Archives of Rehabilitation Research and Clinical Translation (2020) 2, 100049

ACRM AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Rehabilitation Research and Clinical Translation

Archives of Rehabilitation Research and Clinical Translation 2020;2:100049

Available online at www.sciencedirect.com

Original Research

Musculoskeletal Pain Outcomes Pre- and Post Intrathecal Baclofen Pump Implant in Children With Cerebral Palsy: A Prospective Cohort Study

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KEYWORDS
Cerebral palsy;
Musculoskeletal pain;
Pediatrics;
Rehabilitation

Abstract *Objective:* To characterize musculoskeletal pain intensity, duration, frequency, and interference with activities of daily living in children with cerebral palsy (CP) before and after intrathecal baclofen pump placement.
Design: Prospective cohort study.
Setting: Children's tertiary hospital.
Participants: Participants were children with CP (N = 32; 53% male; mean age, 9.9y; age range, 4-17y). The majority of participants had a CP diagnosis of quadriplegia (76%) and relied on wheeled mobility (91%).
Interventions: Assessments were completed pre- and post intrathecal baclofen pump implant.
Main Outcome Measures: Because of considerable patient heterogeneity, both pain measures (Brief Pain Inventory, Dalhousie Pain Interview) were completed by proxy (parent) report at the time of the procedure and approximately 6 months after intrathecal baclofen (ITB) pump placement.
Results: Prior to implant, 31% of participants were living with constant pain, which reduced to 6% post ITB implant ($P<.001$). Based on Wilcoxon signed rank tests, pain duration significantly decreased post ITB pump implant ($P<.01$).

List of abbreviations: BPI, Brief Pain Inventory; CP, cerebral palsy; DPI, Dalhousie Pain Interview; ICF, International Classification of Functioning, Disability and Health; ITB, intrathecal baclofen; MAS, Modified Ashworth Scale.

Supported by Eunice Kennedy Shriver NICHD (grant no. 73126) and the Gillette Children's Foundation.
Disclosures: none
Presented to the American Pain Society, May 17–20, 2017, Pittsburgh, PA.
Cite this article as: Arch Rehabil Res Clin Transl. 2020;2:100049.

https://doi.org/10.1016/j.arrct.2020.100049

Conclusions: This prospective analysis supports the anecdotal and retrospective evidence that musculoskeletal pain decreases in CP following ITB pump implant. The greatest effect appears to be on the duration of pain experience. Pain did not decrease for all individuals, and it would be worth further investigation to better understand the relation between patient characteristics and pain outcomes.

Cerebral palsy (CP) is the most common motor disability in childhood and is considered a group of disorders that affect movement and posture, causing limitations in activities attributed to nonprogressive disturbances to the immature brain.[1] Spasticity is common in CP, reported in approximately 70% of individuals, and is a condition characterized by velocity dependent increases in muscle resistance.[2] Spasticity can interfere with movement, daily care, speech, and gait.[1] Spasticity, depending on severity, can result in chronic musculoskeletal pain due to muscle strain and contracture that interferes with function and comfort.[3,4] In CP intrathecal baclofen (ITB), a muscle relaxant medication, is indicated for the treatment of spasticity.[5] ITB treatment goals can relate to function, comfort, ease of care provision, or the prevention or treatment of deformity.[6] Initial and subsequent reviews of ITB in children with CP and related neurologic conditions repeatedly reach the same conclusion, most notably in 2010 by the American Academy of Neurology's Practice Committee and in 2018 by the American Academy of Cerebral Palsy and Developmental Medicine, that the evidence grade is relatively low and there remains a need for prospective trials using validated and reliable outcome measures addressing all levels of the International Classification of Functioning, Disability and Health (ICF), including pain and comfort (ICF Body Function and Structure).

There are several related issues surrounding ITB and CP specific to pain outcomes. Pain can be difficult to assess among individuals with communicative, motor, and cognitive impairments associated with CP.[7,8] As mentioned, reviews spanning over 3 decades reach the candid conclusion that the scientific merit of the majority of studies investigating ITB is often limited, based primarily on retrospective chart reviews and clinical case series with evidence grades precluding robust causal inferences between ITB and treatment effects.[6] Although almost all studies report changes in tone, historically the evidence specific to pain outcomes in pediatric samples is typically anecdotal and almost entirely retrospective or data specific to patients with CP cannot be extrapolated.[6] Reports in which ITB use was evaluated in relation to improvements in function are decidedly mixed. Some report improvements in positioning, activities of daily living, sleep, and comfort while others do not.[9] The variability is problematic because it is preventing our ability to communicate with individuals and families with certainty about expected outcomes. Our scientific understanding of that variability is weak primarily because of inadequately designed studies that, for our purposes, have not included an in-depth examination of pain outcomes.[10]

The goal of the current study was to measure pain intensity, duration, and frequency in response to ITB in children with CP. We used a cohort study design and prospectively examined the within-group effects of ITB implant specific to musculoskeletal pain in a clinical sample of children and adolescents with CP. Our primary outcome was anchored to a pain scale designed for nonverbal individuals with developmental disabilities completed prospectively by proxy (parents) specific to multiple musculoskeletal pain dimensions (intensity, duration, frequency of pain episodes), with a secondary outcome specific to pain interference with activities of daily living. Our specific objective was to measure musculoskeletal pain pre- and post ITB pump implant. We hypothesized that relevant pain dimensions specific to intensity, frequency, and duration would decrease post implant.

Methods

Participants

Following IRB ethical approval and subsequent informed consent, a clinical convenience sample of 46 participants was formed through consecutive enrollment based on scheduled ITB pump implant surgery. Thirteen participants did not return for follow-up clinical care and were excluded from these analyses. One participant family did not speak English and therefore could not complete the questionnaires and was excluded from these analyses. The remaining sample included 32 participants with CP (mean age, 9.9±3.08y; range, 4-17y; 53% male).

Inclusion/exclusion

Children were identified as eligible for the study if they (1) had cerebral palsy and (2) were scheduled for initial intrathecal baclofen pump implant surgery. Children were excluded from the study if (1) their parent(s) or guardian(s) did not consent to the study,(2) they had compounded dosing (ie, opioid adjunctive to baclofen) through their pump, (3) they had comorbid psychiatric disorders (eg, major depression, routinely screened for clinically as part of the presurgical evaluation), or (4) they had a co-occurring chronic pain condition, such as juvenile

idiopathic arthritis (routinely screened for clinically as part of the presurgical evaluation). The type of CP was collected from the medical record; half of the sample had spastic CP, and half the sample had mixed tone CP (table 1). Mixed tone CP indicates symptoms of more than 1 type of tone classification are present (eg, spasticity and dystonia). Presence of dystonia was determined by clinician assessment of examination and historical information. The majority of participants had quadriplegia (76%), relied on wheeled mobility (91%; Gross Motor Function Classification System level IV-V), and were white (82%). The majority of participants were not taking pain medications on a regular basis (78%; see table 1 for full sample clinical characteristics). Participants were initially identified from the ITB surgical schedule, and criteria for inclusion were determined. Enrolled participants' clinical schedules were screened on a weekly basis to identify clinically indicated visits where follow-up data could be collected.

Table 1 Participant clinical information (N=32)

Demographic Information	Mean ± SD or n (%)
Age (y), mean ± SD	9.9±3.08
Age range (y)	4.35-17.25
Male, n (%)	17 (53.1)
Ethnicity, n (%)	
White	24 (75.0)
Black	4 (12.5)
Native American	2 (6.3)
Other	5 (15.6)
Multiple	3 (9.4)
CP topography, n (%)	
Quadriplegia	26 (81.3)
Diplegia	5 (15.6)
Hemiplegia	1 (3.1)
CP classification, n (%)	
Spastic	16 (50)
Mixed tone	6 (19)
Spastic mixed tone	4 (13)
Spastic and dystonic mixed tone	6 (19)
GMFCS level, n (%)	
I (ambulant without assistance)	0 (0)
II (ambulant without assistive devices, limitations outside the home)	1 (3.1)
III (ambulant with assistive devices, wheelchair required outside home)	2(6.3)
IV (nonambulatory, self-mobile in wheelchair with limitations)	4 (12.5)
V (nonambulatory, self-mobility very limited)	25 (78.1)
Cognitive impairment (n=31), n (%)	
None	3 (9.7)
Mild/moderate	18 (58.1)
Severe/profound	10 (32.3)
Pain medications pre-ITB, n (%)	
Acetaminophen	3 (9.4)
Ibuprofen	2 (6.2)
Gabapentin, ibuprofen, and acetaminophen	1 (3.1)
Acetaminophen or ibuprofen as needed	4 (12.5)
Pain medications post-ITB	
Acetaminophen	6 (18.8)
Ibuprofen	1 (3.1)
Acetaminophen & ibuprofen	3 (9.4)
Oxycodone	1 (3.1)
Acetaminophen or ibuprofen as needed	6 (18.8)

NOTE. Other ethnicities included Asian (n=1), Hispanic/Latino (n=1), African (n=1), Jamaican (n=1), and Somali (n=1); multiple ethnicities indicates the number of participants that identified as more than 1 ethnicity.
Abbreviation: GMFCS, Gross Motor Function Classification System.

Procedures

For all participants, pain (Brief Pain Inventory [BPI]; Dalhousie Pain Interview [DPI]) assessments were completed by parent report, which has become the accepted approach for individuals with compromised self-report skills because of motor, communicative, and/or intellectual impairment.[11,12] Parent-reported assessments were completed once before (day of surgery: time 1) and once approximately 6 months after ITB implant (mean, 5.61±3.29mo, range 1.30-16.90mo: time 2). Parents completed the pain measures (described below) at a pediatric tertiary care hospital on an iPad with the assistance of a researcher. Measures were completed during the child's surgery (time 1) and during a clinical appointment (time 2). Enrollment and initial data collection for time 1 occurred between October 2013 and February 2018. Follow-up data collection for time 2 occurred between March 2014 and July 2018. Participant clinical characteristics were available from chart review and preoperative evaluation.

Clinical outcome measures

Dalhousie Pain Interview

The DPI provided a measure of proxy-reported estimates of pain frequency, duration, and intensity.[12] The DPI consists of 10 items designed explicitly as an interview and/or survey script. Specific items are anchored to whether there has been pain in the past week (number of pain events [ie, frequency]), its general description, estimated duration, and estimated intensity. While all pain types were recorded, for the purposes of this study analyses were focused on musculoskeletal pain (in the same manner previously reported in Barney et al).[13] The DPI was used as an outcome measure in a prior study specific to pain in children with CP receiving botulinum toxin (Botox) injections for spasticity management.[14]

Brief Pain Inventory

The BPI provided a measure of pain interference (ie, the degree to which ongoing pain interfered with daily living).[11] The BPI is a 12-item, 11-point scale (0=did not interfere, 10=completely interfered). The items include general activity, mood, mobility, work school or chores, relationships with other people, sleep, enjoyment of life, self-care, recreational activities, and social activities. In our prior

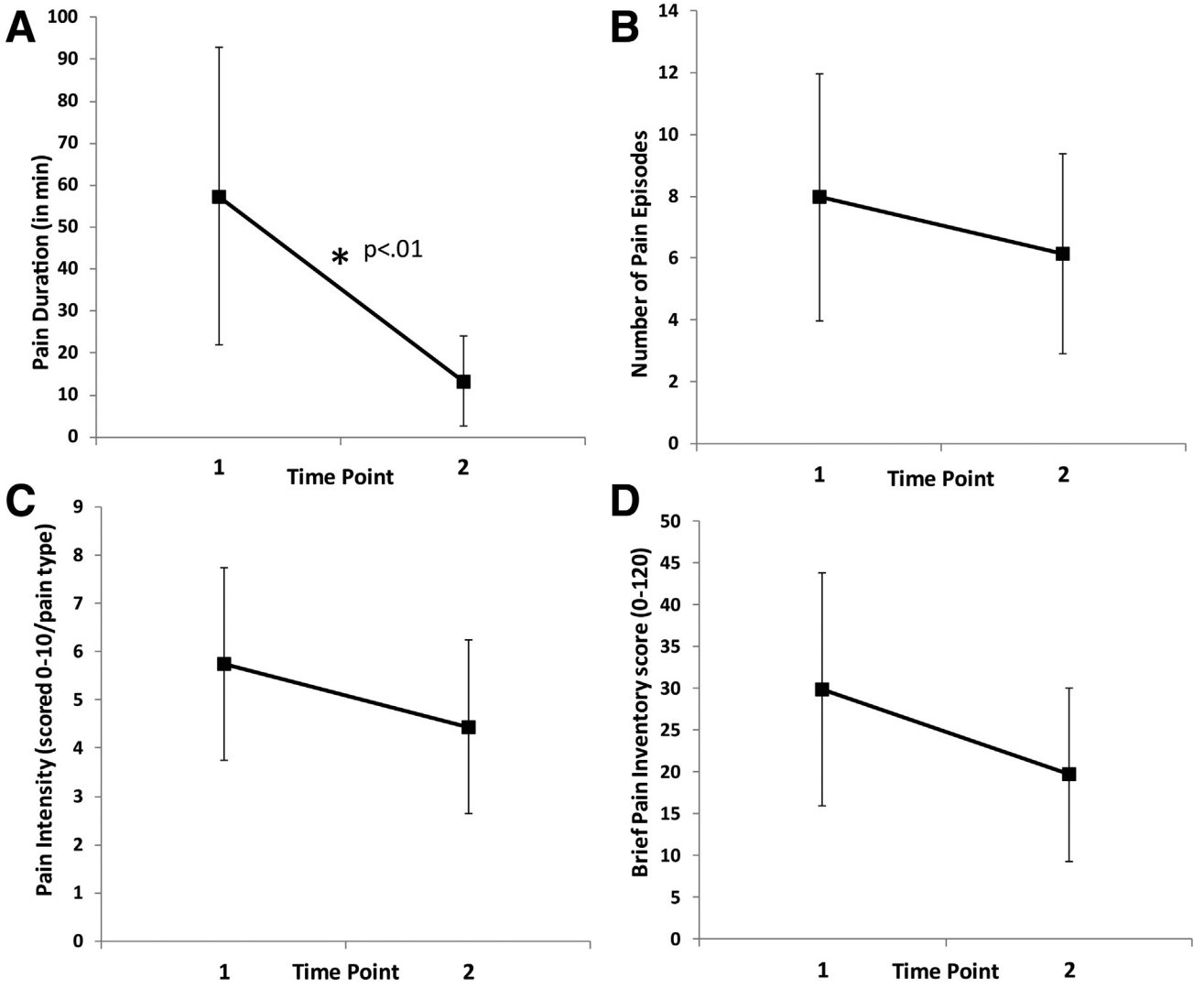

Fig 1 Mean pain scores collected pre-ITB pump implant (time point 1) and post ITB pump implant (time point 2). Scores reflect mean pain experienced in the previous 7 days. Pain scores include pain duration (A), pain frequency (number of episodes) (B), pain intensity (C), and pain interference with activities of daily living scored using the BPI (D). Error bars indicate standard deviation.

work with the BPI and a large representative clinical sample of children with CP with and without cognitive impairment (n=167; 47% male; mean age, 9.1y), we established very good to excellent psychometric measurement properties for the BPI. These properties included excellent internal consistency (Cronbach α=.96) and pain validity evidence based on significant correlations with numerical ratings intensity scores (ρ=0.67, P<.001), DPI pain intensity (ρ=0.65, P<.001), pain frequency (ρ=0.56, P=.02), and pain duration scores (ρ=0.42, P=.006).[15] The Cronbach α for the BPI in the current sample was 0.97 with corrected item-total correlations $\geq$0.81 for all 12 items.

Modified Ashworth Scale

The MAS is designed to measure spasticity in individuals with lesions of the central nervous system.[16] Scores range from 0, indicating no increase in muscle tone, to 4, indicating the affected limb is rigid. The modified version of the Ashworth Scale differs from the original version by providing a response option of 1+ indicating resistance/spasticity during less than half of the movement. In original assessment of interrater reliability of the MAS, assessors agreed on 87% of their ratings. However, MAS scores in the current sample were abstracted from the medical record and were completed by only 1 rater (an advanced practice nurse or a physical medicine and rehabilitation physician); thus, there was no way of assessing interrater reliability in the current sample. Because the information provided in the medical record was highly variable in terms of which and how many muscles were tested, we opted to collect the highest MAS score listed for the lower extremities at each time point. We focused on lower extremity MAS scores because ITB is thought to be more effective for lower extremity spasticity.

Statistical analyses

Normality of data was estimated using the Shapiro-Wilk test. Internal consistency was assessed using Cronbach α.

Table 2 Musculoskeletal pain and spasticity outcome by group (N = 32)

Variables	Pre-ITB Pump Time 1	Post ITB Pump Time 2	*P* Value
Pain interference (scored 0-120)			
Mean ± SD	29.91 (34.96)	19.75 (24.31)	.10
Median (IQR)	18.00 (0-48.25)	7.5 (0-42.75)	.11
Pain frequency (episodes/wk)			
Total episodes (n)	255	196	
Mean ± SD	7.97 (10.23)	6.13 (8.95)	.39
Median (IQR)	3.00 (1.00-13.00)	2.50 (0-9.75)	.47
Pain duration (h/wk)			
Mean ± SD	57.35 (77.58)	13.30 (41.39)	.002
Median (IQR)	2.17 (0.05-168.00)	0.06 (0.00-3.10)	.003
Constant pain, n (%)	10 (31.25)	2 (6.25)	
Pain intensity (scored 0-10)			
Mean ± SD	5.75 (5.00)	4.44 (4.31)	.14
Median (IQR)	5.00 (2.00-9.50)	5.00 (0.00-7.00)	.12
Spasticity (MAS scored 0-4)*			
Mean ± SD	1.87 (0.97)	1.74 (0.75)	.61
Median (IQR)	2.0 (1-3)	2.0 (1-2)	.56

NOTE. Scores represent averages for all members of the group including those with and without pain. Statistical significance in the right hand column is calculated using paired samples *t* tests for mean comparisons and Wilcoxon signed rank tests for median comparisons.
Abbreviation: IQR, interquartile range.
* Signifies n = 28.

Wilcoxon signed rank test for related samples was used to assess significant changes in pain scores pre- and post ITB pump implant. DPI subscales used in analysis included pain intensity, pain frequency, and pain duration. Pain parameters for the DPI are summed to include data for all pain types and/or locations reported. Because multiple types of pain often coexist, the summary data can exceed the 0-10 scale or the number of hours in a week. Missing data constituted <5%, and therefore missing values were dropped and not imputed. Significance was set at $P<.05$ for all tests. All statistical tests were completed using SPSS version 25.[a] A simple linear regression was used to determine that sex did not significantly predict pain intensity ($F_{1,30}=0.366$, $P=.550$), duration ($F_{1,29}=1.401$, $P=.246$), frequency ($F_{1,30}=0.163$, $P=.690$), or interference ($F_{1,29}=0.111$, $P=.741$) post ITB pump. Results remained unchanged when participants (n = 3) with Gross Motor Function Classification System level II or III were excluded from analyses. The main results tended to hold when participants (n = 6) taking daily pain medications at the time of surgery were excluded from analyses ($P=.054$, pre/post pain intensity).

Results

Pain outcomes

There was a significant decrease in pain duration (in the week prior to assessment) from pre- (median, 2.17h) to post ITB pump (median, 0.06h; $Z=-3.00$; $P=.003$) with a medium effect size ($r=-0.38$) (fig 1). Median pain frequency and intensity remained unchanged (table 2). See fig 2 for descriptive depiction of the individual differences in percentage change in pain intensity, duration, and interference for the entire sample.

Chronic pain, pain interference, and medications

Prior to ITB pump implant 31% of participants were reported to be living in constant chronic pain (ie, chronic pain was considered any pain that had lasted more than 3mo; constant was considered when pain was reported to be present every minute of every day, ie, constantly). Post-ITB pump implant reduced the number to 6% (McNemar test of paired nominal proportions; unsigned difference = 0.25; 2-tailed = 0.007, 1-tailed = 0.004). Pain interference on activities of daily living did not decrease significantly from pre- (scored 0-120; median, 18.00) to post ITB pump implant (median, 7.50; $Z=-1.615$; $P=.11$). Pre-ITB participants were taking pain medications daily (n = 6) or as needed (n = 4). Of those taking pain medications daily, their post-ITB pain medication use was unchanged (n = 3) or reduced to as needed (n = 3). Post ITB, 8 participants were taking pain medications daily who were not taking pain medications pre-ITB.

Spasticity

There was no statistically significant change in MAS scores from pre- (median, 2) to post ITB pump (median, 2; $Z=-0.587$; $P=.56$). There was variability in MAS score outcomes after surgery, with MAS scores decreasing (n = 9; 28%), increasing (n = 7; 22%), staying the same (n = 8; 25%), or going unreported in the medical record (n = 8; 25%).

Bivariate relations between outcome measures

BPI pain interference score significantly correlated with pain duration ($\rho=.62$, $P<.001$), intensity ($\rho=.70$, $P<.001$), and frequency $\rho=.55$, $P<.001$). Pain intensity also correlated

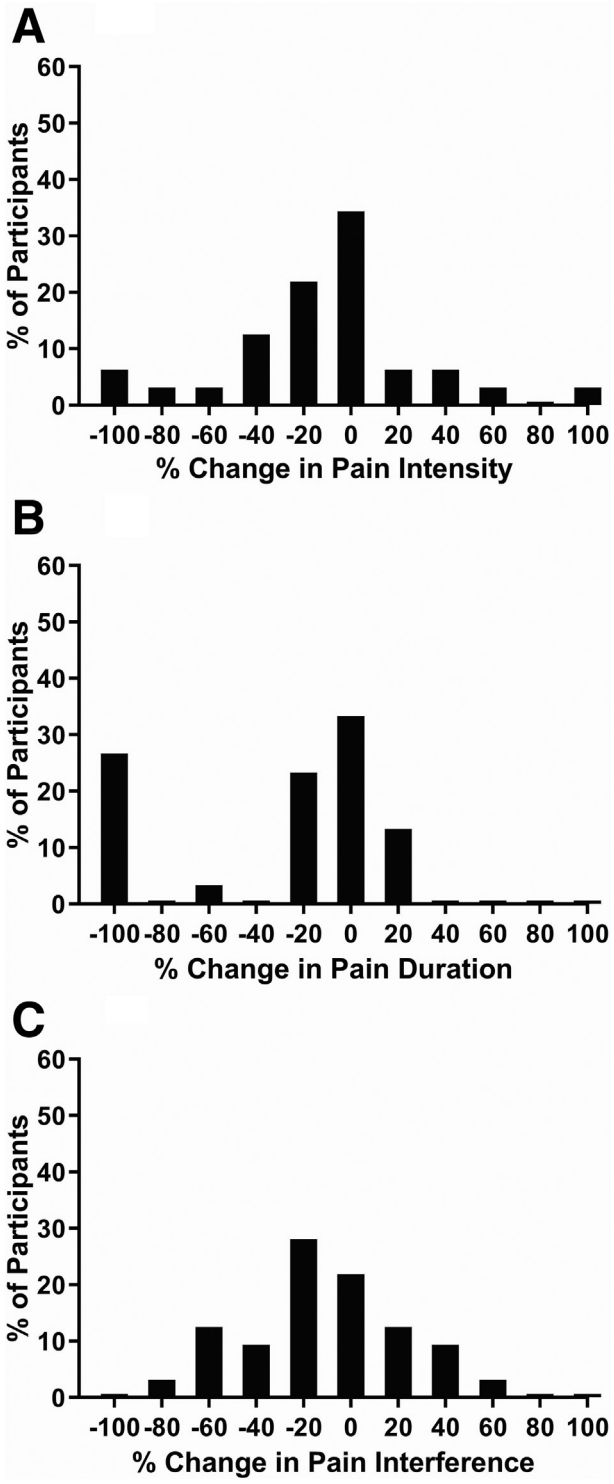

Fig 2 Depiction of the percentage of the sample (y-axis) that had various percent change (x-axis) in pain intensity (A), pain duration (B), and pain interference with activities of daily living scored using the BPI (C). Positive values on the x-axis indicate the percent of participants for whom pain increased post ITB pump implant. Negative values indicate the percent of participants for whom pain decreased post ITB implant.

significantly with pain frequency ($\rho = .80$, $P < .001$) and duration ($\rho = .70$, $P < .001$). Pain duration correlated significantly with pain frequency ($\rho = .49$, $P < .001$).

Discussion

CP is the most common cause of physical disability in children affecting approximately 2-3/1000 live births.[17] Spasticity is reported in approximately 70% of those with CP and, depending on severity, can result in chronic pain that interferes with function and comfort.[3,4] ITB is regarded as relatively effective in the reduction of lower limb spasticity and is frequently used to treat hypertonicity associated with CP.[18] ITB outcomes specific to pain are not well documented or understood. In this study cohort, our objective was to measure musculoskeletal pain pre- and post ITB pump implant. We used pain measurement scales specific to developmental disability and documented prospectively that within group pain duration significantly decreased post ITB pump implant. The proportion of children reported to experience constant pain was also significantly reduced. Although not statistically significant, there was a trend toward decreased pain interference scores post ITB pump implant. Pain intensity and frequency of pain episodes remained unchanged. Interestingly, average MAS spasticity scores did not differ from pre- to post ITB pump implant, and in some cases spasticity scores increased. This finding may be influenced by variability in clinical measurement of the MAS (ie, the same muscles were not consistently assessed) or by the way in which the MAS was reported and therefore extracted from the medical record (highest lower extremity scores recorded).

Our analysis based on standardized proxy-report pain measures used in populations with intellectual and developmental disabilities adds prospective evidence to the accumulated evidence that pain decreases related to ITB pump implant in children with CP. The greatest effect appears to be on the duration of pain experience. This is among the few prospective studies specific to CP and pain showing sustained reductions in pain approximately 6 months post ITB pump implant. The study adds to the 2018 systematic review completed by Ostojic et al in which authors noted the existence of moderate evidence to support the efficacy of ITB for the reduction of spasticity-related pain.[19] Our results are also consistent with the prior 4 studies reporting on prospective protocols similar to what we have described here (pre/post ITB measurement strategy within CP).[10,18,20] Hoving et al found ITB was effective for pain reduction in 12 children compared with standard of care. Two measures for pain were included: a visual analog scale of satisfaction with pain pre- and post implant as well as 1 item from the Child Health Questionnaire specific to pain and/or discomfort.[18] Morton et al compared 2 time points in treated ($n = 18$) and untreated ($n = 18$, waitlist control) children and documented significant improvements in those treated with ITB based on the Caregiver Questionnaire, which included a comfort dimension but was not pain specific.[10] Ramstad et al relied on a within-group design evaluating change before

implant and then again approximately 6 and 18 months post implant.[20] Their reported pain outcome measure showed improvements between baseline (before implant), time 1 (approximately 6mo) and time 2 (approximately 18mo). The Intrathecal Baclofen in Dyskinetic Cerebral Palsy trial assessed the efficacy of ITB using a double-blind, placebo-controlled, multicenter, randomized clinical trial in 30 children with CP.[21] The primary outcome variable was goal attainment scaling, which assesses attainment of personalized goals for each patient. Goal attainment scores at 3 months were significantly greater for participants in the ITB condition; however, pain and comfort assessments (0-10 visual analog scales) did not differ between groups. These are important studies broadening the scope of outcomes by including pain and comfort specific to pediatric samples, but, as with any single study, there were limitations including small sample sizes,[18,21] ad hoc measures with limited reliability and/or validity evidence for the sample,[18,21] and a nonpain-specific measure.[10]

Study limitations

In terms of study limitations, there are several points to consider. We relied on proxy report for all participants. This approach has become the industry standard for individuals with compromised self-report.[6] It does not mean it is without problems; most importantly, it does not guarantee an accurate (truthful) measure of the individual's pain experience but rather a proxy's judgment. There may also be issues with burden, such that asking parents a detailed list of questions may add to caregiving burden and affect the proxy report. That said, our experience in relying on parents is based on accepted convention that they are the individuals who know best their child's idiosyncrasies, mood, and affective displays. Anecdotally in this sample, we did not perceive or receive any feedback from parents that completing the measures was stressful, problematic, or otherwise burdensome. It is also possible that parents completing the measures during their child's surgery might have been under undue stress and also possibly inclined to (consciously or subconsciously) emphasize their child's pain to justify putting their child through the procedure. Similarly, parents may tend to inflate the procedure's benefits after it takes place for the same reason. From a measurement perspective, one next step would include further study of the proxy assessment tools used in this study with adolescents and adults with CP with no cognitive impairment focused on assessing the utility of the measures for use as a self-report tool. This would help determine whether the pain assessment tools are feasible for use in that age/ability group. Additionally, there are limitations associated with assessing pain at a single time point before and after surgery. Pain is variable, and therefore a single time point sampling (although our sampling was based on a 7-d recall) may not accurately or completely represent the participants' pain experiences.

Conclusions

Overall, in this specific sample, it was clear that the majority of parents perceived and reported on positive changes in their child's musculoskeletal pain reduction post ITB implant. The reduction in constant chronic pain is noteworthy. From a clinical care perspective, one of the problems created by the limited scientific study of a broader range of ITB treatment outcomes in CP (informed by ICF) is a corresponding lack of patient selection criteria designed to optimize outcome by producing decision aides for who is most likely to benefit and in what ways. Pain response in CP should continue to be described in relation to the treatments provided to this vulnerable patient group, as should work to improve pain outcome measurement and further define pain response profiles in relation to quality of life outcomes.

Supplier

a. SPSS Statistics for Windows version 25; IBM.

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Acknowledgments

We are grateful for the participants and their families who generously shared their time and energy to help make this study a success. We thank Rachel Katoch, CCRC, Kristin Frenn, MBA, and Lisa Lykken, R EEG T, for supporting the data collection for this study.

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