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S P T S

Case Study

Gait training using a hybrid assistive limb after botulinum toxin treatment for cerebral palsy: a case report

Mayumi Matsuda Kuroda, PhD, RPT[1)*], Hirotaka Mutsuzaki, PhD, MD[2)],
Kenichi Yoshikawa, PhD, RPT[3)], Haruka Ohguro, MD[4)], Iwasaki Nobuaki, PhD, MD[4)]

[1)] Department of Physical Therapy, Ibaraki Prefectural University of Health Sciences: 4669-2 Ami,
Ami-machi, Ibaraki 300-0394, Japan
[2)] Center for Medical Science, Ibaraki Prefectural University of Health Sciences, Japan
[3)] Department of Physical Therapy, Ibaraki Prefectural University of Health Sciences Hospital, Japan
[4)] Department of Pediatrics, Ibaraki Prefectural University of Health Sciences Hospital, Japan

Abstract. [Purpose] Hybrid Assistive Limb® (HAL; Cyberdyne, Tsukuba, Japan) is a wearable robot that assists patients based on their voluntary movements. We report gait training with HAL after botulinum toxin treatment for spasticity of the lower limb in cerebral palsy (CP). [Participant and Methods] The participant was a 36 year-old male with spastic diplegia due to periventricular leukomalacia, with Gross Motor Function Classification System (GMFCS) level II. HAL training was performed in 20-minute sessions (3 sessions/week for 4 weeks). The outcome measures were range of motion, spasticity, walking ability, muscle strength, gross motor function measure (GMFM), Canadian Occupational Performance Measure (COPM), and Pediatric Evaluation of Disability Inventory measured before, immediately after, and one, two, and three months after HAL training. [Results] No adverse events were observed during training. After the HAL intervention, gait speed, step length, cadence, 6-min walking distance (6MD), knee extension strength, GMFM, and COPM increased, and Physiological Cost Index declined. Three months post-intervention, gait speed, step length, cadence, 6MD, and GMFM remained higher than those observed within the first two months. [Conclusion] Gait training with HAL can be a safe and feasible method for patients with CP who undergo botulinum toxin treatment to improve walking ability and motor function.
Key words: Robotics, Robot assisted gait training, Botulinum toxin

INTRODUCTION

Cerebral palsy (CP) presents functional motor disabilities and abnormal gait patterns[1)], as well as failure of gait function, such as increase of energy cost in walking and lowering of gait speed[2, 3)]. Crouching, or an equine gait pattern, is a well-known complication in patients with CP, notably among patients with spastic-type CP. The hip-joint contracts with flexion and adduction, the knee joint with flexion, and the ankle joint with plantarflexion[4, 5)]. The muscles causing these conditions are the adductor longus and gracilis in the hip joint, the hamstrings in the knee joint, and the gastrocnemius and soleus muscles in the ankle joint. It has been reported that in CP, the greater the walking ability, the greater the accomplishment of life habits (activities of daily living and social roles)[6)]. Therefore, it is expected that the accomplishment of life habits can be heightened when gait function is improved by rehabilitation.

Botulinum toxin A is an effective and safe treatment of spasticity in CP[7)]. Particularly, for lower limb spasticity, botulinum toxin treatment was found to effectively reduce muscle tone and improve a passive range of movement. On a review of CP

treatment by Novak et al., botulinum toxin treatment showed the high effect value on the spasticity management[8]. Botulinum toxin A treatment is injected in spastic muscles to block the release of acetylcholine at the neuromuscular junction. This effect manifests approximately four–seven days or more after the injection and persists for approximately three months. Repeated treatment, as needed, is recommended[9]. Studies have reported that botulinum toxin treatment for lower limb spasticity in CP improved muscle tone and increased lower limb joint angles during walking[10, 11]. After botulinum toxin treatment, effectiveness of a physical therapy program of muscle strengthening exercises was also reported[12]. Another study also reported that combined physical therapy (such as casting, stretching, muscle strengthening exercises, and gait training) after botulinum toxin treatment increases lower limb joint angles during gait[13].

Hybrid Assistive Limb® (HAL; Cyberdyne, Tsukuba, Japan) is a novel robotic device that can assist voluntary walking based on the intention of the wearer. HAL is a wearable robot suit that assists torque and drive of hip and knee joint actuators based on real-time information from the patient's voluntary muscle activities (hip and knee flexors and extensors) via electromyography electrodes and/or ground reaction force signals. In this way, the patients can repeat and continue near-normal gait[14, 15].

Robot-assisted gait training using HAL is effective for stroke and spinal cord injury. Specifically, walking ability and walking endurance were improved in adult patients[16, 17]. Previously, we reported the safety and immediate effects of a single session of gait training using a small-sized HAL in adolescent CP patients[18, 19]. We also reported that multiple repetitions of robot-assisted gait training using HAL improved walking ability, walking endurance, and gross motor function in adolescent CP patients[20].

In addition to botulinum toxin treatment for upper limb spasticity in adult stroke patients, the combined use of HAL and botulinum toxin treatment is reported to have improved upper limb function and activity using single-joint HAL[21]. However, gait training with HAL after botulinum treatment in CP has not been reported.

We considered that gait training using HAL could be safely performed even after botulinum treatment in CP with bilateral lower limb spasticity and that it may improve walking ability and motor function. In this case report, we performed gait training with HAL after botulinum treatment for lower limb spasticity in a patient with CP.

PARTICIPANT AND METHODS

A 36 year-old male (height: 165 cm, weight: 51.3 kg) with CP and spastic diplegia was admitted to our hospital. Although there was no obvious abnormality at birth, there was gradual delay of motor development. Magnetic resonance imaging of the head revealed periventricular leukomalacia. Botulinum treatment was carried out periodically for 8 years. The participant's gross motor ability on Gross Motor Function Classification System (GMFCS) was level II. The daily transfer was independent using bilateral Lofstrand crutches. His tendon reflex was enhanced, and his gait pattern was crouching and equinus. It was difficult to touch down the total plantar area on bare feet, so an ankle foot orthosis was worn. The communication ability on Communication Function Classification System (CFCS) was level II. The participant received botulinum toxin A (BOTOX for injection, GlaxoSmithKline, Japan) treatment for lower limb spasticity 12 days before the start of HAL intervention. Botulinum toxin treatment was administered by a pediatric doctor. A total of 250 units were injected: 50/50 units (right foot/left foot) for the hamstrings, 20/30 units for the gastrocnemius, 15/35 units for the soleus, and 25/25 units for the tibialis posterior.

We utilized the lower-limb-type, S-size HAL for medical use in the cybernic voluntary control mode. Briefly, 20 min (excluding intermission) of gait training using HAL was completed in each session, depending on the patient's condition (e.g., fatigue, facial expression, and pulse). In total, 12 sessions were completed. The torque tuner and balance tuner were optimized for the patient. We addressed requests from him by modifying the level of assistance received[15]. We performed training using HAL in addition to conventional rehabilitation during hospitalization. During hospitalization, each rehabilitation session with physical therapy and occupational therapy is accomplished in 40–60 minutes, at five times a week. After discharge from the hospital, no physical or occupational therapy was implemented (Fig. 1).

Measurements were recorded before, immediately after, and at one, two, and three months post-intervention using HAL. Pre- and post-intervention measurements were recorded during hospitalization, and measurements one, two, and three months post-intervention were performed after the patient was discharged from the hospital.

Outcomes measured were as follows: knee and ankle joint range of motion (ROM) and Modified Tardieu Scale (MTS), gait speed (m/s), step length (cm), cadence (step/min) over the 10-m walking test (10MWT), 6-min walking distance (6MD), and physiological cost index (PCI) over the 6-min walking test (6MWT)[22]. The 10MWT and 6MWT performance were measured as the patient was walking using bilateral Lofstrand crutches. Maximum isometric knee extension strength was determined by a hand-held dynamometer (Mobie MT-100, Sakai, Tokyo, Japan)[23] and Gross Motor Function Measure (GMFM)[24], Pediatric Evaluation of Disability Inventory (PEDI) Functional Skills Scale was used to measure self-care and mobility domain[25], and Canadian Occupational Performance Measure (COPM)[26] was used to perform subjective evaluations as secondary outcome measures.

The study protocol was approved by the ethics committee of Ibaraki Prefectural University of Health Sciences (approval nos. 682, e83, e119). The patient and his parents provided written informed consent.
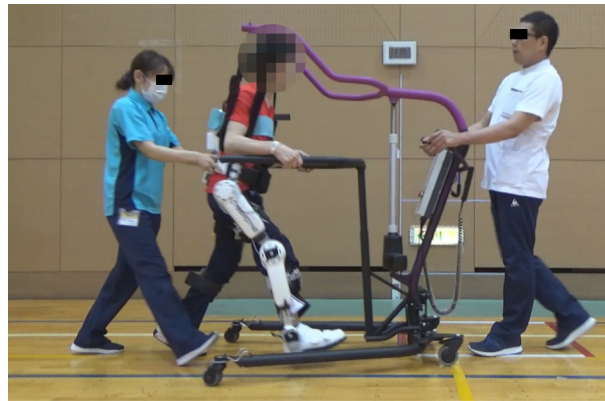
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Fig. 1. Gait training using the lower-limb-type, S-size Hybrid Assistive Limb with All-in-One Walking Trainer.

RESULTS

The participant was able to complete gait training with HAL without any adverse events interrupting the intervention. The mean gait time and distance in each session were 20 (range, 14–24) min and 540 (range, 280–720) m, respectively. The mean degree of fatigue during the training, as measured on the Borg scale, was 7.2 (range, 7–12). Knee extension ROM of the left leg improved post-intervention. However, ankle dorsal flexion ROM of the left leg declined, while there was no change in the knee and ankle ROM of the right leg. While the ankle dorsal flexion MTS of both legs improved post-intervention, knee extension MTS of both legs declined (Table 1).

The participant's self-selected walking speed (SWS) increased from immediately post-intervention to two months post-intervention, compared with pre-intervention. Cadence of SWS increased from immediately post-intervention to one month post-intervention. Step length of SWS decreased one month post-intervention, but increased again at two months post-intervention. Although SWS, step length, and cadence were lowered slightly three months post-intervention, they maintained at a higher value than that immediately post-intervention.

The maximum walking speed (MWS) and cadence of MWS slightly decreased and step length increased after HAL intervention in comparison with those at pre-intervention. Step length of MWS increased from immediately post-intervention to two months post-intervention compared with pre-intervention. MWS and cadence were increased 1 month post-intervention and decreased again two months post-intervention. Although MWS and cadence were increased three months post-intervention compared with those two months post-intervention, they remained at a lower value than at pre-intervention.

As shown in Table 1, 6MD was increased from immediately post-intervention to two months post-intervention compared with pre-intervention. Although 6MD was slightly lowered three months post-intervention, 6MD maintained at a higher value than was recorded immediately post-intervention. PCI was decreased from immediately post-intervention to two months post-intervention, compared with that at pre-intervention. PCI at three months post-intervention increased up to the same value as that at pre-intervention. Isometric maximum knee extension torque of the right leg increased post-intervention, when compared with that at pre-intervention, and decreased slightly from one month to three months post-intervention, compared with that immediately post-intervention, but remained higher than that at pre-intervention even at three months post-intervention. Isometric maximum knee extension torque of the left leg peaked at one month post-intervention compared with that at pre-intervention. Although it was slightly lowered over two to three months post-intervention, the high value was maintained immediately post-intervention, even at three months post-intervention.

GMFM increased from immediately post-intervention to two months post-intervention compared with that at pre-intervention. Although GMFM slightly lowered three months post-intervention, GMFM maintained a higher value than that at post-intervention. PEDI functional skills scale score did not change from pre- to post-intervention in any of the self-care and mobility domains. Conversely, the COPM of performance and satisfaction peaked at one month post-intervention. Although COPM was slightly lowered after two and three interventions, the high value was maintained from the pre-intervention period.

DISCUSSION

We performed gait training using HAL after botulinum toxin treatment for lower limb spasticity in a patient with spastic diplegia CP. No adverse events occurred during the intervention, suggesting that gait training using the HAL can be safely performed even after botulinum treatment for CP. In addition, SWS, 6MD, GMFM, leg muscle strength, and COPM improved after the intervention. Furthermore, as regard the effect persistence after HAL intervention, SWS, 6MD, and GMFM

Table 1. Change of outcome measure

Outcome measure		Pre HAL	Post HAL	Post-HAL after 1 month	Post-HAL after 2 months	Post-HAL after 3 months
ROM	Knee (R/L°)	−20/−30	−20/−20	—	—	—
	Ankle (R/L°)	0/−10	0/−20	—	—	—
MTS	Knee (R/L°)	−25/−35	−35/−40	—	—	—
	Ankle (R/L°)	−30/−35	−25/−30	—	—	—
Gait speed at SWS	(m/s)	0.69	0.74	0.81	0.87	0.80
Step length at SWS	(cm)	43	45	43	48	48
Cadence at SWS	(step/min)	95	98	112	110	101
Gait speed at MWS	(m/s)	1.08	1.06	1.14	0.87	1.02
Step length at MWS	(cm)	33	36	38	48	40
Cadence at MWS	(step/min)	195	177	178	110	153
6MD	(m)	269	361	404	423	369
PCI	(beat/min)	0.9	0.7	0.7	0.6	0.9
Knee extension strength	(R/L Nm)	68/43	96/58	92/74	87/71	78/64
GMFM total	(% 0–100)	66	70	77	78	71
PEDI-FSS self-care	(score 0–100)	81.4	81.4	81.4	81.4	81.4
PEDI-FSS mobility	(score 0–100)	71.6	71.6	71.6	71.6	71.6
COPM–performance/satisfaction average	(score 0–10)	2.2/3.8	7.8/6.6	9.0/10	7.8/7.6	6.8/5.4
1. Increase lower limb flexibility		3/3	10/7	10/10	7/7	6/4
2. No toe pain while walking		1/2	7/6	10/10	6/9	9/5
3. Can walk for 1–2 hours		1/4	9/9	10/10	10/10	9/6
4. Reduce increased muscle tone during movement		5/3	6/5	5/10	7/5	5/7
5. Easier to swing out during walking		1/7	7/6	10/10	9/7	5/5

6MD: 6-minute walking distance; COPM: Canadian Occupational Performance Measure; FSS: Functional Skills Scale; GMFM: Gross Motor Function Measure; HAL: Hybrid Assistive Limb®; MTS: Modified Tardieu Scale; MWS: maximum-selected walking speed; PCI: physiological cost index; PEDI: Pediatric Evaluation of Disability Inventory; ROM: range of motion; SWS: self-selected walking speed.

peaked at two months after HAL intervention and had slightly decreased from peak at three months post-intervention, but remained higher than the values immediately after HAL intervention. These results suggest that gait training using HAL is effective in patients with CP after botulinum toxin treatment. A study reported that combined interventions, such as stretching and gait training, improve gait speed and GMFM compared with CP treated with botulinum toxin treatment alone[13]. In addition, botulinum toxin injection for limb spasticity should be combined with rehabilitation with the aim of improving active motor functions[27]. In this participant, improvement was shown in gait speed and step length, walking endurance, leg muscle strength, and GMFM when botulinum toxin treatment was used jointly with robotic gait training using HAL. The effectiveness of using HAL as a rehabilitation technique after the botulinum toxin treatment was thus indicated.

Regarding intervention using HAL after botulinum treatment, it has been reported that single joint HAL after botulinum toxin treatment for adult stroke patients with upper extremity spasticity improves Fugl-Meyer Assessment and upper extremity activity[21]. Alessandro et al. compared a group of stroke patients treated with botulinum toxin treatment alone and another group treated with robotic gait training using the G-EO System Evolution (Reha Technology, Olten, Switzerland). They found no difference in the improvement in muscle tone, but 6MD had significantly increased in the group that received robotic gait training[28]. Our participant demonstrated partial improvement of ROM and muscle tone. However, the muscle strength of the quadriceps femoris muscle, an antagonist muscle of the hamstrings that injected botulinum toxin increased. In addition, "lower limb flexibility" and "toe pain while walking" in COPM improved after the HAL intervention. Therefore, in addition to the effect of botulinum toxin treatment, the improvement of muscle strength and muscle flexibility was obtained by gait training, without increasing the muscle tone, with HAL assistance.

Neuroplasticity and/or motor learning should be improved by assisted walking based on the patient's voluntary efforts[29]. HAL is a robot that assists the voluntary walking of a patient according to the intention of the wearer and is distinct from other robots that support the walking passively such as the G-EO System. Therefore, it might be supposed that this CP patient using HAL, which assists voluntary walking, should be able to achieve further improvement of walking ability and motor function beyond the effect seen until now.

As regards the persistence of intervention effects, a comparative study of a group that received botulinum toxin treatment for stroke followed by gait training with RoboGait® (BAMA Technology, Turkey, Ankara) and a group that received

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only physical therapy showed that the improvement in balance and gait functions was maintained even after three months post-treatment in the group that received robot training[30]. In our participant, improvement in gait function and GMFM was maintained until three months after robotic gait training. When walking with HAL assistance, step length was increased more than usual. Therefore, greater joint movement and center of gravity movement may have been facilitated by performing gait training using HAL, during the period when muscle tone was reduced by botulinum toxin treatment.

With respect to physical strategies, modern concepts of motor learning recommend a task-specific repetitive approach that induces skill acquisition relevant to the patient's daily life[31, 32]. This study investigated the effects of HAL-assisted gait training after botulinum toxin treatment on performance using PEDI and COPM, not only body structure/function. In our participant, a qualitative improvement in activities of daily living was clinically observed, but it was not detected as a change in PEDI score. PEDI functional skills scale score is dichotomous, with a score of 1 indicating capability of performing the described task independently and a score of 0 indicating inability to perform a task or requiring assistance[24]. Therefore, it might be difficult to reflect qualitative change in activities of daily living. In the future, to objectively show change in activities of daily living in CP, it may be necessary to develop a more sensitive scale. On the other hand, COPM significantly improved after HAL intervention. The items of COPM related to gait endurance and gait posture correlated with the results of 6MD and gait function, suggesting that functional improvement was reflected in daily living activity.

In addition, many outcome measures showed a peak at two months and a slight decrease from peak at three months after HAL intervention. The pharmacological effect of botulinum toxin is expected to persist for three or four months[33]. This participant received botulinum toxin treatment every three−four months. During our study period, he received botulinum toxin treatment two months after HAL intervention again. Therefore, in this participant, the pharmacological effect of botulinum toxin did not seem to have disappeared during the follow-up period after the intervention. Therefore, repeated botulinum toxin treatment and HAL-assisted gait training may further improve motor function.

Thus, it was expected that the combination of robotic rehabilitation, such as HAL assisted gait training, and efficacy of botulinum treatment begins approximately 10 days after treatment, and produce further therapeutic effects[9].

There are several limitations to this study. First, this study was a single-case design. Second, the follow-up on the study protocol was short. Further studies are needed to accumulate more cases and compare them with those in the usual rehabilitation group after they received botulinum toxin treatment.

The present study suggests that gait training using HAL after botulinum toxin treatment for lower limb spasticity in spastic diplegia CP was a safe and feasible intervention and improves walking ability, walking endurance, motor function, and subjective assessment.

Conflict of interest

The authors declare no conflict of interest.

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