less satisfactory. Young age and low body weight are certainly not a contraindication for ITB therapy. The smallest patient in our cohort being successfully implanted without any complications at 11 months of age with a bodyweight of 6, 4 kg, and a length of 63 cm (Fig. 1) responded very well to ITB therapy, although we had to wait for about 5 months after indication of ITB therapy for him to grow enough to reach the required 8-cm diameter in the "pump triangle" of the right flank. Despite oral baclofen therapy, we observed two muscle tone–related femoral fractures until we could implant the pump in this particular child. In general, age and bodyweight are not principal limitations for the feasibility of ITB therapy in infants, but the diameter of the abdomen. Once patients have reached a body size comparable with an 8-cm incision in the "pump triangle," implantation is possible. Smaller pumps than 20-ml volume are available, but keep in mind that smaller volumes go hand in hand with a higher frequency of refills.

The single pump infection in our patient group occurred after subcutaneous implantation in 2007, leading to a change of surgical strategy at our institution. After this event, all pumps were implanted in subfascial technique and vancomycin powder was administered at the pump implantation site. Since changing the surgical technique to subfascial implantation and administering vancomycin, we did not see any other pump infection, neither in the group of infants and small children reported nor in the other 119 pediatric cases, unlike

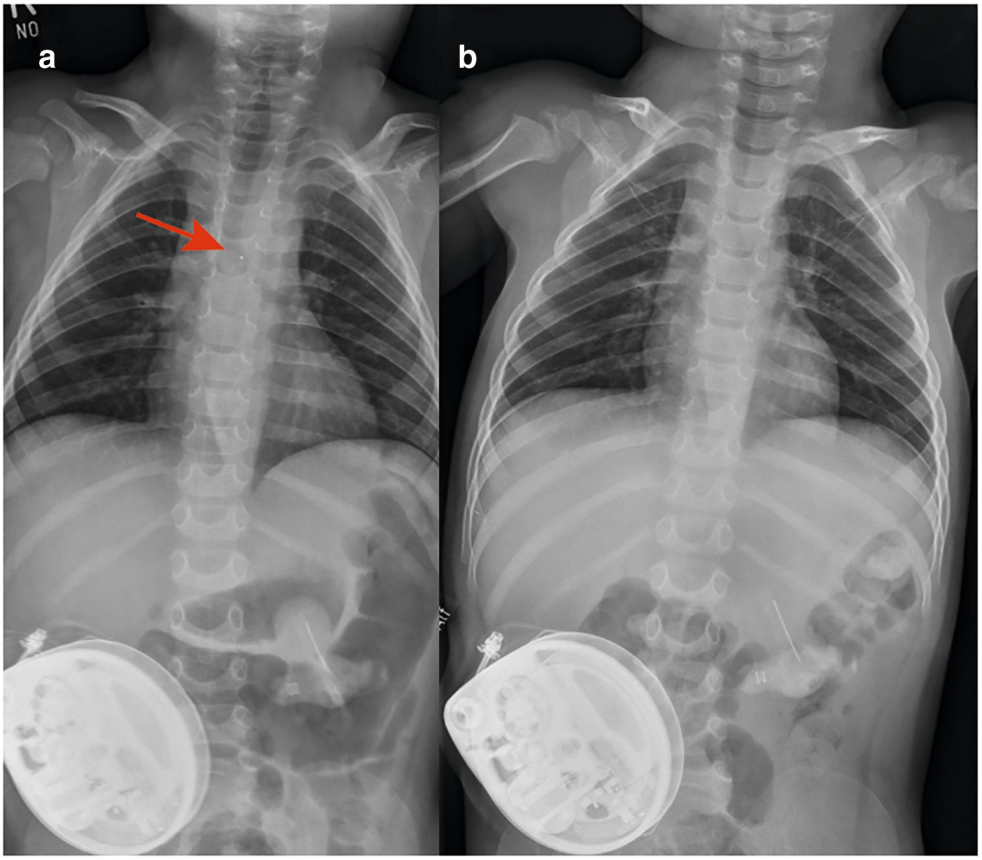

Fig. 2 Catheter slide due to surgical failure using a radiolucent Ascenda catheter by Medtronic. **a** X-ray at 3rd-day post-surgery, notice the small radiopaque mark at the tip of the catheter. Although catheter tip was located at T1 during implantation, it shows already significant sliding to T5. B: Few days later, the patient developed baclofen withdrawal, and the catheter tip is no longer visible on X-ray. The entire catheter lay rolled up behind the pump at revision

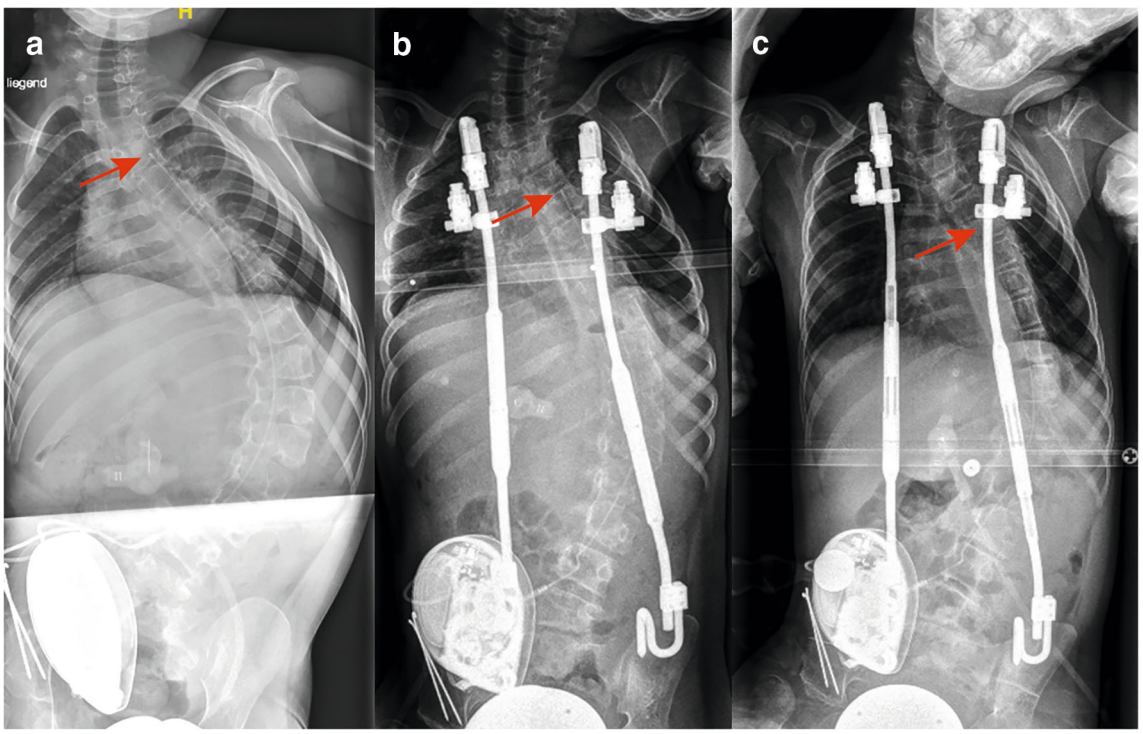

Fig. 3 Catheter slide due to spine surgery and elongation of magnetically elongated growing rods in neuromuscular scoliosis. **a** Scoliosis and tip position at T3. **b** Tip position after implantation of growing rods. **c** Tip position after frequent elongation of the growing rods

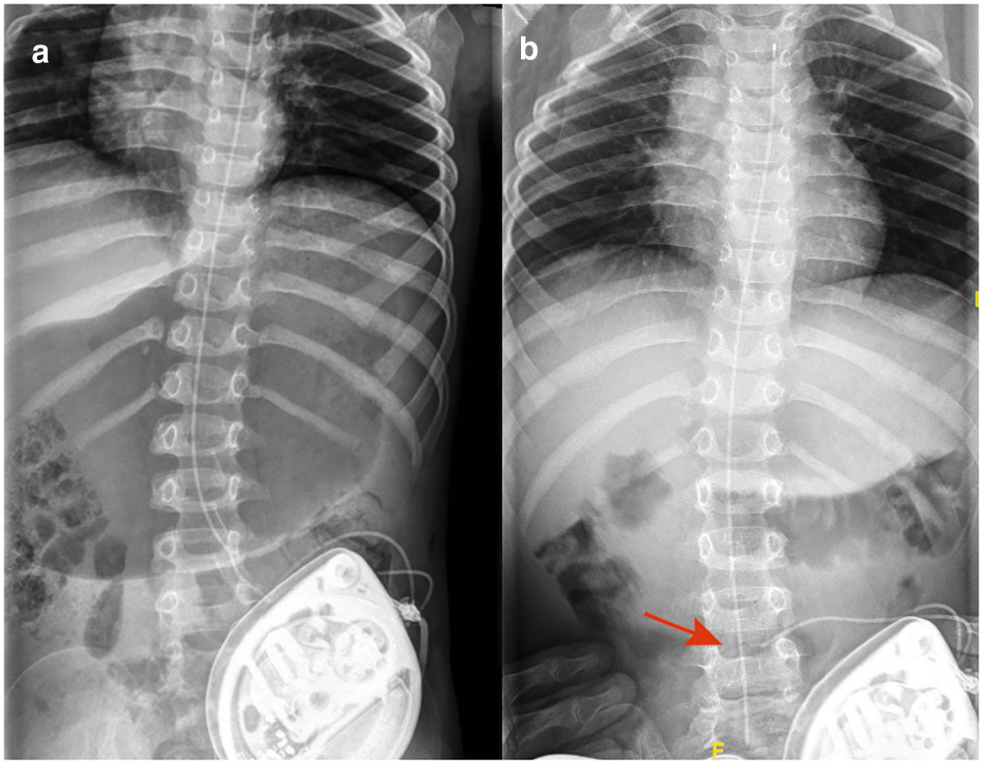

Fig. 4 Catheter transection due to dystonia (radiopaque catheter Indura 1P). **a** X-ray after implantation. **b** Baclofen withdrawal on day 6 of titration phase after dystonic opisthotonus, which led to transection of the catheter

others who reported up to 9, 8% infections in pediatric cases [6, 16]. Nevertheless, the use of vancomycin at the implantation site is the authors' preference, as reports are published which do not support the efficacy of onsite vancomycin, but again, we had no single pump infection since 2007 [17].

All the reported 17 infants and small children receive the baclofen in a simple continuous fashion, and they were titrated over the years according to their needs during the refill sessions, showing mostly an increasing dose over several months after implantation as reported by Gilmartin et al. [18]. All refill sessions were performed by authors; therefore, there was a close relationship between patients, parents, caregivers, and treating doctors.

Catheter events leading to revision surgery are still occurring but we see them more seldom, and we recommend to implanting them in subfascial technique as well because we believe that there is more resistance for the catheter to slide if implanted in subfascial technique. In subcutaneous implantation technique, we have seen dislocations despite the anchoring system. One case of transection occurred in a dystonic child in the severe opisthotonic state while still in early titration phase and the catheter was cut in between vertebral arches (Fig. 4). At revision, an interlaminar fenestration was performed at the catheter entry zone to avoid future catheter transections in this particular child. Overall, 23% of cases required revision surgery, an incidence of complications similar to those reported by others [10, 19].

Catheter tip placement should be considered in every case according to the spasticity and expected growth. Due to the assumed rather limited range of baclofen distribution in the cerebrospinal fluid away from the catheter tip, there seems to be a significant loss of concentration just a few centimeters away from the catheter tip as reported by Flack and Bernards [3]. Therefore, especially in quadriplegic patients in whom reduction of spasticity also at the upper extremities is an important goal, we recommend placing the catheter tip in the cervical region, like others [8]. Due to expected growth, there might be a loss of effect regarding the upper extremities following catheter slide over the years and even the need to exchange the catheter in the same session as pump exchange surgery due to battery depletion, which is normally due between 6 and 7 years after implantation depending on the performance of the pump.

Conclusion

ITB in infants and small children is as safe and effective as reported for elder pediatric cases and adults in the literature. We have successfully implanted a pump in an 11 months old infant with 6, 4-kg bodyweight, and 63-cm length once this patient reached the appropriate size to place an 8-cm incision in the "pump triangle" of the right flank. Subfascial implantation technique of the entire system seems to reduce infection and dislocation. Dose titration should be slowly and carefully

to avoid overdosing, which can lead to bradycardia and apnea. As this is a retrospective analysis with a limited number of patients, the level of evidence is 4.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Woolf SM, Baum CR (2017) Baclofen pumps: uses and complications. Pediatr Emerg Care 33(4):271–275
2. Abe T, Taniguchi W, Nishio N, Nakatsuka T, Yoshida M, Yamada H (2019) Molecular mechanisms of the antispasticity effects of baclofen on spinal ventral horn neurons. Neuroreport 30(1):19–25. https://doi.org/10.1097/WNR.0000000000001155
3. Flack SH, Bernards CM (2010) Cerebrospinal fluid and spinal cord distribution of hyperbaric bupivacaine and baclofen during slow intrathecal infusion in pigs. Anesthesiology 112(1):165–173
4. Albright AL, Cervi A, Singletary J (1991) Intrathecal baclofen therapy for spasticity in cerebral plasy. JAMA 265:1418–1422
5. Dickey MP, Rice M, Kinnett DG, Lambert R, Donauer S, Gerber MA, Staat MA (2013) Infectious complications of intrathecal baclofen pump devices in a pediatric population. Pediatr Infect Dis J 32(7):715–722. https://doi.org/10.1097/INF.0b013e318287f02a
6. Spader HS, Bollo RJ, Bowers CA, Riva-Cambrin J (2016) Risk factors for baclofen pump infection in children: a multivariate analysis. J Neurosurg Pediatr 17(6):756–762. https://doi.org/10.3171/2015.11.PEDS15421
7. Stewart K, Hutana G, Kentish M (2017) Intrathecal baclofen therapy in paediatrics: a study protocol for an Australian multicentre, 10-year prospective audit. BMJ Open 7(6):e015863. https://doi.org/10.1136/bmjopen-2017-015863
8. Skalsky AJ, Fournier CM (2015) Intrathecal baclofen bolus dosing and catheter tip placement in pediatric tone management. Phys Med Rehabil Clin N Am 26(1):89–93. https://doi.org/10.1016/j.pmr.2014.09.011
9. Ammar A, Ughratdar I, Sivakumar G, Vloeberghs MH (2012) Intrathecal baclofen therapy–how we do it. J Neurosurg Pediatr 10(5):439–444
10. Motta F, Antonello CE (2014) Analysis of complications in 430 consecutive pediatric patients treated with intrathecal baclofen therapy: 14-year experience. J Neurosurg Pediatr 13(3):301–306. https://doi.org/10.3171/2013.11
11. Berman CM, Eppinger MA, Mazzola CA (2015) Understanding the reasons for delayed referral for intrathecal baclofen therapy in pediatric patients with severe spasticity. Childs Nerv Syst 31(3):405–413
12. Buizer AI, Martens BHM, Grandbois van Ravenhorst C, Schoonmade LJ, Becher JG, Vermeulen RJ (2019) Effect of continuous intrathecal baclofen therapy in children: a systematic review. Dev Med Child Neurol 61(2):128–134. https://doi.org/10.1111/dmcn.14005
13. Kopell BH, Sala D, Doyle WK, Feldman DS, Wisoff JH, Weiner HL (2001) Subfascial implantation of intrathecal baclofen pumps in children: technical note. Neurosurgery. 49(3):753–756 discussion 756-7
14. Chan DY, Chan SS, Chan EK, Ng AY, Ying AC, Li AC, Chiu CC, Cheung N, Mak WK, Sun DT, Zhu CX, Poon WS (2018) Blessing or burden? Long-term maintenance, complications and clinical outcome of intrathecal baclofen pumps. Surg Pract 22(3):105–110. https://doi.org/10.1111/1744-1633.12308
15. Saulino M, Anderson DJ, Doble J, Farid R, Gul F, Konrad P, Boster AL (2016) Best practices for intrathecal baclofen therapy: troubleshooting. Neuromodulation 19(6):632–641. https://doi.org/10.1111/ner.12467
16. Fjelstad AB, Hommelstad J, Sorteberg A (2009) Infections related to intrathecal baclofen therapy in children and adults: frequency and risk factors. J Neurosurg Pediatr 4(5):487–493. https://doi.org/10.3171/2009.6.PEDS0921
17. Ghobrial GM, Thakkar V, Singhal S, Oppenlander ME, Maulucci CM, Harrop JS, Jallo J, Prasad S, Saulino M, Sharan AD (2014) Efficacy of intraoperative vancomycin powder use in intrathecal baclofen pump implantation procedures: single institutional series in a high risk population. J Clin Neurosci 21(10):1786–1789. https://doi.org/10.1016/j.jocn.2014.04.007
18. Gilmartin R, Bruce D, Storrs BB, Abbott R, Krach L, Ward J, Bloom K, Brooks WH, Johnson DL, Madsen JR, McLaughlin JF, Nadell J (2000) Intrathecal baclofen for management of spastic cerebral palsy: multicenter trial. J Child Neurol 15(2):71–77
19. Pucks-Faes E, Hitzenberger G, Matzak H, Fava E, Verrienti G, Laimer I, Fritz J, Saltuari L (2018) Eleven years' experience with Intrathecal Baclofen - complications, risk factors. Brain Behav 8(5):e00965. https://doi.org/10.1002/brb3.965