

Intrathecal Baclofen Therapy for Hypertonia

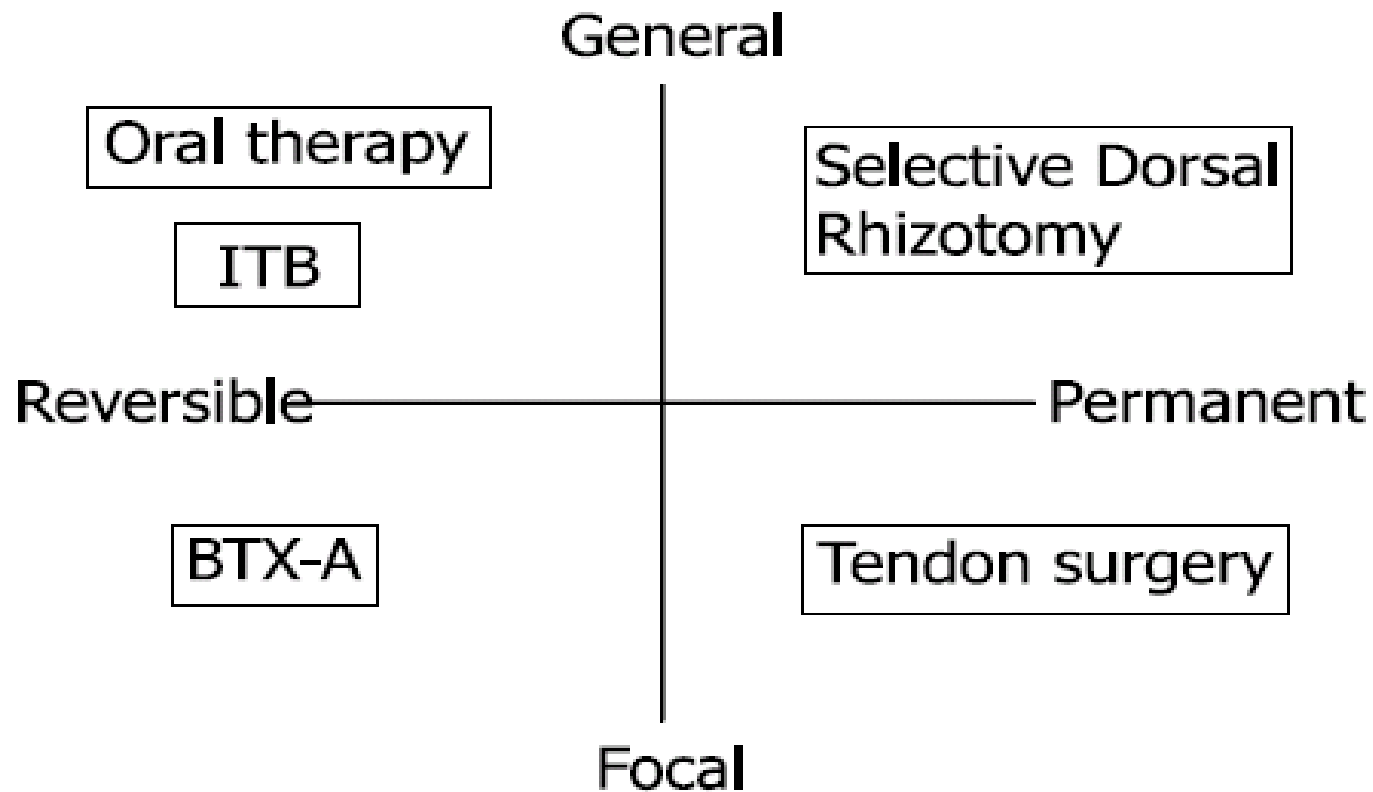
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Yonsei University College of Medicine**





Treatment for Spasticity & Dystonia





Treatment for Spasticity & Dystonia

- Medical Treatment

Medication : baclofen, diazepam, dantrolene, tizanidine

Botulinum toxin, phenol & alcohol injection

- Surgical Treatment

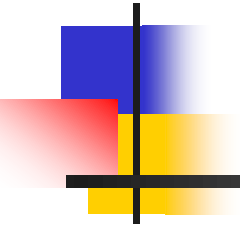
Orthopedic surgery for spasticity & bone deformity

Selective posterior rhizotomy for spasticity

Deep brain stimulation for dystonia

Intrathecal baclofen pump (ITBP)

**Outcomes of Deep Brain Stimulation
in Primary Dystonia &
Adults with Cerebral Palsy**



GPI-DBS in Dystonia

- DYT1(+) generalized dystonia
genetic dystonia : dramatic improvement
effective treatment after 5 years (Sobstyl et al.)
- DYT1(-) generalized dystonia
effective procedure after 2 years (Krauss et al.)
- Secondary dystonia and choreoathetosis
limited benefit in 2 patients of 4 CP (Krauss 2002)

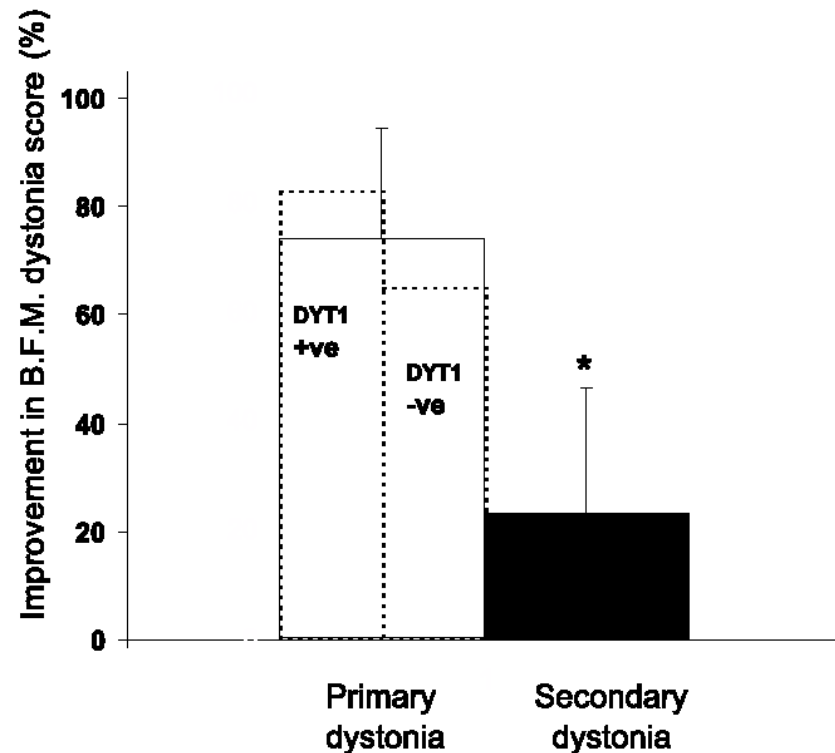




Figure 1 Mean percentage improvements in the Burke-Fahn-Marsden Dystonia Rating Scale for movement (Burke *et al.*, 1985) after bilateral pallidal surgery (either DBS or lesioning) from the literature.

Bilateral pallidal deep brain stimulation for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study

	Preoperative	1 year	p
Movement scale			
Neck and trunk (0-24)	8.73 (5.86)	6.28 (4.71)	0.05
Upper and lower limbs (0-64)	29.79 (15.10)	23.07 (15.05)	0.01
Face: eyes and mouth (0-16)	3.23 (3.36)	3.00 (1.98)	0.55
Speech and swallowing (0-16)	4.10 (1.55)	3.86 (2.63)	0.53
Total	44.23 (21.12)	34.69 (21.87)	0.01
Disability scale			
Speech (0-4)	1.96 (0.92)	1.46 (0.66)	0.02
Writing (0-4)	2.46 (0.99)	1.77 (0.93)	0.01
Feeding (0-4)	1.77 (0.56)	1.46 (0.52)	0.08
Eating and swallowing (0-4)	0.92 (0.73)	0.62 (0.77)	0.24
Hygiene (0-4)	1.39 (0.80)	1.23 (0.73)	0.50
Dressing (0-4)	1.35 (0.75)	1.15 (0.56)	0.40
Walking (0-6)	2.73 (1.39)	2.55 (1.33)	0.48
Total	12.58 (5.03)	10.23 (3.92)	0.01
Pain (0-10)	2.72 (2.66)	1.79 (2.14)	0.33

Data are mean (SD). A reduction in a score indicates an improvement in dystonia. Pain: visual analogue scale (0=no pain, 10=maximum pain).

Table 2: Burke-Fahn-Marsden subscores at baseline and after 1 year of continuous stimulation

	Preoperative	1 year	p
General health	67.31 (22.70)	77.85 (15.98)	0.12
Physical functioning	54.23 (29.92)	57.69 (34.44)	0.48
Role (physical)	56.92 (38.97)	61.54 (40.33)	0.72
Role (emotional)	35.89 (37.18)	58.98 (43.36)	0.06
Social functioning	64.42 (20.95)	65.38 (27.55)	0.76
Body pain	61.00 (31.64)	79.54 (25.92)	0.04
Vitality	51.15 (27.32)	53.46 (20.14)	0.82
Mental health	52.62 (22.56)	65.54 (18.22)	0.05

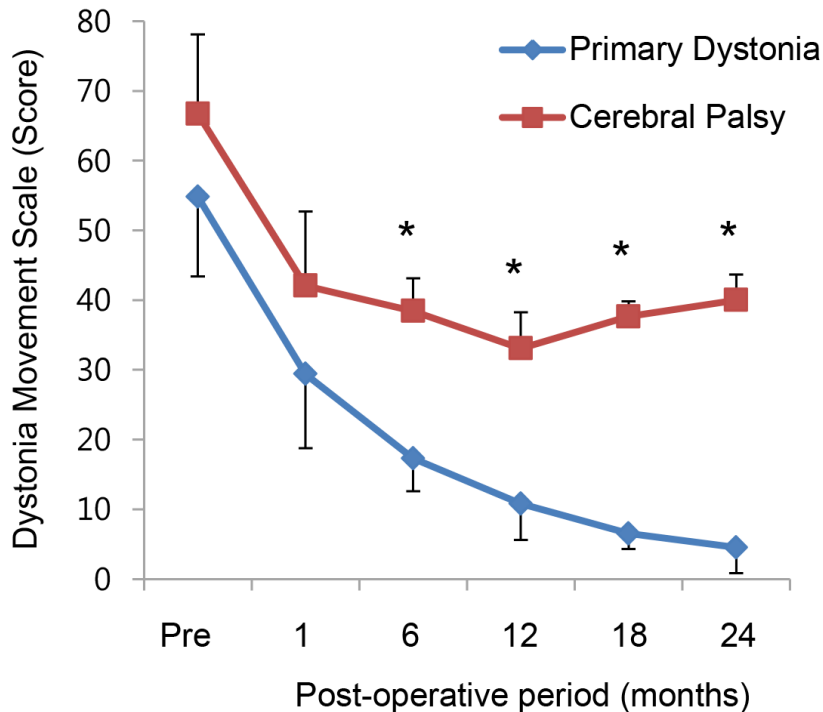
Data are mean (SD). Possible scores range from 0-100. An increase in a score indicates an improvement in function.

Table 3: Health-related quality of life subscores (SF-36) at baseline and after 1 year of continuous stimulation

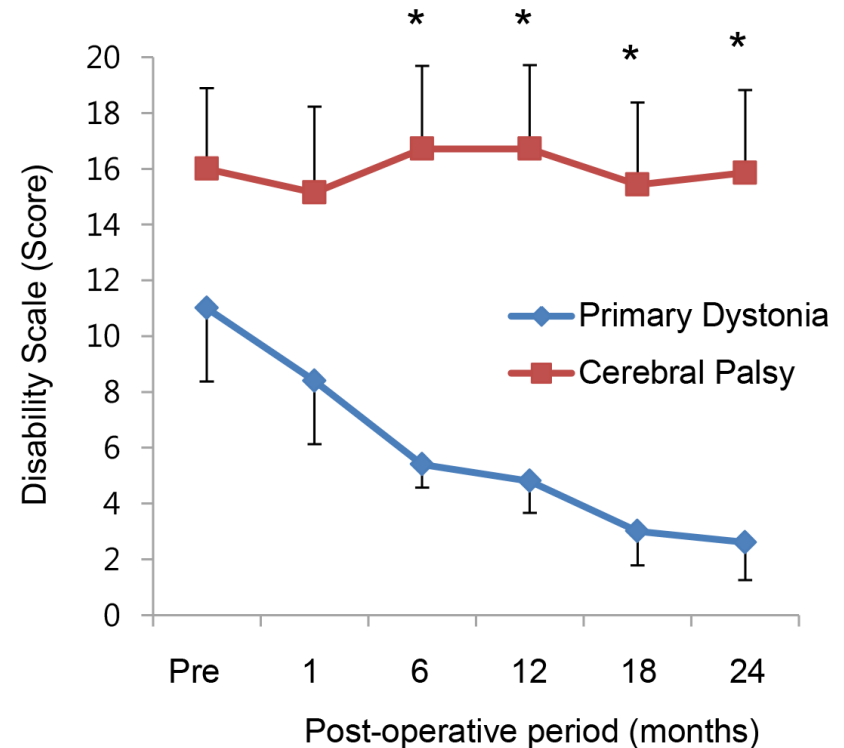
Two-Year Outcomes of Deep Brain Stimulation in Adults With Cerebral Palsy

Ae Ryoung Kim, MD¹, Jin Woo Chang, MD, PhD², Won Seok Chang, MD²,
Eun Sook Park, MD, PhD¹, Sung-Rae Cho, MD, PhD^{1,3,4,5}

A

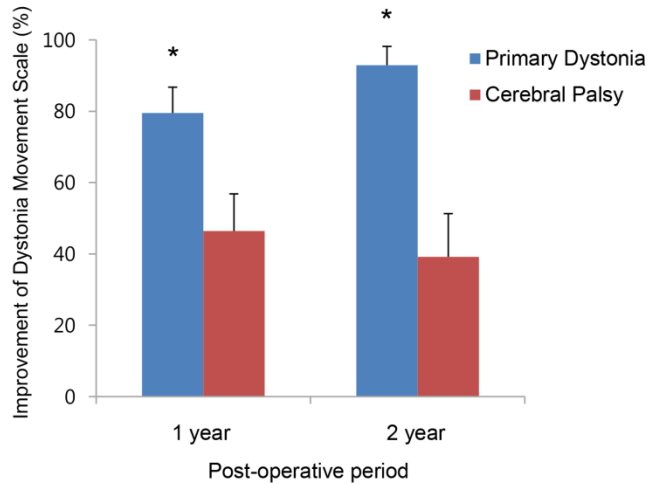


B

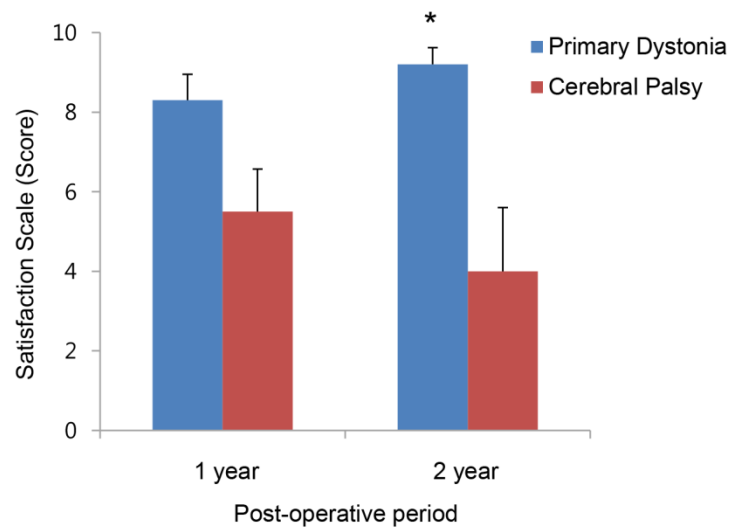
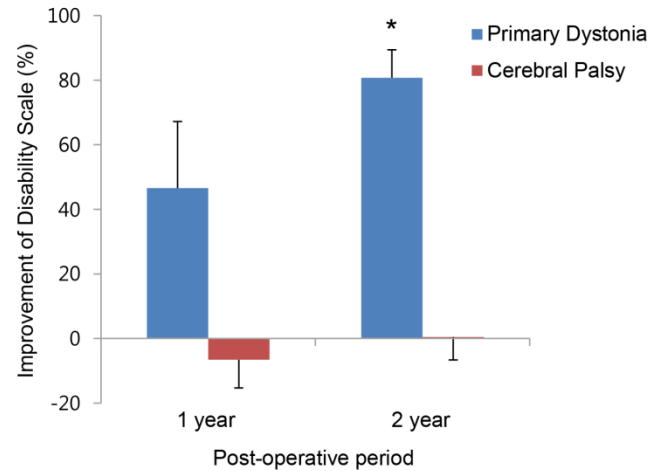


Improvement of dystonia movement, but no improvement of disability

A



B

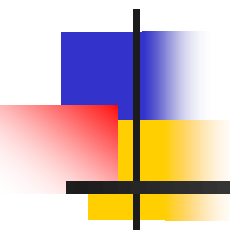




Conclusions

- After GPi DBS :
 - Dramatic improvement in DYT1(+) primary dystonia
 - Limited effect in adult CP with dyskinetic type
 - GPi DBS as an alternative strategy in dystonia which was not responsive to medication and botulinum toxin
- **Limitation :**
 - Some CP felt unsatisfied compared to pre-operative state
 - More study is necessary to anticipate which movement pattern will be responsive to GPi DBS in dyskinetic CP

**Outcomes of Intrathecal Baclofen
Therapy in Cerebral Palsy
& Acquired Brain Injury**



Intrathecal Baclofen Pump (ITBP)



[명의&인의를 찾아서-(133) 세브란스병원 뇌신경센터 바클로펜/모르핀 펌프 클리닉] 중증 통증 완화

이기수 의학전문기자 입력 2017.10.31 05:06 수정 2017.10.31 09:16 댓글 1개

Multidisciplinary approach



- Department
 - Neurosurgery
 - Neurology
 - Rehabilitation Medicine
- Patients
 - Cerebral Palsy
 - Traumatic Brain Injury
 - Hypoxic Brain Injury
 - Hereditary Spastic Paraplegia
 - Spinal Cord Injury, Syringomyelia

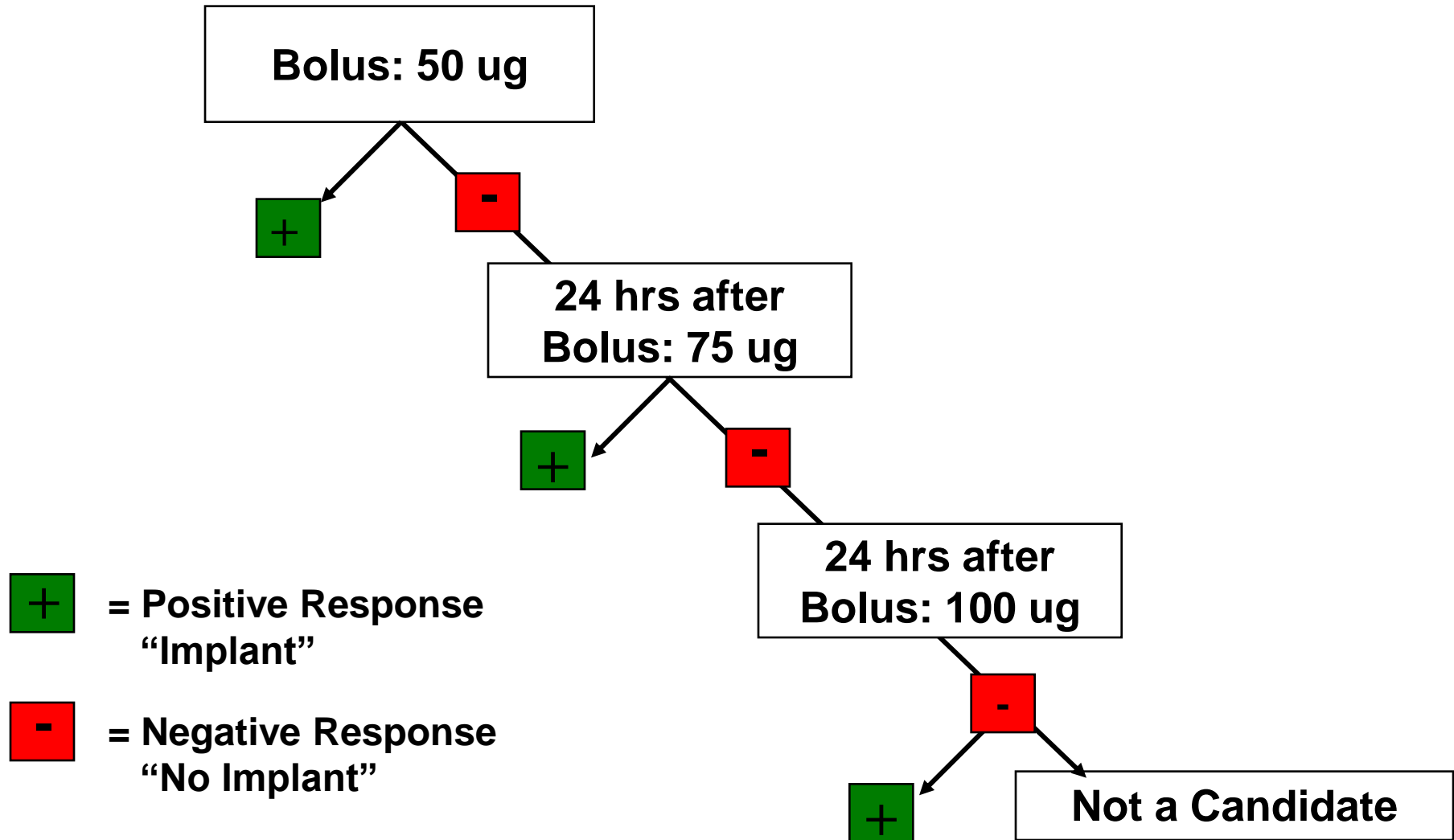
연세대 세브란스병원 뇌신경센터 바클로펜/모르핀 펌프 클리닉 다학제 협진 의료진. 뒷줄 왼쪽부터 시계 방향으로 신경외과 장원석 교수와 유범석 전공의, 연세암병원 종양내과 최혜진, 신경외과 정나영 교수, 뇌신경센터 박선영 간호사, 재활의학과 조성래, 신경과 신하영 교수, 뇌신경센터 박상금 코디네이터, 연세암병원 완화의료센터 박지영, 뇌신경센터 김혜인 간호사, 권은정 코디네이터.세브란스병원 제공



Baclofen metabolism

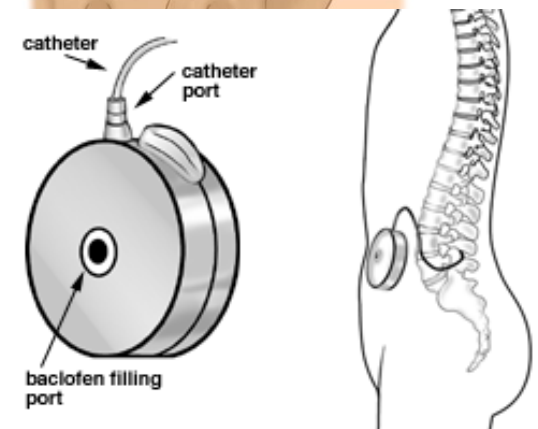
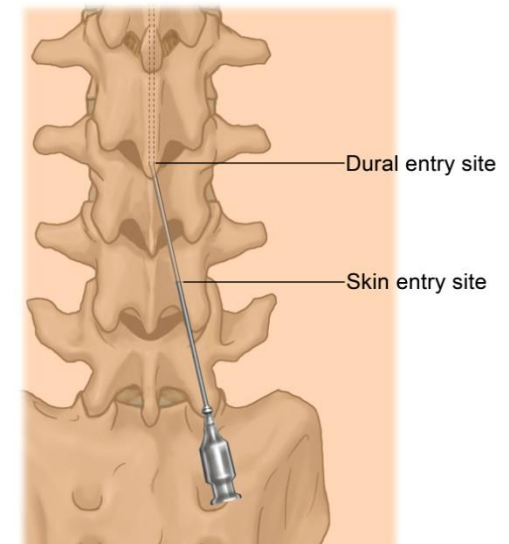
- Baclofen could pass BBB, but only partially permeates
 - partially metabolized in the liver
 - largely excreted unchanged in the kidneys
- Direct intrathecal baclofen permits effective CSF concentration to be achieved with resultant plasma concentration **100 times** less than those occurring with oral administration

Screening Test Flow Chart



Surgical implantation procedure

- Implanted in subcutaneous or subfascial pocket in anterior abdominal wall
- Catheter is threaded to enter lumbar subarachnoid space at L3-4 or L4-5, and advanced superiorly
 - CP spastic diplegia: T10-12
 - CP spastic quadriplegia: C7-T2
 - Generalized secondary dystonia: cervical



intrathecal baclofen pump system

Outcomes of intrathecal baclofen therapy in patients with cerebral palsy and acquired brain injury

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Abstract

Intrathecal baclofen (ITB) has been known to reduce spasticity which did not respond to oral medications and botulinum toxin treatment. However, few results have been reported comparing the effects of ITB therapy in patients with cerebral palsy (CP) and acquired brain injury. This study aimed to investigate beneficial and adverse effects of ITB bolus injection and pump therapy in patients with CP and to compare outcomes to patients with acquired brain injury such as traumatic brain injury and hypoxic brain injury. ITB test trials were performed in 37 patients (19 CP and 18 acquired brain injury). Based on ambulatory function, CP patients were divided into 2 groups: 11 patients with nonambulatory CP and 8 patients with ambulatory CP. Change of spasticity was evaluated using the Modified Ashworth Scale. Additional positive or negative effects were also evaluated after ITB bolus injection. In patients who received ITB pump implantation, outcomes of spasticity, subjective satisfaction and adverse events were evaluated until 12 months post-treatment. After ITB bolus injection, 32 patients (86.5%) (CP 84.2% versus acquired brain injury 88.9%) showed a positive response of reducing spasticity. However, 8 patients with CP had negative adverse effects. Particularly, 3 ambulatory CP patients showed standing impairment and 1 ambulatory CP patient showed impaired gait pattern such as foot drop because of excessive reduction of lower extremity muscle tone. Ambulatory CP patients received ITB pump implantation less than patients with acquired brain injury after ITB test trials ($P = .003$ by a chi-squared test). After the pump implantation, spasticity was significantly reduced within 1 month and the effect maintained for 12 months. Seventeen patients or their caregivers (73.9%) were very satisfied, whereas 5 patients (21.7%) suffered from adverse events showed no subjective satisfaction. In conclusion, ITB therapy was effective in reducing spasticity in patients with CP and acquired brain injury. Before ITB pump implantation, it seems necessary to perform the ITB bolus injection to verify beneficial effects and adverse effects especially in ambulatory CP.

Abbreviations: CP = cerebral palsy, ITB = intrathecal baclofen.

Keywords: acquired brain injury, cerebral palsy, intrathecal baclofen, spasticity

Table 1**Baseline characteristics in patients with CP and acquired brain injury.**

	Nonambulatory CP (N = 11)	Ambulatory CP (N = 8)	Acquired brain injury (N = 18)
Sex, M:F	9: 2	5: 3	16: 2
Age, years	36.6 ± 2.5	34.1 ± 3.9	33.7 ± 3.6
BMI	19.4 ± 1.6	22.3 ± 1.1	18.4 ± 0.6
Duration, years	36.6 ± 2.5	34.1 ± 3.9	1.7 ± 0.4*
MAS			
Upper extremity	4.1 ± 0.2	2.6 ± 0.7 [†]	3.6 ± 0.3
Lower extremity	4.2 ± 0.2	2.5 ± 0.5 [†]	3.8 ± 0.3
FIM	54.7 ± 7.1	90.6 ± 11.1*	18.2 ± 0.2
MBI	20.5 ± 5.7	58.1 ± 13.4*	0
ITBP: No ITBP	7: 4	1: 7	15: 3

BMI = body mass index, FIM = functional independence measure, ITBP = intrathecal baclofen pump, MAS = modified Ashworth scale, MBI = modified Barthel index.

* $P < .05$ compared with the other groups.

[†] $P < .05$ compared with nonambulatory CP.

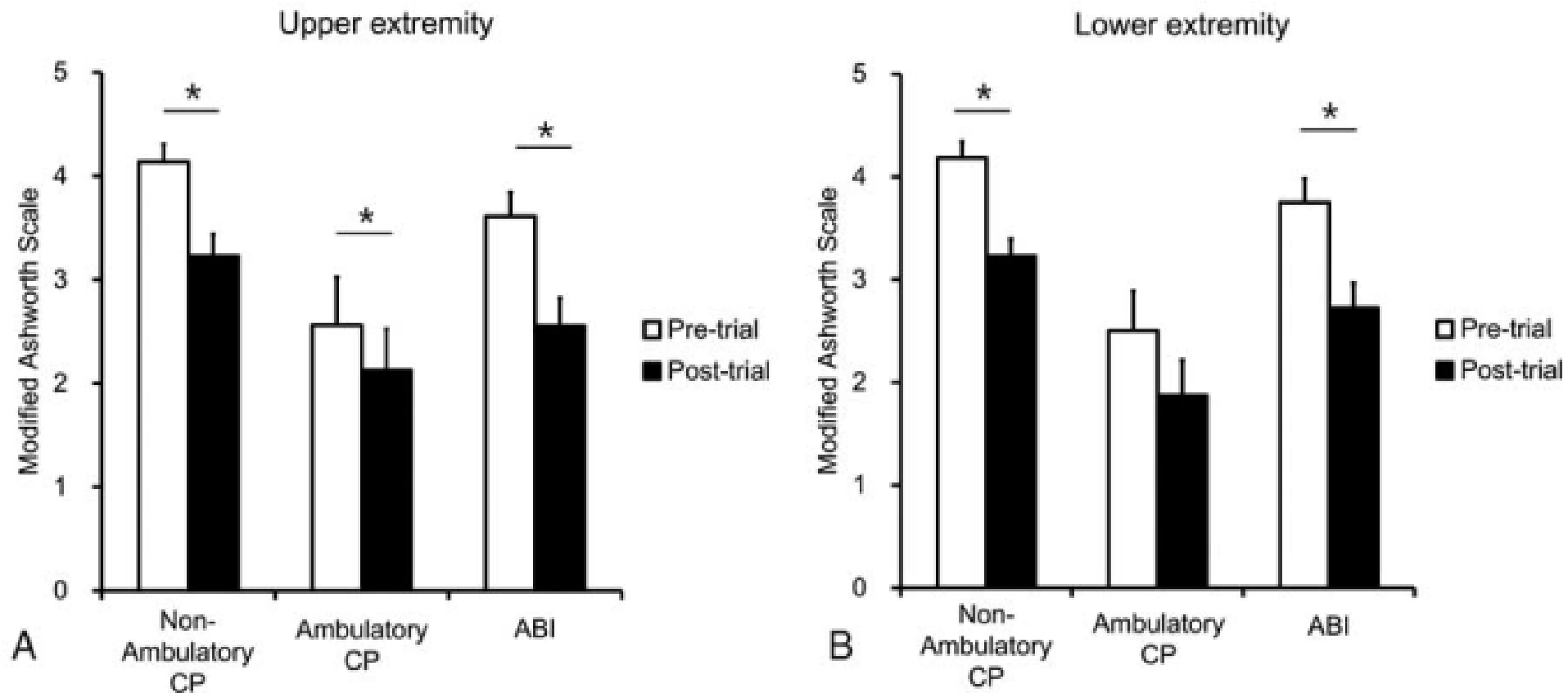
Table 2**Baseline characteristics in the ITBP Group and No ITBP Group.**

	ITBP group (N = 23)	No ITBP group (N = 14)	Total (N = 37)
Sex, M: F	20: 3	10: 4	30: 7
Age, years	36.0 ± 2.7	32.3 ± 3.1	34.7 ± 2.1
BMI	18.6 ± 0.6	21.4 ± 1.4	19.6 ± 0.7
Duration, years	14.8 ± 4.0*	26.0 ± 4.5	19.1 ± 3.1
MAS			
Upper extremity	3.8 ± 0.2	3.1 ± 0.4	3.5 ± 0.2
Lower extremity	3.9 ± 0.3	3.1 ± 0.4	3.6 ± 0.2
FIM	30.0 ± 5.2*	65.4 ± 12.1	41.1 ± 5.9
MBI	10.3 ± 3.9*	35.1 ± 11.8	18.1 ± 5.0
CP: ABI	8: 15	11: 3	

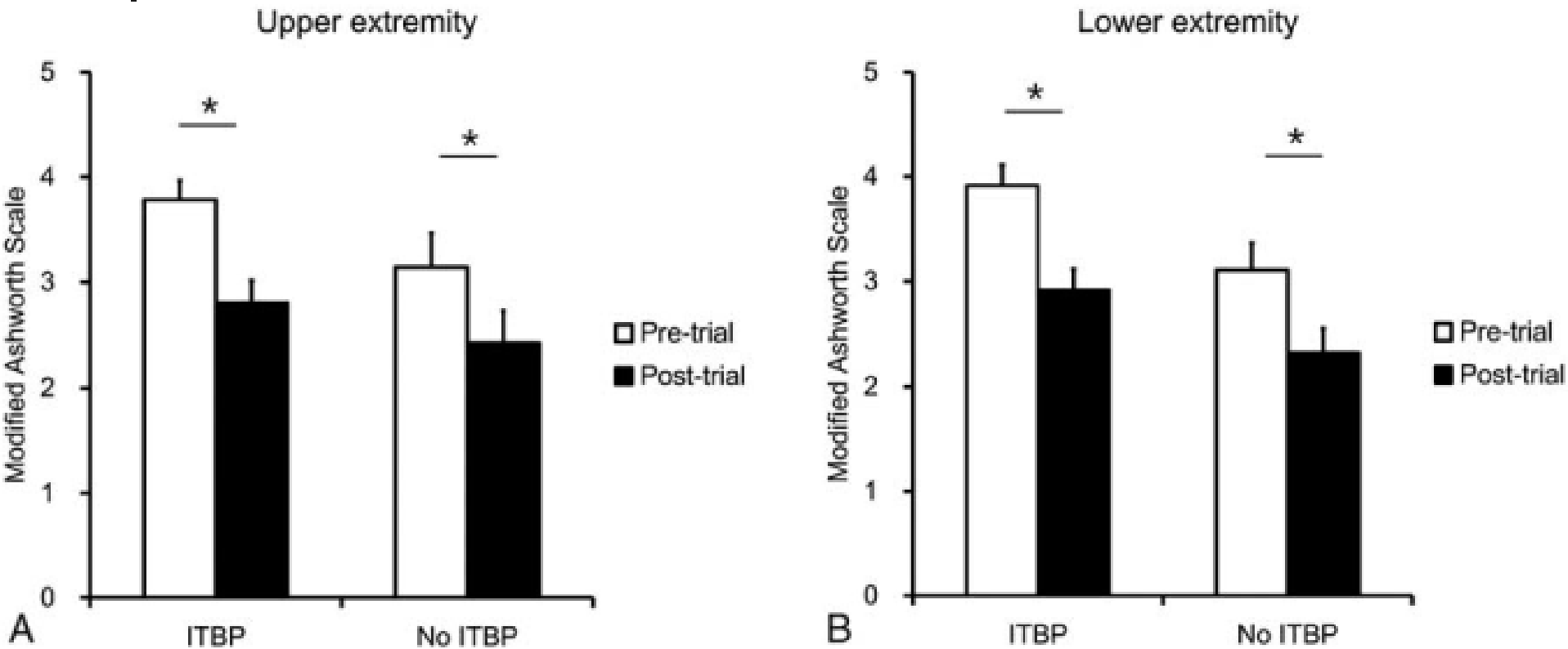
BMI = body mass index, FIM = functional independence measure, ITBP = intrathecal baclofen pump, MAS = modified Ashworth scale, MBI = modified Barthel index.

* $P < .05$ compared with no ITBP group. Values are presented as mean ± SE.

Effects of intrathecal baclofen bolus injection in CP and acquired brain injury



Effects of intrathecal baclofen bolus injection in ITBP and no ITBP groups



Outcomes of the ITB test trials (N=37)




Positive effects

- Decreased spasticity (MAS) 32 (86.5%)
- Decreased dystonic movement 8 (21.6%)
- Decreased chronic pain 6 (16.2%)
- Decreased excessive sweating 4 (10.8%)
- Improved sitting posture 4 (10.8%)
- Improved sleep pattern 3 (8.1%)

Negative effects

- Impaired standing 3 (8.1%)
- Impaired gait pattern 1 (2.7%)
- Voiding difficulty 1 (2.7%)
- Dysarthria 1 (2.7%)
- Headache, Nausea, Vomiting 1 (2.7%)
- Posterior neck pain 1 (2.7%)

Process to ITBP implantation after the ITB test trials



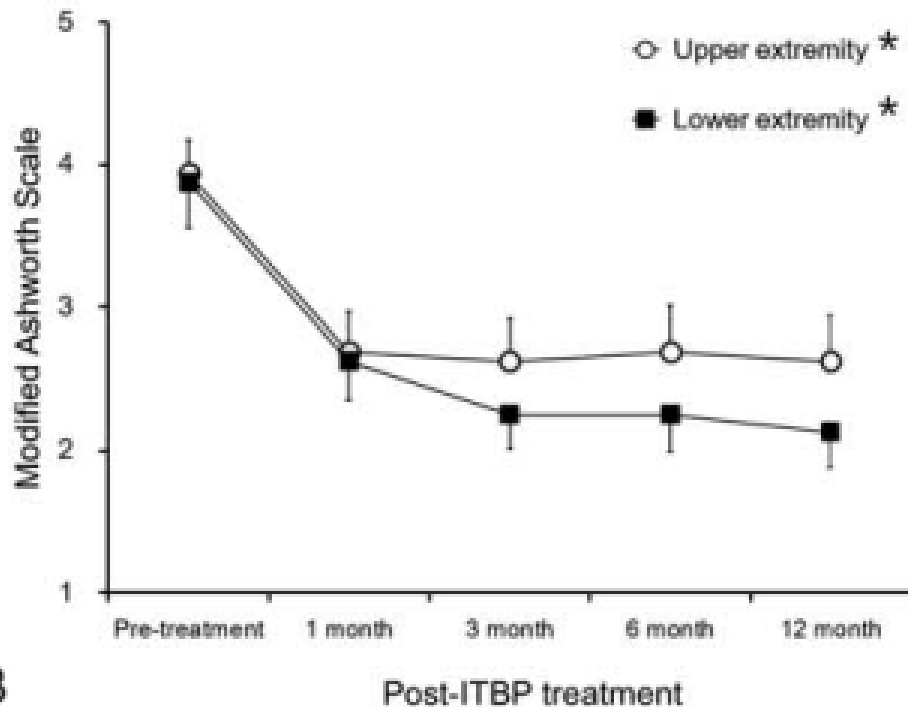
Diagnosis	ITBP (N=23)	No ITBP (N=14)	Total (N=37)
Cerebral Palsy	8 (42.1%)	11 (57.9%)	19 (100%)
Non-ambulatory CP	7	4	11
Ambulatory CP	1	7	8
Acquired Brain Injury	15 (83.3%)	3 (16.7%)	18 (100%)
Hypoxic Brain Injury	4	1	5
Traumatic Brain Injury	11	2	13

ITBP 62.2% vs. no ITBP 37.8%

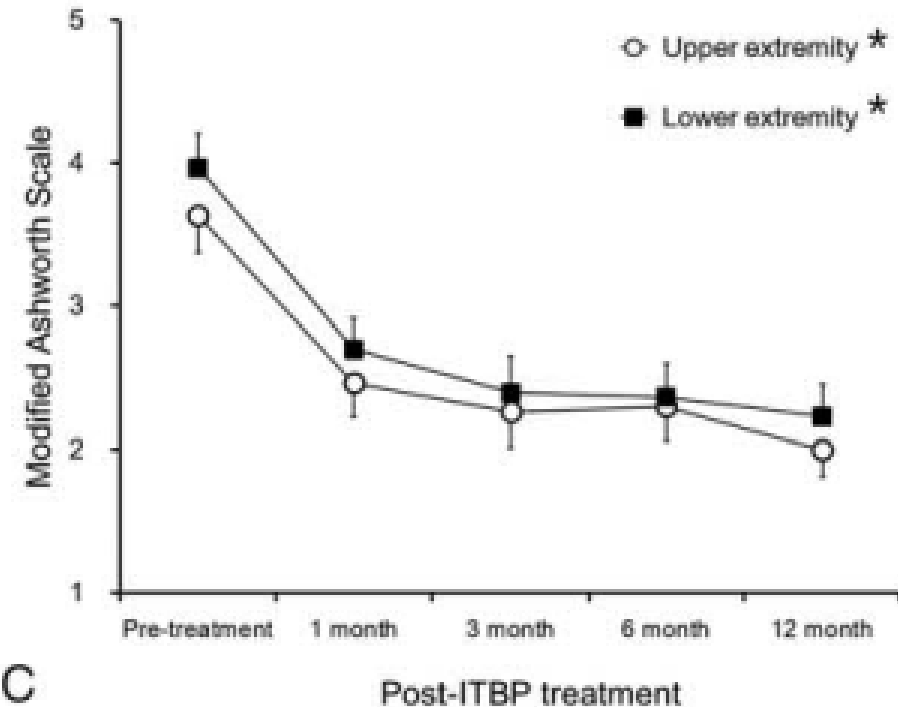
$P=.003$ by a chi-squared test

Effects of intrathecal baclofen pump implantation

CP



Acquired Brain Injury



Responses of subjects with intrathecal baclofen pump implantation.

Case		Spasticity (MAS)					Adverse events	Satisfaction (10-point grading scale)
		Pre	1 month	3 months	6 months	12 months		
Traumatic brain injury	Upper	4/3	3/3	1/1	1/1	1/1	Decreased sitting balance	Caregiver 9
	Lower	4/4	3/4	1/1	1/1	1/1		
Traumatic brain injury	Upper	4/4	3/3	3/3	3/3	3/3	Catheter disconnection Withdrawal symptoms	Caregiver 0
	Lower	4/4	4/4	4/4	4/4	4/4		
Traumatic brain injury	Upper	5/5	5/4	5/5	5/5	2/2		Caregiver 9
	Lower	5/5	4/4	3/4	3/4	3/3		
Traumatic brain injury	Upper	4/4	3/4	4/4	3/3	4/3		Caregiver 9
	Lower	5/5	3/4	4/4	4/4	3/3		
Traumatic brain injury	Upper	4/1	1/1	1/1	1/1	1/1		Caregiver 8
	Lower	1/1	1/1	1/1	1/1	1/1		
Traumatic brain injury	Upper	5/1	1/1	1/1	1/1	1/1		Patient 9
	Lower	5/5	3/3	3/3	3/3	3/3		
Traumatic brain injury	Upper	1/1	1/1	1/1	1/1	1/1		Caregiver 9
	Lower	4/4	2/2	2/2	2/2	2/2		
Traumatic brain injury	Upper	3/3	1/1	1/1	1/1	1/1		Caregiver 9
	Lower	4/4	2/2	2/2	1/1	1/1		
Traumatic brain injury	Upper	3/3	3/2	3/2	3/2	3/2		Caregiver 8
	Lower	3/3	3/3	3/3	3/3	3/3		
Traumatic brain injury	Upper	5/5	1/2	1/0	1/1	0/1		Caregiver 9
	Lower	5/5	1/2	0/0	1/1	0/1		
Traumatic brain injury	Upper	3/3	1/1	2/2	2/2	2/2	Drowsiness	Caregiver 0
	Lower	2/1	1/1	2/0	2/0	2/0		
Hypoxic brain injury	Upper	4/1	3/3	3/3	4/3	3/2	Wound infection	Caregiver 9
	Lower	3/3	1/1	1/1	1/1	1/1		
Hypoxic brain injury	Upper	5/5	4/4	4/1	4/3	3/3	Wound dehiscence Catheter disconnection	Caregiver 0
	Lower	5/5	4/4	3/4	4/4	4/4		
Hypoxic brain injury	Upper	5/5	4/4	3/4	3/3	3/3		Caregiver 7
	Lower	5/5	4/4	4/4	3/3	3/3		
Hypoxic brain injury	Upper	5/5	3/3	3/3	3/3	3/3		Caregiver 9
	Lower	5/5	3/3	3/3	3/3	3/3		

Table 4**Responses of subjects with intrathecal baclofen pump implantation.**

Case		Spasticity (MAS)					Adverse events	Satisfaction (10-point grading scale)
		Pre	1 month	3 months	6 months	12 months		
Nonambulatory CP	Upper	4/4	3/1	3/1	3/1	3/1	Headache	Caregiver 9
	Lower	4/4	3/3	3/3	3/3	3/3		
Nonambulatory CP	Upper	4/4	3/3	4/4	3/3	3/3	Drowsiness Impaired standing balance	Caregiver 0
	Lower	4/4	3/3	3/3	1/1	1/1		
Nonambulatory CP	Upper	5/5	4/3	4/3	4/3	3/3		Patient 7
	Lower	5/5	1/1	1/1	1/1	1/1		
Nonambulatory CP	Upper	2/4	1/3	1/2	1/2	1/2	CSF leakage	Patient 0
	Lower	4/4	4/3	1/2	1/2	1/2		
Nonambulatory CP	Upper	3/3	1/1	1/1	1/1	1/1		Patient 7
	Lower	4/4	3/3	3/3	3/3	2/2		
Nonambulatory CP	Upper	5/5	4/4	3/4	3/4	3/4		Patient 8
	Lower	5/5	4/4	3/3	3/3	3/3		
Nonambulatory CP	Upper	5/4	3/3	3/2	3/2	3/2		Caregiver 8
	Lower	3/5	2/3	2/3	3/4	3/4		
Ambulatory CP	Upper	3/3	3/3	3/3	4/5	4/5		Patient 3
	Lower	1/1	1/1	1/1	2/2	2/2		

Among 23 patients with ITBP

Very satisfied -17 (73.9%)

Somewhat satisfied - 1 (4.3%)

No satisfaction - 5 (21.7%)

Among 37 patients with ITB test trials

Very satisfied - 17 (45.9%)

Satisfied - 18 (48.6%)



Conclusions

- After intrathecal baclofen therapy,
 - Control severe spasticity & dystonia
 - Control chronic pain & excessive sweating
 - Improve sitting posture & sleep pattern
 - Improve function in specific patients
- Through intrathecal baclofen test trials,
 - evaluate positive beneficial & negative adverse effects

2014 척수강내 약물주입펌프이식술 (PUMP) 보험급여 혜택

Ref) 건강보험요양급여비용 (2014년 7월판) 사단법인대한병원협회 / 보건복지부 고시 제2014-84호

항 목	자-484 척수강내 약물주입펌프이식술 (Implantation of Intrathecal Drug Infusion Pump)
제 목 1	자-484 척수강내 약물주입펌프이식술의 세부사항 인정기준
세 부 인 정 사 항	<p>척수강내 약물주입펌프이식술은 다음과 같은 경우에 요양급여를 인정함.</p> <p style="text-align: center;">[다 음]</p> <p>가. 6개월 이상의 적절한 통증치료(약물치료와 신경차단술 등)에도 효과가 없고, 심한 통증(VAS 통증점수 7 이상)이 지속되는 불인성 통증이 있는 경우</p> <p>나. 고용량의 모르핀(1일 200mg) 경구투여나 또는 동등 역가의 타 마약성 진통제 투여를 하였음에도 통증이 제어되지 않는 암성통증(VAS 통증점수 7 이상)으로 여명이 1년 이상으로 예상되는 경우</p> <p>다. 모르핀 또는 타 마약성 진통제의 부작용 등 약물투여를 할 수 없는 암성통증(VAS 통증점수 7 이상)으로 여명이 1년 이상으로 예상되는 경우</p> <p>라. 적절한 경직치료(약물치료 등)에도 불구하고 경직척도(MAS)가 하지 3등급 이상 또는 상지 2등급 이상인 중추신경계 손상에 의한 경직(spasticity)으로 시험적 약물주입술에서 1등급 이상 호전된 경우</p>