ORIGINAL ARTICLE

Effect of Intrathecal Baclofen Bolus Injection on Lower Extremity Joint Range of Motion During Gait in Patients With Acquired Brain Injury

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ABSTRACT. Horn TS, Yablon SA, Chow JW, Lee JE, Stokic DS. Effect of intrathecal baclofen bolus injection on lower extremity joint range of motion during gait in patients with acquired brain injury. Arch Phys Med Rehabil 2010;91:30-4.

Objectives: To evaluate lower extremity joint range of motion (ROM) during gait before and after intrathecal baclofen (ITB) bolus administration, and to explore the relation between changes in ROM and concurrent changes in gait speed and muscle hypertonia.

Design: Case series.

Setting: Tertiary care rehabilitation center.

Participants: Adults (N=28) with muscle hypertonia due to stroke, trauma, or anoxia.

Interventions: 50-μg ITB bolus injection via lumbar puncture (75 and 100μg in 2 cases).

Main Outcome Measures: Ashworth score, self-selected gait speed, and sagittal plane ROMs in hip, knee, and ankle joints before and 2, 4, and 6 hours after ITB bolus.

Results: A significant decrease in the mean Ashworth score on the more involved side (2.0 to 1.3) and an increase in gait speed (41 to 47cm/s) were noted at different intervals after ITB bolus injection. Ankle ROM significantly increased on the more involved (13° to 15°, $P<.01$) and less involved (22° to 24°, $P<.05$) sides. ROM significantly improved, significantly worsened, or showed no significant change in 42%, 34%, and 24% of individual joints, respectively. The peak change in ROM did not coincide with the peak decrease in Ashworth score. Peak changes in ROM and speed coincided more often ($P<.001$) in participants who increased gait speed after ITB bolus compared with those who decreased speed. The absolute change in ROM after ITB bolus injection correlated better with the concurrent changes in speed ($r=.41$, $P<.001$) than with the baseline speed ($r=.18$, $P<.05$).

Conclusions: ITB bolus injection produces variable changes in joint ROM during gait, with significant improvements in the ankles only. Timing and magnitude of peak changes in ROM are associated with concurrent changes in speed but not muscle hypertonia.

Key Words: Brain injuries; Gait; Muscle hypertonia; Rehabilitation.

CONTINUOUS INTRATHECAL baclofen infusion therapy effectively reduces lower extremity spastic hypertonia in ambulatory and nonambulatory patients with ABI resulting from trauma or stroke.[1,2] Screening protocols for determining clinical response to baclofen administration before pump implantation typically use manual evaluation of muscle stiffness after ITB bolus injection. The implications of change in muscle hypertonia after a bolus or continuous ITB administration on functional activities, such as walking, are less clear. This is not surprising considering that the contribution of muscle tone to gait impairment after stroke remains controversial.[3-7] In addition, transient changes in gait after ITB bolus injection may be subtle and not readily discernible by clinical or observational gait assessment. Thus, computer-assisted motion analysis has been used to better understand changes in various gait parameters after bolus[8] and continuous[9] ITB administration.

Our recent investigation of walking performance in 28 pump candidates with ABI revealed a consistent decrease in the lower extremity Ashworth score after ITB bolus injection.[8] The effects on speed and other time- and distance-based gait parameters were unrelated to the decrease in Ashworth score, however, and greatly varied in terms of timing and magnitude of changes between 2 and 6 hours of ITB bolus administration. In this follow-up investigation, we examined the changes in lower extremity joint ROM during ambulation in the same 28 participants.

We generated 3 hypotheses based on previous results. First, we predicted that joint ROM during gait would increase after ITB bolus injection, as may be observed with other antispasticity treatments such as botulinum neurotoxin chemodenervation[10,11] and dorsal rhizotomy.[12,13] Second, assuming a positive correlation between changes in sagittal plane ROM and gait speed in patients after stroke,[14] we postulated a temporal relation between changes in ROM and speed after ITB bolus injection. That is, the improvement in ROM during gait would coincide with the largest increase in speed after ITB bolus administration. Lastly, providing that the latter relation between ROM and speed holds true, changes in ROM during gait should not be associated with changes in the resting Ashworth score, since we previously found no association between

List of Abbreviations

ABI	acquired brain injury
ITB	intrathecal baclofen
ROM	range of motion

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changes in speed and muscle hypertonia after ITB injection in the same sample.[8]

METHODS

Participants

Twelve men and 16 women, ranging in age from 19 to 56 years (mean ± SD, 35±12y), were recruited from a spasticity and motor disorders clinic led by one of the investigators. The etiology of ABI included stroke (13 participants), trauma (12 participants), and hypoxic encephalopathy (3 participants). The average time ± SD postinjury was 45±34 months. Additional descriptive information about the sample has been provided elsewhere.[8] All participants had experienced persisting motor impairments associated with muscle hypertonia despite prior administration of oral antispasticity agents, botulinum toxin chemodenervation injections, or both. ITB was thus considered a potential treatment option with the goal of improving overall motor function, including gait. Each participant had been scheduled for bolus injection before enrollment in this study as a part of the screening for possible ITB pump implantation. Additional criteria for referral were (1) muscle hypertonia resulting from ABI; (2) age 16 years or older; (3) no known allergy to baclofen; (4) ability to safely walk independently or with some assistance; and (5) no fixed contracture in the lower extremity joints. The study was approved by the institutional review board for human research, and each participant signed the informed consent before enrollment in the study.

Evaluation Protocol

On day 1, a physical therapist evaluated muscle hypertonia in hip flexor, hip extensor, knee flexor, knee extensor, and ankle plantarflexor muscle groups using the Ashworth score on a scale of 1 to 5.[15] Each participant then underwent baseline gait evaluation using the video-based motion analysis protocol. The next morning, participants received a 50-μg bolus of baclofen injected into the lumbar intrathecal space. Two participants received 75 and 100μg, respectively, because of equivocal clinical responses from a previous 50-μg bolus. Clinical assessment of muscle hypertonia and computerized gait analysis were repeated at 2, 4, and 6 hours after the bolus injection. The same therapist measured the Ashworth score across all evaluation points in a given patient. The reflective markers attached to body segments were kept in place between 2 and 6 hours after the injection. To minimize the occurrence of postlumbar puncture headache, participants rested in bed except when gait data were being acquired.

Gait Data Acquisition and Processing

Spherical reflective markers 2.5cm in diameter were affixed with adhesive tape to bony landmarks on the lower extremity in accordance with the Helen Hayes biomechanical model.[16] After the baseline assessment, the locations of the reflective spheres were marked on the patient's skin with indelible ink. Participants walked at a self-selected speed, either barefoot or with preferred footwear, and with their customary assistive device, if any. Video images were acquired at a sampling frequency of 60 fields/s using a 6-camera motion capture system.[a] Data acquisition started after participants had taken a few steps and terminated before they reached the end of a 4-m walkway. At least 5 walking trials, comprising 2 to 5 gait cycles each, were recorded during every evaluation session, providing 10 to 25 total gait cycles for analysis.

Images of the reflective markers were computer digitized to derive their 3-dimensional positions for each walking trial. The raw data were normalized to 1% interval of each gait cycle. Normalized data were then averaged to produce mean hip, knee, and ankle joint angle curves for each evaluation session. In addition to previously reported temporospatial outcome measures,[8] maximum flexion and extension angles for the hip, knee, and ankle joints were calculated (Orthotrak gait modeling software[a]) and used to derive joint ROM values for the more and less involved sides.

Data were processed for group and individual analyses. For the group analysis, the greatest difference from baseline was defined as the participant's peak response, and the evaluation session at which it occurred (2, 4, or 6h) was defined as time of peak response. Peak response was considered to be the most representative individual outcome and thus most suitable for the before-after group comparison. Considering variable changes in ROM across participants, joints, and evaluation time points, individual ROM data were transformed into categorical outcomes. For that purpose, baseline, 2-, 4-, and 6-hour data of each participant were submitted to the analysis of variance with planned post hoc comparison to determine the statistical significance of each participant's response to ITB bolus injection.[8] Depending on whether the level of significance was reached ($P<.05$) and the direction of ROM change, 1 of 3 possible outcome categories (significant improvement, significant worsening, no significant change) was ascribed to each joint (hip, knee, ankle) on both sides for each evaluation session (2, 4, and 6h postbolus). ROM was considered improved when the absolute deviation from the normative data[a] decreased after the injection. The reverse indicated ROM worsening. The frequencies of the 3 possible ROM outcomes were tabulated for each joint across all participants and compared between the 3 evaluation time points after ITB injection.

Statistical Analysis

To examine changes in joint ROM after ITB bolus injection across the entire group (hypothesis 1), the paired *t* test was applied to test the difference between baseline and peak response values for each joint. For descriptive purposes, the frequency of individual ROM outcomes was related to the time of postbolus evaluation using the chi-squared statistic. The chi-squared statistic was also used to determine whether the timing of peak changes in ROM coincided with peak changes in speed (hypothesis 2) and Ashworth score (hypothesis 3). As per a priori planned comparisons, the magnitude of change in ROM at the time of peak change in speed was compared between the subsets of participants who increased speed and those who decreased speed, by using analysis of variance and controlling for joint and side, as appropriate. Correlations between ROM and speed, and between ROM and Ashworth score were explored in secondary analyses using the Pearson product-moment correlation and the Spearman rank correlation, respectively. A *P* value of less than .05 was considered significant. Statistical analyses were performed using Prism 3.0[b] and SAS[c] software.

RESULTS

Range of Motion During Gait Before Intrathecal Baclofen Bolus

Mean ROM results per joint and side are presented in table 1 for all 28 ABI participants along with normative values. On average, baseline ROM was within normal limits only at the hip joint on the less involved side. At the more involved hip, ROM was 10°, or approximately 2 SD, below normal. Knee ROM was 35° (7 SD) below normal on the more involved side and 12°

Table 1: ROM at Baseline and at the Time of Peak Response After ITB Bolus Injection With the Distribution of Individual Outcomes

Joint (Normal Values*) Side	Baseline (deg)	Peak Response (deg)	$P^{\dagger}$	Improved n (%)	Largest Improvement (deg)	Worsened n (%)	Largest Worsening (deg)	Unchanged n (%)
Hip (38±5)								
More involved	28±11	27±12	.532	10 (36)	8.4	9 (32)	−12.7	9 (32)
Less involved	38±9	39±9	.345	9 (32)	8.3	12 (43)	−12.0	7 (25)
Knee (62±5)								
More involved	27±15	29±17	.250	10 (36)	13.5	9 (32)	−16.5	9 (32)
Less involved	50±14	48±11	.856	10 (36)	13.1	11 (39)	−41.1	7 (25)
Ankle (28±3)								
More involved	13±6	15±7‡	.008‡	16 (57)	10.7	5 (18)	−5.9	7 (25)
Less involved	22±8	24±8‡	.031‡	15 (54)	11.6	11 (39)	−8.3	2 (7)

NOTE. Values are mean ± SD or as otherwise indicated.
*Motion Analysis Corp, Santa Rosa, CA.
†*t* test.
‡Significant results.

(3 SD) below normal on the less involved side. Ankle ROM was 15° (5 SD) below normal on the more involved side and 6° (2 SD) below normal on the less involved side. Overall, ROM was significantly larger on the less involved side than on the more involved side for all 3 joints ($P<.001$). The ratio of ROM values between the more and less involved sides (ROM symmetry) was 72% at the hip, 55% at the knee, and 59% at the ankle. Baseline ROM values at the less involved hip joint ($r=.54$, $P<.01$) and the more involved ankle joint ($r=.40$, $P<.05$) were correlated with preferred walking speed but not Ashworth score.

Peak Changes in Range of Motion After Intrathecal Baclofen Bolus (Hypothesis 1)

Across all participants, mean changes in hip and knee ROM during gait were less than ±2° at the time of peak response after ITB bolus injection (see table 1). ROM significantly increased in both ankles, however, from 13° to 15° on the more involved side ($P<.01$) and from 22° to 24° on the less involved side ($P<.05$). ROM symmetry increased at the knee and ankle joints from 55% to 60% and from 59% to 63% on average, respectively, but decreased from 72% to 69% at the hip.

Distribution of Peak Range of Motion Outcomes Across Joints and Time

Across all participants and joints (n=168), ROM at the time of peak response significantly improved in 70 joints (42%) (fig 1), significantly worsened in 57 (34%), and did not change in 41 (24%). Peak changes in ROM tended to be statistically significant more often in the ankle (93%) than either the hip (75%) or the knee (75%) joint on the less involved side ($\chi^2=3.3$, $P=.06$). Significant ROM improvement, in comparison with significant ROM worsening, also tended to be more frequent in the ankle (66%) than in the hip joint (48%) across the 2 sides combined ($\chi^2=3.0$, $P=.08$).

ROM improvement, worsening, and no change were distributed differently across the 3 postbolus sessions ($\chi^2=0.3$, $P=.08$). In general, ROM worsening occurred more frequently at 2 hours after ITB bolus injection (60%), whereas ROM improvement was more often seen later (65% at 4 hours and 60% at 6 hours, $\chi^2=6.4$; $P<.05$).

Relation Between Changes in Range of Motion and Gait Speed (Hypothesis 2)

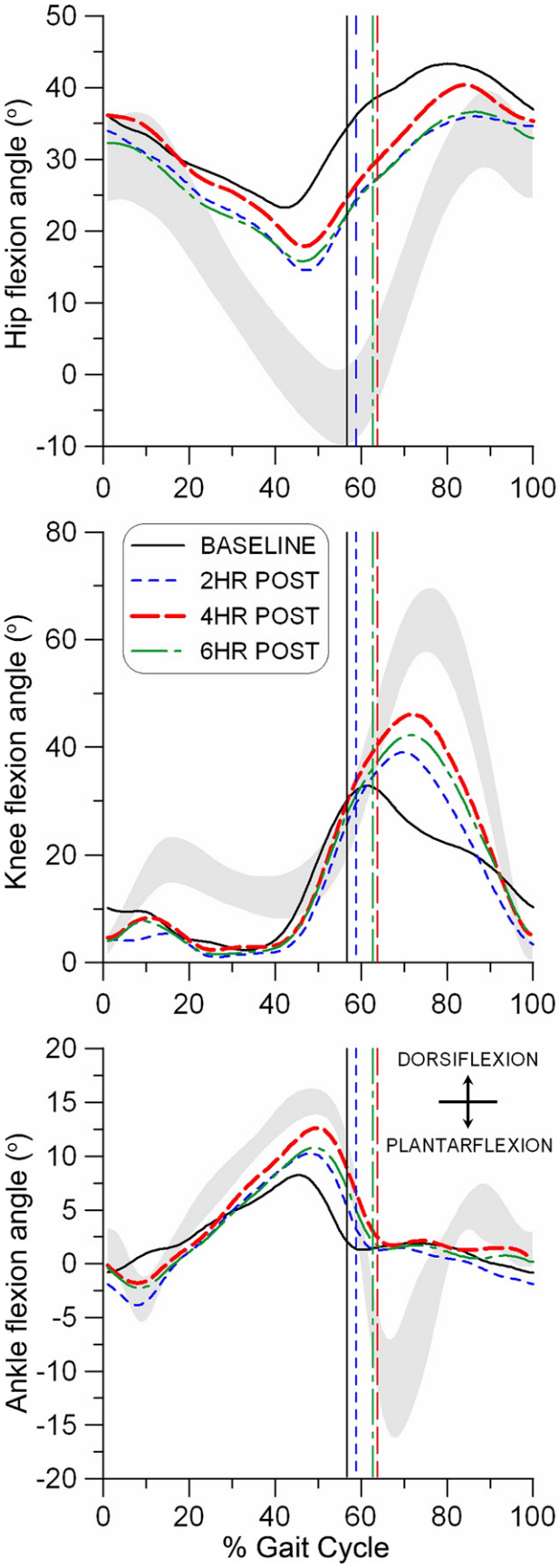
Baseline gait speed (41±26cm/s) in the study participants was significantly ($P<.001$) slower compared with the normative values (125±18cm/s, age >21y). Across the study pool, mean velocity increased significantly from 41±26cm/s at baseline to 47±31cm/s at the time of peak response ($P<.001$).[8] When analyzed individually, 16 participants significantly increased speed (45 to 57cm/s, on average), 5 significantly decreased speed (13 to 7cm/s), and 7 showed no significant change. Peak changes in ROM coincided with peak changes in speed significantly more often in participants who significantly increased speed after ITB bolus injection, whether compared with those with a significant speed decrease and no change combined (70% vs 30%, $\chi^2=6.6$, $P<.01$) or only with those participants with a significant speed decrease (94% vs 6%, $\chi^2=12.5$, $P<.001$). The corresponding magnitude of peak changes in ROM was significantly different ($P<.001$) depending on speed outcome. That is, peak ROM improved by 2° across all joints at times when speed significantly increased, but worsened by either 3.5° when speed significantly decreased or by 1.5° when speed did not increase (ie, no change and significant decrease combined, $P<.001$). There was no significant effect of either joint or side. Lastly, the magnitude of change in ROM at the time of peak speed response after ITB injection was significantly correlated with the magnitude of concurrent change in speed (Pearson $r=.41$, $P<.001$) and less so with the baseline speed ($r=.17$, $P<.05$).

Relation Between Changes in Range of Motion and Ashworth Score (Hypothesis 3)

The average lower extremity Ashworth score on the more involved side decreased from 2.0±0.5 at baseline to 1.6±0.4 at 2 hours, 1.4±0.4 at 4 hours, and 1.3±0.3 at 6 hours ($P<.001$ for all comparisons with baseline). The distribution of ROM outcomes (significant vs nonsignificant change or significant improvement vs significant worsening) was not significantly different at the time of peak change in Ashworth score. The lack of association also prevailed when analyzed by joint or side. Accordingly, the correlation between the magnitude of peak changes in Ashworth score after ITB bolus and the magnitude of concurrent changes in ROM was not significant.

DISCUSSION

This study tested 3 related hypotheses to discern the relation between ITB bolus–related changes in joint ROM during walking, self-selected walking speed, and muscle stiffness at rest. Our main finding is that joint ROM after ITB bolus injection showed little change across the entire group because of large individual variability, increasing significantly only at the ankle.



This partially confirms our first hypothesis, as similar changes were also postulated for the hip and knee joints. Our second hypothesis was fully supported by the finding that the improvement in joint ROM was significantly associated with an increase in self-selected speed after ITB bolus injection, both in terms of the timing and the magnitude of change. This is further supported by the significant positive correlation between the magnitude of peak changes in speed and the magnitude of corresponding changes in ROM. Our third hypothesis also proved correct, as we found no relation between the timing or magnitude of peak changes in muscle stiffness (Ashworth score) and the corresponding changes in ROM. The overall findings indicate that ITB bolus injection can lead to variable changes in ROM across different joints that are not related to alteration in resting muscle stiffness but rather to neuromuscular adaptation underlying changes in self-selected walking speed.

The participants in this study underwent the ITB bolus trial as part of a clinical screening protocol for possible pump implantation. Their baseline gait was characterized by decreased ROM in the hip, knee, and ankle joints, often found bilaterally, in addition to a number of temporospatial deviations.[8] Gait impairments observed in this relatively large sample appear representative of ambulatory persons with ABI,[17] including patients considered for the ITB pump to control hypertonia and improve walking.

ROM during gait significantly increased in both ankles after ITB bolus injection across the entire group, but the magnitude of change was modest. In a study similar to ours, Remy-Neris and coworkers[9] evaluated 7 participants with ABI before and at 4 hours after ITB bolus injection. No significant changes were seen in hip, knee, and ankle ROM or self-selected speed. We also observed inconsistent changes in joint ROM during gait after ITB bolus injection, but self-selected speed significantly increased on average. Inconsistent ROM results reflect large variability in terms of outcome (significant improvement and significant worsening in 75% of joints), timing, and magnitude of peak changes across different joints. This is exemplified by a more frequent decrease in ROM at 2 hours after ITB injection compared with a more frequent increase in ROM at 4 and 6 hours. These findings may reflect either transient changes in ITB diffusion in the cerebrospinal fluid or neuromuscular adaptations in gait to altering muscle tone.

The variability of changes in ROM after ITB injection allowed testing of our 2 remaining hypotheses concerning the relation between changes in gait ROM, speed, and muscle stiffness (Ashworth score) at rest. The results indicate that the largest change in ROM (whether improvement or worsening) should be expected at the time when the speed increase is greatest after ITB injection. Moreover, changes in ROM and speed are positively related, indicating that improvement in ROM is associated with a significant speed increase and vice versa. Increased ROM may be due to higher joint angular velocities seen at faster walking speeds[18] as a result of better neuromuscular coordination after ITB bolus injection. In-

Fig 1. Joint angle curves for hip (top), knee (middle), and ankle (bottom) joints on the more affected side at baseline (solid bold line) and at 2 (short broken line), 4 (long broken bold line), and 6 (short-long broken line) hours after the ITB bolus injection. The corresponding vertical lines indicate toe-off for each time point. ROM significantly improved in the knee (30° to 44°) and ankle (9° to 15°) at 4 hours after the injection. Although there was no significant change in the hip, the overall curve shifted toward normative values. At the same time, the mean Ashworth score decreased from 2.4 to 1.2.

creased ROM generally leads to better advancement of the swing leg and more effective push off, which increases the step length and thereby speed. In contrast, changes in ROM were not related to the timing or the magnitude of decrease in Ashworth score. Although the clinical implications of this finding are unclear, they suggest that "static" measures of muscle stiffness are poor indicators of "dynamic" neuromuscular response to an ITB bolus.

Despite the relatively large sample size, consecutive recruitment of potential candidates for continuous ITB administration, and use of video-based gait analysis in conjunction with clinical evaluation, we recognize several factors that may limit the degree to which our findings can be generalized. First, an open-label design and lack of a control group may have introduced a selection and observer bias. On the other hand, the study design and broad inclusion criteria also allowed observation of both improvements and worsening in kinematic and temporospatial[8] gait parameters after ITB bolus injection, consistent with previous reports.[9,19] Moreover, use of computer-aided motion analysis mitigated the influence of possible observer bias. Second, it could be argued that some of the ROM outcomes were misclassified because they were compared with the normative ROM data[a] from healthy subjects walking at 125cm/s on average. However, changes in ROM due to slower speed are likely smaller than the magnitude of changes of significant ROM outcomes observed in this study. Any misclassification of nonsignificant outcomes is inconsequential because they were already designated as "no change." Third, most participants wore a nonrigid ankle-foot orthosis on the more involved side during gait evaluation for safety reasons. This may have restricted ankle motion and thereby affected the ROM change in hip, knee, and ankle joints. However, the results indicate that the effect of an ankle-foot orthosis on ROM outcomes was not significant. Finally, hypertonia in ABI, particularly in the trauma subsample, may have dystonic features[1] or soft tissue components[20] that are less amenable to treatment with ITB.

CONCLUSIONS

ITB bolus injection results in variable changes in joint ROM during gait, with small but significant improvements observed only at the ankles. The timing and magnitude of peak changes in ROM are associated with concurrent changes in speed but not muscle stiffness. Future longitudinal studies in a larger sample size are needed to evaluate gait outcomes and identify optimal ambulatory candidates for continuous ITB administration.

The results of this and our previous investigation[8] have several clinical implications. They indicate ITB bolus injection leads to transient changes in gait in most cases, but the results are unpredictable and not necessarily favorable. Moreover, the changes in resting muscle hypertonia are not related to temporospatial or kinematic outcomes.

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Suppliers

a. Motion Analysis Corp, 3617 Westwind Blvd, Santa Rosa, CA 95403.
b. GraphPad Software, 11452 El Camino Real, San Diego, CA 92130.
c. SAS Institute Inc, 100 SAS Campus Dr, Cary, NC 27513.