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# Intrathecal Baclofen Therapy for Adults with Spinal Spasticity: Therapeutic Efficacy and Effect on Hospital Admissions

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**ABSTRACT:** A prospective trial to demonstrate the efficacy of intrathecal baclofen therapy by implanted pump for adults with spasticity due to spinal cord injury or multiple sclerosis was initiated in our hospital. Of the 140 patients assessed, 7 met the following criteria for inclusion in the study: a modified Ashworth score > 3, a spasm frequency score > 2, and an inadequate response to oral anti-spasticity drugs, (i.e., baclofen, clonidine and cyproheptadine). All patients responded to intrathecal bolus injection of baclofen in the double blind, placebo-controlled screening phase (mean bolus dose = 42.8 µg). Programmable Medtronic pumps were implanted in 4 patients while 3 patients received non-programmable Infusaid pumps. Post-implantation, a marked decrease in spasticity occurred with a significant reduction of the Ashworth score (mean = 1.8,  $p < .005$ ), a reduced spasm score (mean = 0.8,  $p < .005$ ), and an improved leg swing in the pendulum test. These effects were maintained during a follow-up of 24 - 41 months (average infusion dose = 218.7 µg/day). The gross cost-savings due to reduced hospitalizations related to spasticity was calculated by comparing the cost for the two year period before pump implantation to the same period after treatment for 6 of the 7 patients. The cost of in-hospital implantation as well as the cost of the pumps were deducted from the gross savings. There was a net cost-saving of \$153,120. Our findings agree with the reported efficacy and safety of intrathecal baclofen treatment, and illustrate the cost-effectiveness of this treatment.

**RÉSUMÉ:** Le baclofen intrathécal chez les adultes avec spasticité spinale: efficacité thérapeutique et conséquences sur les admissions hospitalières. Cette étude prospective avait pour but de démontrer l'efficacité du baclofen intrathécal, administré au moyen d'une pompe, chez des adultes avec spasticité due à un traumatisme de la moelle épinière ou à la sclérose en plaques. Des 140 patients évalués, seulement 7 répondaient à nos critères d'inclusion au projet soit: pointage à l'échelle Ashworth modifiée > 3, pointage de la fréquence des spasmes > 2, réponse inadéquate aux médicaments antispastiques oraux tels que le baclofen, la clonidine et la cyproheptadine. Tous les sujets ont répondu à l'injection d'un bolus intrathécal de baclofen dans la phase de sélection impliquant une épreuve à double insu avec placebo (dose moyenne du bolus: 42.8 µg). La pompe programmable Medtronic a été implantée chez 4 patients et la pompe non programmable Infusaid chez 3 patients. Suite à l'implantation, nous avons observé une diminution remarquable de la spasticité, une réduction significative du pointage à l'échelle Ashworth (moyenne 1.8,  $p < 0.005$ ) et de la fréquence des spasmes (moyenne 0.8), ainsi qu'une augmentation de l'amplitude du mouvement de la jambe dans l'épreuve pendulaire. Ces effets ont été maintenus pendant une période de 24 à 41 mois avec une dose d'infusion moyenne de 218.7 µg/jour. Le coût total des soins hospitaliers pendant les deux ans qui ont précédé l'implantation de la pompe a été comparé au coût total de ces soins pendant les deux années suivant l'implantation chez 6 des 7 patients. Du montant brut épargné suite à une réduction des hospitalisations reliées à la spasticité on a soustrait le coût de l'implantation en milieu hospitalier ainsi que le coût des pompes. Le montant net épargné est de \$153,120. Nos résultats sont en accord avec des études antérieures démontrant l'efficacité et la sécurité de cette méthode de traitement. De plus, nous démontrons ses avantages économiques.

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One of the better known inhibitory transmitters in the central nervous system is gamma aminobutyric acid (GABA). Baclofen is a GABA<sub>B</sub> receptor agonist that has been used as an oral medication for the treatment of spasticity since its introduction in Europe in 1966.<sup>1,2</sup> Although oral baclofen has been shown to be effective,<sup>1-15</sup> when given intrathecally, it has a more potent effect requiring approximately 1/100th of the oral dose. The development of

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reliable implantable drug delivery systems has permitted baclofen to be administered by chronic slow infusion into the intrathecal space. Several studies, most of which were conducted in the United States and Europe, have demonstrated the effectiveness of intrathecal baclofen for the treatment of spasticity.<sup>16-25</sup> However, intrathecal baclofen therapy is still considered investigational in Canada. Considering the costs of the pumps and associated components (currently approximately \$7000 per patient) and the ever increasing constraints on health care resources, both the therapeutic effectiveness and health-cost effectiveness of this new treatment needed to be evaluated. Thus, the purpose of this prospective study is to confirm the therapeutic effectiveness of this treatment on patients with severe spasticity resulting from injury to the spinal cord. In addition, a retrospective analysis was performed to examine the effect of the treatment on the need for hospitalization. In the present study, the results of using intrathecal baclofen to treat 7 adults suffering from severe spasticity are reported. Preliminary results have been presented previously.<sup>26</sup>

## METHODS AND MATERIALS

The protocol was approved by the University of Manitoba Human Ethics Committee and the Health Sciences Centre Research Committee. Approval for the use of intrathecal baclofen as a new investigational drug was obtained from the Health Protection Branch, Ottawa. Each subject signed an informed consent form.

### Pre-screening phase

#### Patient selection

Over a three year period, 140 patients were referred to our clinic because of severe spasticity due to spinal cord injury (SCI) or multiple sclerosis, their neurologic impairment was assessed in terms of a spinal level (sensory or motor) and the completeness of the spinal level as a Frankel grade.<sup>27</sup> The Frankel grades used are as follows: A) no voluntary motor or sensory function below the level of the spinal cord injury; B) some sensory function, but no motor function evident below the level of injury; C) motor function below the level of injury which is not functional; and D) motor function below the level of the injury which is functional.

Patients were considered candidates for intrathecal baclofen therapy if their spasticity had been unremitting for at least 12 months and a satisfactory reduction in spasticity, after oral medication, had not been achieved. Since most patients required oral antispasticity treatment, we attempted to optimize their antispastic therapy with either oral baclofen, clonidine or cyproheptadine, alone or in combination, according to individual requirements. The maximum doses prescribed were as follows: clonidine (0.025 mg twice daily), cyproheptadine (8 mg four times daily), and baclofen (20 mg four times daily). Once patients had achieved their best response to oral medication, baseline measurements of the degree of spasticity were determined. The primary dependent measures were the clinical assessment of leg tone using a modified Ashworth score<sup>15,28</sup> (see Table 1), and the amplitude of the knee swing by a videomotion analysis of the pendulum test.<sup>29</sup> The secondary dependent measure was a self-reported spontaneous spasm frequency score<sup>19</sup> (see Table 2).

The Ashworth score was determined with the patient in a supine position. The patient's leg was moved by a single

**Table 1.** Modified Ashworth Scale

1 = No increase in tone
2 = Slight increase in tone, giving a "catch"
3 = More marked increase in tone but limb easily moved
4 = Considerable increase in tone - passive movement difficult
5 = Limb rigid in flexion or extension

**Table 2.** Spasm Frequency Score

0 = No spasms
1 = Mild spasms induced by stimulation
2 = Infrequent full spasms occurring less than once per hour
3 = Spasms occurring more than once per hour
4 = Spasms occurring more than 10 times per hour

experienced examiner through the available range of motion to assess the following passive movements: hip flexion/extension, hip adduction/abduction, knee flexion/extension, and ankle flexion/extension. Patients were accepted for the screening trial if the spasm score was > 2 and the average Ashworth score in the lower limb was > 3.

#### Pendulum test

The pendulum test assessed the ability of the leg to passively swing in a pendular manner at the knee. One inch styrofoam hemispheres covered with reflective tape were positioned on each patient over the following points: greater trochanter, lateral aspect of the knee joint line (mid-point), and lateral malleolus. During the videotape recording of the pendulum test, a high intensity halogen light source was directed toward the patient.

Each patient was comfortably positioned on a padded examination table in a supine position such that the leg was allowed to dangle, unsupported over the edge of the table. The right foot of the patient was elevated slowly by the examiner such that the knee was moved to full passive extension. The foot was released and allowed to swing freely at the knee. The test was performed three times. The video motion analysis was accomplished by using a Peak Performance 2D video motion analysis system. The movements of the reflective tape covered markers were digitized and the angular displacement and velocity of the knee were analyzed. The amplitude of the first knee swing was operationally defined as the difference of knee angle in full extension compared to the angle of knee flexion at which the knee angle velocity became zero and the leg began to move in the opposite direction within 1 second of foot support release.

The advantage of using a quantified pendulum test to assess changes in leg tone is that it provides an objective measurement, sensitive to any changes brought about by antispasticity treatment.<sup>30</sup>

#### Bladder and respiratory functions

Bladder and respiratory function in these patients was assessed before implantation of the baclofen pump and 3 months post-implantation. The bladder capacity was determined by the volume of fluid contained in the bladder when the intracystic pressure was observed to suddenly rise in association with either voiding around the catheter or dyssynergic urethral sphincter activity as

monitored by electromyography.<sup>31</sup> Respiratory function was assessed by the following standard spirometric measurements: forced vital capacity (FVC), forced expiratory volume in one second (FEV<sub>1.0</sub>), inspiratory capacity (IC),<sup>32</sup> and maximum inspiratory mouth pressure measured at residual volume (Pimax).<sup>33</sup>

### Screening phase

Under local anesthesia, a temporary subcutaneous access port was implanted in the ventrolateral abdominal wall and an attached catheter was directed circumferentially under the skin into the lumbar subarachnoid space. The catheter position and patency of the spinal subarachnoid space was confirmed by monitoring the distribution of Indium 111 DPTA following its injection into the access port.<sup>34</sup> During the double blinded screening phase, patients received daily bolus injections of either baclofen or placebo. Leg muscle tone was measured before the injection and at 30 minutes and 1, 2, 4, 8 and 24 hours after the injection by a single observer. Neither the observer nor the patient had knowledge of the injection content (i.e., baclofen or placebo). The minimum baclofen bolus dose was 12.5 µg and increased in subsequent trials to 25, 50, 75 and 100 µg as necessary to achieve a therapeutic response. A therapeutic response was defined as a decrease in the Ashworth and spasm scores by 1 full grade.

### Pump implantation and follow-up

Patients demonstrating a therapeutic response during the screening phase received either a programmable battery powered (Synchromed, Medtronic Inc.<sup>35</sup>) pump, or a nonprogrammable vapour pressure powered infusion pump (Infusaid Inc.<sup>36</sup>). At the time of pump implantation, the access port was removed from its subcutaneous pocket in the abdominal wall and was replaced by a pump which was then connected to the lumbar intrathecal catheter. After determining the optimal daily infusion dose (initially set at 2 times the therapeutic bolus dose), patients were discharged from hospital and returned to the clinic every 30 days for reassessment of spasticity and refilling of the pump reservoir with baclofen. The Synchromed pump reservoir holds 18 ml. The Infusaid pump reservoir holds 48 ml.

### Statistical Analysis

Statistical analyses were carried out using the analysis of variance (ANOVA) with simple effects applied post hoc<sup>37</sup> (Anova, version 1.1, Clear Lake Research, Tulsa, Oklahoma).

### Hospitalization Cost Analysis

The cost of in-hospital treatment for problems directly related to spasticity for a two year period before intrathecal baclofen pump implantation was compared to the same period after initiation of therapy. A hospitalization related to spasticity was deemed to have occurred when the history revealed that spasticity was causally related to the reason for admission. When medical problems other than spasticity were treated concurrently during the course of a particular admission it was sometimes difficult to determine the proportion of the stay that should be attributed to the treatment of spasticity alone. Therefore, in addition to reviewing the chart, the attending physician was consulted in an effort to clarify the reasons for ongoing hospitalization and estimate the proportion of the stay that was attributable to spasticity. The cost of hospitalization was derived by multiplica-

tion of the number of in-patient days with the current cost per day for hospitalization in the Health Sciences Centre in Winnipeg, \$813.00 per day. In Manitoba, the daily hospital rate of \$813 is all inclusive for all hospital-based resources except for special areas such as the Intensive Care Unit. The cost of the infusion devices as well as the cost of the days in hospital for the screening phase, implantation and for the treatment of any complications were then subtracted, resulting in our estimate of the net cost-saving. The Manitoba Health Services Commission corroborated these data for each patient.

### RESULTS

Of the 140 patients initially referred, treatment of aggravating factors such as bladder infection, poor urinary drainage, bladder stones, constipation, leg fracture, anal fistula and skin ulceration, decreased the spasticity in 38 patients. Optimization of oral antispastic medication with either baclofen, clonidine or cyproheptadine resulted in improvement in another 92 patients. Ten patients met the criteria for entry into the screening phase of the study; 2 of these did not wish to have a treatment that required surgery, and 1 patient lived 400 km from the study site. Of the 133 patients who did not enter this study, 20 had multiple sclerosis (13 females and 7 males with mean ages of 46 and 55, respectively, and Ashworth scores of 3.5 and 2.9, respectively). The remaining 113 patients had SCI; 54 had Frankel A SCI (3 females and 51 males with mean ages of 36.5 and 36 respectively, and Ashworth scores of 1.9 and 2.7, respectively; and 59 had Frankel B, C or D SCI (13 females and 46 males with mean ages of 37 and 43, respectively, and Ashworth scores of 2.8 and 2.5, respectively).

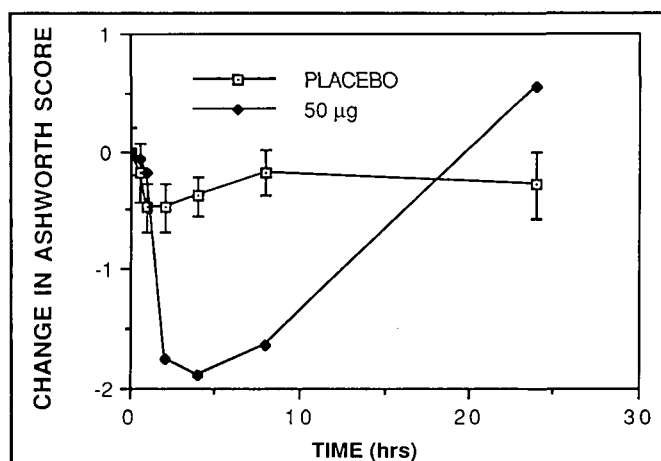
All 7 patients entering the screening phase completed the final phase of the study which included the implantation of the intrathecal drug delivery device. The level, Frankel grade and duration of spinal cord injury, as well as the gender, age and baclofen dosage for the screening bolus and current 24 hour infusion are summarized for each patient in Table 3. All patients utilized wheelchairs for mobilization. Four patients were implanted with the Synchromed Medtronic pump and three with the Infusaid pump.

The responses of patient 7 to intrathecal injections are shown in Figure 1. Intrathecal placebo (0.9% sodium chloride) injection had a brief but therapeutically insignificant antispasticity effect, whereas 50 µg of intrathecal baclofen decreased the average Ashworth score. A therapeutic response, defined as a decline in the average Ashworth score by at least 1 unit, was obtained in all 7 patients (mean maximum change in the Ashworth score following baclofen injection was a decrease of 2.5 units). No patient showed a therapeutic response after injection of 12.5 µg of baclofen. Two patients responded to 25 µg, three patients responded to 50 µg and two patients responded to 100 µg of intrathecal baclofen. The mean bolus dose eliciting a therapeutic response was 42.8 µg.

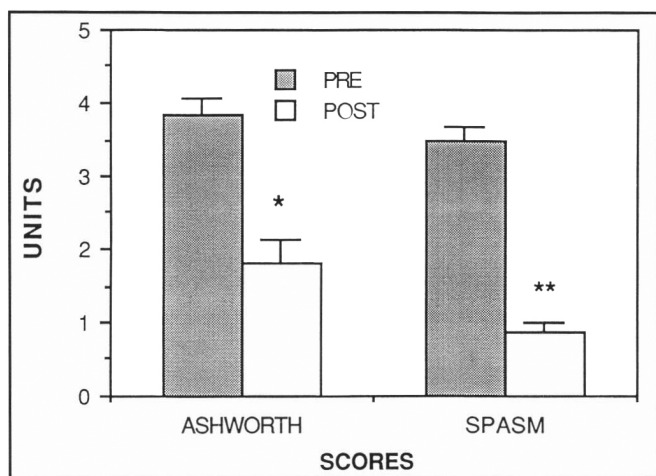
Chronic continuous infusion of intrathecal baclofen by means of an implanted pump markedly reduced the mean Ashworth and spasm frequency scores from 3.840 +/- 0.23 and 3.50 +/- 0.19, respectively, before pump implantation, to 1.80 +/- 0.32 and 0.860 +/- 0.14, respectively, seven days after pump implantation ( $p < .005$  for both comparisons). Figure 2 demonstrates the change in average Ashworth scores and spasm frequency scores before

**Table 3.** Subject Demographics and Baclofen Dosage

Subject	SCI level	Frankel	Injury duration(yrs)	Treatment duration(mths)	Gender	Age(yrs)	Baclofen Dose ( $\mu$ g)	
							Bolus	Current
#1	T8	B	23	41	Male	39	100	308.1
#2	MS T8	A	7	39	Male	39	50	237.5
#3	MS	C	17	35	Female	37	50	203.8
#4	C5(R), C6(L)	A	6	34	Male	46	100	220.0
#5	C5(R), C6(L)	B	4	31	Male	41	25	70.9
#6	C7(R), C8(L)	B	18	27	Male	34	25	286.2
#7	C5	B	8	24	Male	35	50	204.6
Mean			12	33		38.7	57	218.7



**Figure 1:** Dose-effect responses of patient 7 to bolus injections. The values are derived by subtracting each averaged Ashworth score post-injection from the pre-injection score at the beginning of each trial. Values for placebo are means of 3 trials  $\pm$  SE, indicated by bars.



**Figure 2:** The effect of intrathecal baclofen by implanted pump infusion on the Ashworth score and spasm frequency score pre-treatment (closed bars) compared to 3 months post-treatment (open bars),  $p = .0019$  and  $p = .0001$  respectively.

and after treatment. The decrease in tone and spasm scores was maintained in all patients during the follow-up period ranging from 24 to 41 months (mean 33.3 months).

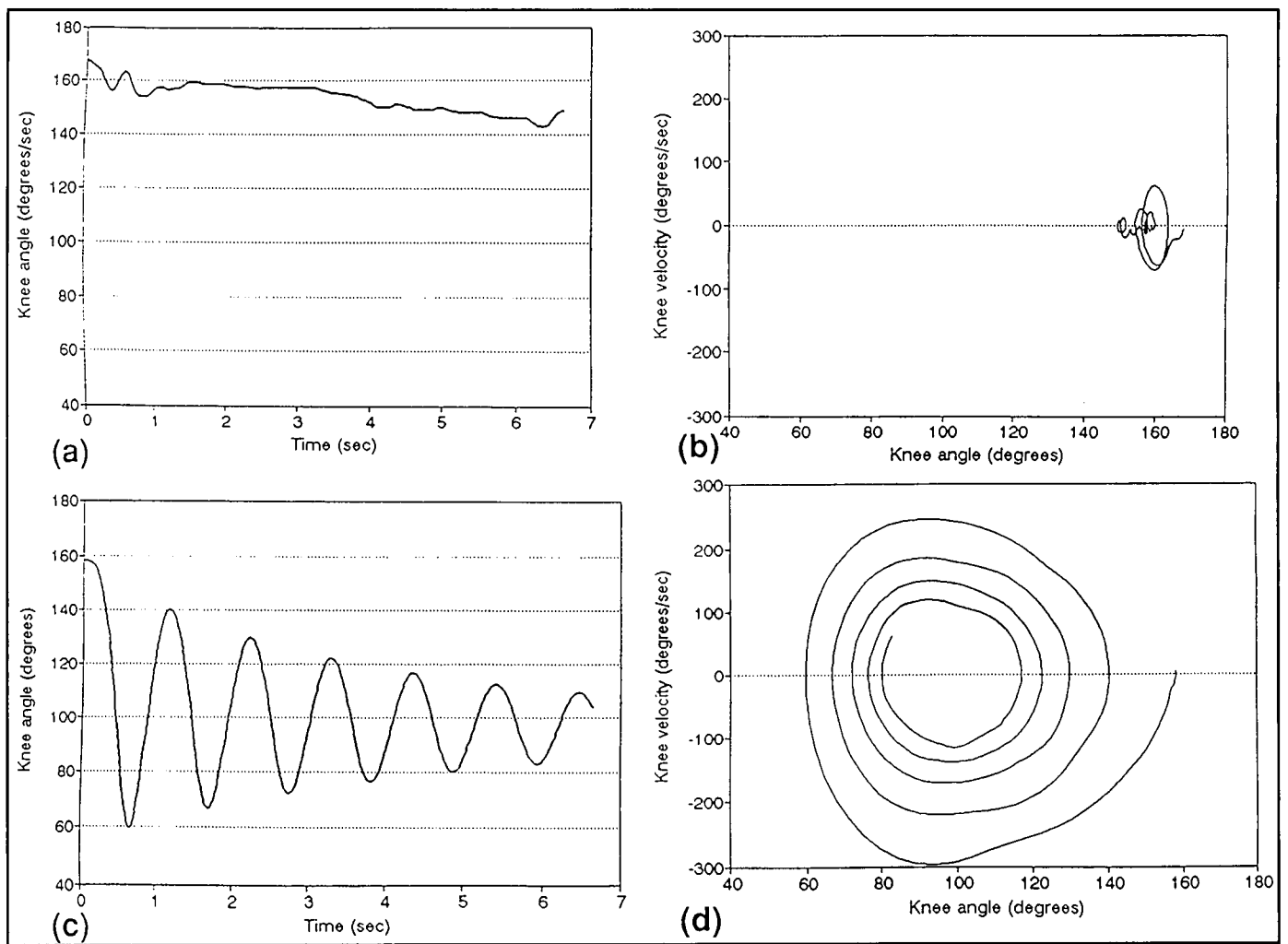
The effect of chronic infusion of intrathecal baclofen on resting leg tone is further illustrated by the results of the pendulum test,

shown in Figures 3 and 4. Resistance to passive movement of the leg was reduced by the infused baclofen. This is shown by an increased angular displacement of the leg (freedom of the leg to swing at the knee) for all leg swings in a pendulum test, such that the amplitude of knee swing of the baclofen treated patients is comparable to able-bodied control subjects for the first three swings and exceeds the controls for the remaining swings. In particular, the amplitude of the first swing increased from a mean of  $28.28 \pm 11.34$  degrees before pump implantation to a mean of  $90.850 \pm 9.83$  degrees after pump-implantation ( $p < .0001$ , see Figure 4).

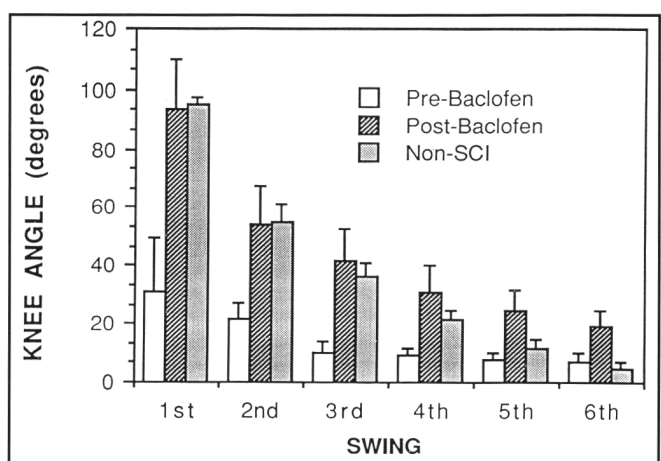
Overall, there was no statistically significant change in any of the bladder or respiratory functions, pre-implantation compared to post-implantation. The mean values ( $\pm$  SE) for the cystometric capacity were  $217.7 \pm 38.5$  ml before baclofen pump implantation, compared to  $275.8 \pm 99.9$  ml after intrathecal baclofen therapy. Four patients used a condom urinary drainage system before intrathecal baclofen therapy with no change after therapy. One patient used intermittent catheterization before and after intrathecal baclofen therapy, but reported needing less oxybutin (Ditropan) to control incontinent episodes. The remaining two patients used indwelling Foley urinary catheters. Both of these patients had urinary drainage problems that remained unchanged by intrathecal baclofen therapy. One patient had frequent leakage around the catheter and received an augmentation cystoplasty with a continent vesicostomy through which intermittent catheterization is now performed. The other patient had difficulty with bladder drainage while sitting upright; a supra-pubic catheter did not improve bladder drainage and indwelling Foley catheterization was resumed.

Table 4 summarizes the results of the respiratory tests. In general, there was no consistent or significant change in respiratory function following intrathecal baclofen therapy compared to before implantation. Of potential concern was the observation that the respiratory parameters for patient 4 decreased considerably after initiation of intrathecal baclofen treatment. This patient's respiratory function after 24 days off intrathecal baclofen therapy was tested again and no change was observed. This patient has no symptoms of respiratory insufficiency, but since the cause of this patient's decrease in FVC, IC and Pimax is currently unclear, long-term respiratory function will be followed.

All subjects reported a marked improvement in their comfort and activities of daily living. One patient regained his ability to transfer from his wheelchair independently. Another patient who



**Figure 3:** Kinematic analysis of the pendulum test in patient 5 before (a, b) and after (c, d) intrathecal baclofen therapy. The obvious improvement in angular displacement of the knee is shown by a greater amplitude of leg swing after treatment (c vs. a). The phase plane plots of angular displacement vs. angular velocity in the treated condition (d) show improvement by the “whirlpool” pattern<sup>47</sup> as compared to the pre-treatment condition (b).



**Figure 4:** The effects of intrathecal baclofen by implanted pump infusion on the angular displacement of the knee in the pendulum test of 7 spinal cord injured subjects before (open bars) vs. 3 months after (hatched bars) intrathecal baclofen,  $p < .0001$ . The average knee swings of 7 age, height and sex matched controls,  $n = 7$  (stippled bars), is shown for comparison.

had not walked for the past 5 years was able to use a functional electrical stimulation system to walk short distances with a walker. One patient was able to return to activities such as wheeling on sidewalks and in shopping malls. Previously, he had been largely housebound because the vibrations encountered over these surfaces were sufficient to provoke spasms that caused him to fall out of his wheelchair. Two patients had a history of chronic skin ulcerations over the ankles, which healed after reduction of limb tone with intrathecal baclofen.

Several complications related to the use of intrathecal baclofen treatment were observed. The occurrence of a displaced intrathecal catheter in patient 1 was confirmed by injection of radio-opaque material through the side-port of the pump. The catheter was then surgically reimplemented. Patient 4 developed a deep vein thrombosis of the right leg 28 days after pump implantation requiring anticoagulation and 12 days of hospitalization. Three months after pump implantation, patient 4 developed an effusion of the left knee from which 12 ml of sterile synovial fluid was removed via needle aspiration without further complication. Two weeks after pump implantation, patient 6 developed a seroma around the pump from which 195 ml of

**Table 4.** Respiratory function tests.

Patient #	Test	FVC <sup>1</sup>	FVC (% pred.)	FEV1.0/FVC	IC <sup>1</sup>	Pimax (cm H <sub>2</sub> O)
1	Pre	4.52	72.00	0.88	2.84	-100.00
	Post	4.17	66.00	0.89	3.23	- 98.00
2	Pre	4.12	85.00	0.82	2.91	-122.00
	Post	4.14	86.00	0.80	2.86	-128.00
3	Pre	2.04	56.50	0.87	1.18	- 25.00
	Post	2.06	57.00	0.80	1.45	- 20.00
4	Pre	1.99	39.00	0.75	1.40	- 40.00
	Post	1.25	25.00	0.88	0.79	- 28.00
5	Pre	2.04	30.00	0.91	1.55	- 60.00
	Post	1.66	24.00	0.89	1.26	- 64.00
6	Pre	3.47	60.00	0.84	1.98	- 73.00
	Post	4.12	72.00	0.83	2.32	- 92.00
7	Pre	3.22	55.00	0.86	2.24	- 65.00
	Post	3.07	53.00	0.82	2.64	- 87.00
Mean ± SE	Pre	3.06 ± 2.48	56.79 ± 0.40	0.85 ± 0.02	2.01 ± 0.26	- 69.29 ± 12.59
Mean ± SE	Post	2.92 ± 0.48	54.71 ± 8.78	0.84 ± 0.02	2.08 ± 0.35	- 73.86 ± 14.73

sterile serosanguinous fluid was drained via needle aspiration. Two days later, an additional 95 ml of fluid was removed without further reaccumulation or complication. The position of the pump in patient 7 required rotation because there was skin breakdown from pressure between the edge of the pump and the anterior rim of the pelvis.

The hospitalization cost analysis involved 6 of the 7 patients. Patient 5 was excluded because his spinal cord injury occurred within two years of receiving intrathecal baclofen therapy and his in-patient course in the acute care hospital as well as the course in the rehabilitation hospital were excluded from the analysis. The cost analysis considered only those hospitalization days related to spasticity. Patient 6, for example, was admitted to the hospital prior to pump implantation for the treatment of a full-thickness ulceration of the ankle that was caused by repeated vigorous involuntary abrasion of the ankles; this was considered a hospitalization related to spasticity. The combined number of days in hospital related to spasticity for the 6 patients during the two years prior to implantation was 376 resulting in a total cost of \$305,688. Following initiation of intrathecal baclofen therapy, there were no admissions for spasticity and therefore, no in-patient hospital days. However, there were admissions for the screening phase, implantation, treatment of problems related to the intrathecal drug delivery devices and for problems possibly or probably related to marked reduction of leg muscle tone. The number of days in hospital as described above are presented for each patient in Table 5.

The cost of the 6 pumps (at approximately \$7,000 each) was \$42,000. The number of in-patient days related to implantation of these devices and the commencement of intrathecal baclofen therapy as well as treatment of complications for the 6 patients was 136 days, costing \$110,568. Subtraction of the combined cost of the pumps and hospitalization for treatment-related problems from the cost of hospitalization for spasticity-related problems before intrathecal baclofen therapy, amounted to a net savings of \$153,120.

## DISCUSSION

Only 5% of the 140 patients pre-screened in our spasticity clinic met our criteria for treatment with intrathecal baclofen. Thus, the majority of patients with spasticity can be effectively managed by treatment of aggravating factors and the use of oral antispasticity medications. However, for patients with severe spasticity, our observations are consistent with previous reports from the United States and Europe, demonstrating the effectiveness of chronic intrathecal baclofen infusion, via an implanted pump.<sup>16-24</sup> The main advantages of continuous infusion of baclofen by implanted pump, compared to intermittent intrathecal baclofen by bolus injection, are the sustained effects of the medication and the marked reduction in the risk of meningitis due to the presence of a bacterial filter in the drug delivery device.<sup>35,36</sup>

All seven patients in our study demonstrated that intrathecal baclofen therapy is effective in reducing spasticity. The efficacy of intrathecal baclofen has been demonstrated in this study by the reduction in the average Ashworth score, an improved knee swing in the pendulum test and a reduction in spasm frequency. In addition to markedly improving these clinical measures of muscle tone, intrathecal baclofen improved the quality of life for these patients.

It has been reported previously that intrathecal baclofen can improve bladder function,<sup>38,39</sup> reduce urethral pressure<sup>40</sup> and permit bladder program upgrade.<sup>22,41,42</sup> Similar to a previous clinical study,<sup>43</sup> but in contrast to another,<sup>21</sup> patients in the present study showed no statistically or clinically significant change in bladder capacity. All four patients with condom urinary drainage had urinary sphincterotomy performed in the past, three were quadriplegic with reduced hand dexterity and none wished to attempt conversion to intermittent urinary catheterization. Of the remaining three patients, one has changed bladder management as a result of a urologic surgery unrelated to intrathecal baclofen therapy.

**Table 5.** Hospitalizations (2 years) before and after intrathecal baclofen therapy.

Patient #	1	2	3	4	5	7	Total
<b>Before</b>							
Hospitalizations (related to spasticity)	3	0	1	0	2	5	11
Hospitalized days	74	0	45	0	71	186	376
Cost at \$813 per day	60,162	0	36,585	0	57,723	151,218	\$305,688
<b>After</b>							
Hospitalizations (for implant & treatment of complications)	3	1	1	2	1	2	10
Hospitalized days	33	11	15	33	18	26	136
Cost at \$813 per day	26,829	8,943	12,195	26,829	14,634	21,138	\$110,568
Cost Saving							\$195,120

Since intracisternal injection of baclofen (10-15 µg/kg) to anesthetized cats,<sup>44</sup> high dose intrathecal baclofen treatment (2000 µg) of tetanus,<sup>45</sup> and accidental intrathecal baclofen overdose<sup>20,24,46</sup> have been reported to cause respiratory suppression requiring mechanical ventilation, we prospectively measured the respiratory function of all patients in our study. This represents the first analysis, to date, of the effect of therapeutic doses of intrathecal baclofen on respiratory function. Overall, a consistent or statistically significant change in respiratory function was not observed. As would be expected, Table 4 shows that the FEV<sub>1.0</sub>/FVC ratio for each patient was well above the range for obstructive airway disease. This contrasts with the single report of a patient with severe asthma whose pulmonary function tests improved after intrathecal baclofen.<sup>21</sup> The data from the present study show that, in general, intrathecal baclofen in doses effective for the treatment of lower limb spasticity has little or no effect on pulmonary function; however, one of the seven patients in this study did show an unexplained deterioration.

The use of a temporary access port prior to pump implantation offers a number of advantages. First, it provides an opportunity to determine the optimal dose for subsequent initiation of pump therapy without exposing the patient to the risks of repeated lumbar puncture during the screening phase. Also, the temporary port allows the patient to experience the effect of intrathecal baclofen prior to pump implantation. Since the pumps are expensive and cannot be re-used, it is important to be confident that a patient will be satisfied with the therapy once the pump has been implanted. Another advantage of the temporary access port is that the positioning of the intrathecal catheter and the patency of the spinal subarachnoid space can be conveniently determined by contrast injection, prior to pump implantation. Radionuclide injection exposes the patient to less radiation and a smaller volume of injection than required using conventional radio-opaque contrast myelography. Indium 111 DPTA was used as the radionuclide because, unlike Technecium 99mDPTA, it is pyrogen free.<sup>34</sup>

Since a slight antispasticity effect of placebo injection can be detected by repeated measurement of the Ashworth score, the authors recommend the inclusion of at least one placebo test dose and that the patient be observed for at least two hours, so that the placebo response can be compared to baclofen. The use of fewer placebo test trials than in the present study will contribute to a shorter hospitalization during the screening phase

and therefore further total cost savings. In this study, the first bolus dose injected was 12.5 µg but the smallest effective bolus dose of baclofen was 25 µg. However, Hugenholtz et al. report that some patients respond to lower doses and therefore suggest initial bolus doses of 10 µg in order to avoid potential overdose.<sup>25</sup>

This study has shown that intrathecal baclofen therapy reduces the need for hospitalization for the treatment of problems related to spasticity. While the frequency of such complications can be expected to vary considerably among different patients, the eventual long-term hospitalization cost benefits that may be realized are potentially substantial, since the savings will be cumulative over the years. However, a more complete survey, that includes other health care utilization factors, is necessary before firm conclusions regarding the overall health-cost effectiveness of the treatment can be determined. For instance, the present analysis has not compared costs such as those related to office visits, pharmaceuticals, personal care services, and consultant fees, before and after pump implantation. Similarly, this study has not attempted to calculate the economic impact for both the patient and society that may result from any improvement in independence and ability to perform more productively following suppression of spasticity. For instance, one patient was able to obtain employment once his spasms were controlled by intrathecal baclofen, and two patients were able to decrease their requirement for personal attendant service.

In conclusion, the majority of patients with spasticity due to spinal cord injury or multiple sclerosis can be adequately treated with attention to spasticity aggravating factors and oral medications. The results of our study concur with previous reports regarding the safety and efficacy of intrathecal baclofen treatment of selected patients with severe spasticity. Furthermore, the hospitalization data suggests that intrathecal baclofen therapy may be a cost-effective means of managing selected patients with severe spasticity.

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