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INDICATION, EFFICIENCY AND COMPLICATIONS OF INTRATHECAL PUMP SUPPORTED BACLOFEN TREATMENT IN SPINAL SPASTICITY

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INTRODUCTION

Spasticity and flexor spasms secondary to lesions of the upper motor neuron at a spinal level are one of the predominant factors of disability reducing the life quality of these patients.

The oral pharmacological treatment of these symptoms is not very efficient, as it needs administration of high doses often with severe side effects [3, 4]. Therefore in severe cases posterior or anterior rhizotomy, in some cases even myelotomy, were performed. Alternatively to these palliative methods local intrathecal pharmacological treatment trials were performed.

In 1984 Baclofen, a GABA analogous selectively acting on GABA-β receptors, administered intrathecally was proved to inhibit polysynaptic reflexes in the spinal cord [5]. On the basis of these results intrathecal Baclofen, continuously administered by a specially developed pump system, was introduced for treatment of spasticity not responding to oral pharmacological treatment [7–10].

MATERIAL AND METHODS

19 patients suffering from severe spinal spasticity of different etiology, who did not respond to oral antispastic pharmacological treatment, were evaluated by intrathecal boli of Baclofen.

The inclusion criteria were:

— insufficient response to physical therapy and oral antispastic pharmacological treatment by mono- or polytherapy, including Baclofen;
— occurrence of severe side effects of oral antispastic treatment;
— severe spasticity reducing life quality;
— patient's informed consent.

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Prior to the bolus application clinical neurological examination as well as lumbar puncture and evoked potentials were performed in all patients. Additional spinal CT-scan, myelography and MRI examinations were done only in patients in whom structural lesions were not diagnosed before.

After an initial intrathecal bolus of 25 µg Baclofen the dosages were increased step by step, each 25 µg, up to a maximum of 100 µg. After each bolus application all patients were monitored continuously for 12 hours.

Spasticity was rated by using the Ashworth scale and the reflexes by a 6 point scale ranging from areflexia to clonus. In addition the motor performance was evaluated by the physician and the physiotherapist.

In some cases a polymyographic recording was performed. First responses to this therapy were observed after 30-60 minutes after intrathecal application, with a dose dependent therapeutical effect for approximately 3-6 hours.

In cases of a good response the patient was scheduled for DAD (drug administration device) implantation under general anesthesia. A 4F-Silastic catheter was introduced through a Tuohy needle between L3 and L4 and the tip positioned in the subarachnoidal space at D10 and connected to a Synchro-MedR 8611H model DAD (Medtronic Inc.) 9 a programmable battery powered pump. The catheter position was confirmed by the CSF backflow through the catheter and by fluoroscopy.

The 11 patients (6 male; 5 female; mean age 42 ys) whom a DAD was implanted, suffered from spinal spasticity secondary to traumatic spinal lesions (n = 4), multiple sclerosis (n = 6) and spinal tumor (n = 1). In all patients the spasticity lasted for more than 8 months (tab. I).

TABLE I

PATIENT CHARACTERISTICS

No	Diagnosis	Age *	Sex	Duration of disease *	Follow-up	Final dosage µg Baclofen/d
1	Trauma	38	m	7¼ years	12 months	305 complex
2	Trauma	32	m	23 months	15 months	200
3	Trauma	33	m	22 months	15 months	380 complex
4	Tumor	40	m	8½ months	9½ months	550
5	Trauma	60	m	34 months	6 months	550
6	MS	49	f	16 years	4 months	400
7	MS	57	f	15 years	18 months	220
8	MS	35	f	11 years	20 months	220
9	MS	49	f	27 years	24 months	185
10	MS	30	f	11 years	2 months	180
11	MS	38	m	6 years	2½ months	230
Mean values ± SD		42 ± 10.3				311 ± 140

* At time of implantation. MS: Multiple Sclerosis.

RESULTS

Out of these 19 patients evaluated for intrathecal Baclofen response only one patient, postoperative to a spinal angioma, who additionally to the spasticity suffered from pain induced by local irritation of the myelon, responded sufficiently to intrathecal bolus application concerning spasticity, although without any influence on pain. The other 18 patients improved markedly to intrathecal Baclofen application.

In 11 patients a DAD was implanted. Two patients refused the operative procedure. Five patients are scheduled for implantation.

After DAD implantation the muscle tonus as well as the reflexes decreased within 2-3 days in all cases. Within 10-14 days the efficient daily dose was reached. The criteria for a therapeutical response judged as positive were: markedly decreased muscle tonus, decreased flexor spasms and missing or reduced reflexes. Within the next 3-5 months an increase of the daily dose of 30-50 % was necessary in most patients. Thereafter only a slight tolerance forcing to dose increase was observed.

A clinically as well as a subjectively reported improvement was reached at a mean daily dose of 311 µg (SD 140 µg) (fig. 1, 2), whereas in supraspinal spasticity the daily dosages exceeded for 100 % those efficient in spinal spasticity.

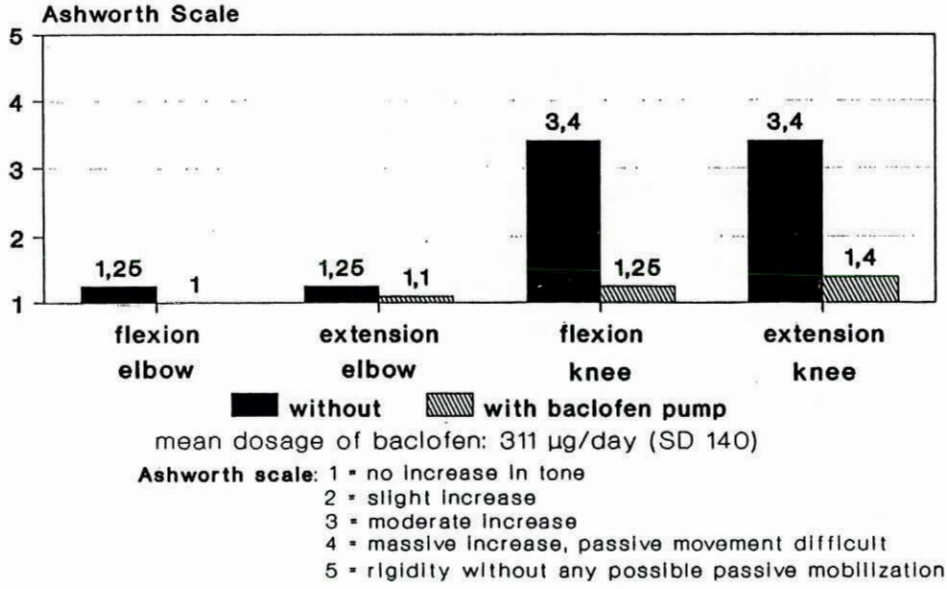

FIG. 1. — Reduction of muscle tone in eleven patients with spinal spasticity and long-term intrathecal baclofen therapy.

4 patients were bedridden due to spasticity and flexor spasms. After reaching the efficient dosages all 4 patients were able to stay in a wheel chair achieving a partial autonomy.

Patient no. 4 not able to walk due to severe paraspasticity was able to walk with help after a daily dose of 220 µg.

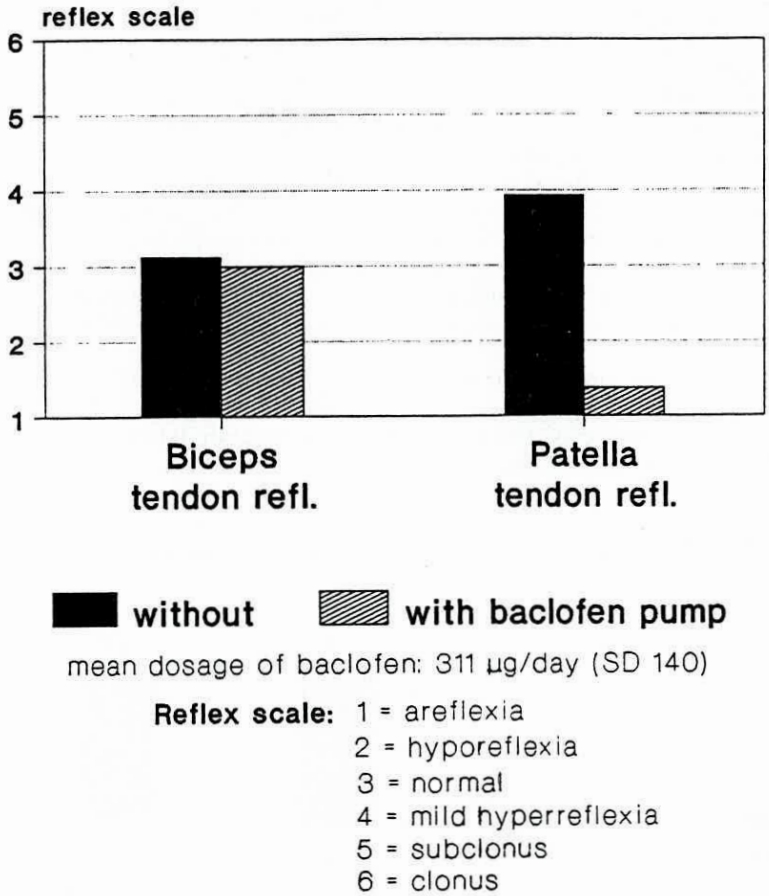

FIG. 2. — Reduction of reflexes in eleven patients with spinal spasticity and long-term intrathecal baclofen therapy.

Patient no. 11 markedly improved his motor performance at a daily dose of 230 µg, thus enabled to use a staircase.

Patients no. 1 and 3 suffered from side effects of high dose oral antispastic treatment, namely a reduction of cognitive functions and were thus unable to carry on their professions. After the DAD implanta-

tion delivering a daily dose of 305 µg and 380 µg respectively, these mentioned central side effects diminished and both were reintegrated.

In 9 patients intrathecal Baclofen was administered continuously, whereas in 2 patients a circadian varying dosage, adapting to circadian varying flexorspasm intensity, was applied.

Bladder function and voiding

The influence of intrathecal Baclofen application on spinal cord lesion induced bladder dysfunction is controversial.

Some authors report on an increased bladder capacity, reduced residual volume, diminished pelvic floor spasms and decreased sphincter dissynergia [7, 2].

According to other authors [13] as well as to our observations no significant improvements of bladder function occurred.

Only in a patient (no. 1) in whom, despite a previously implanted Brindley stimulator, sphincter spasticity seriously hampered voiding, a daily dosage of 305 µg Baclofen combined with the Brindley stimulator enabled a nearly normal (50 ml residual volume) micturition.

Patient no. 2 reported on an impaired erection at a daily dose of 300 µg, which improved after reduction to a daily dose of 200 µg.

Other patients did not report on impaired sexual functions.

Complications

Contrary to our experiences in patients with supraspinal spasticity in none of the patients suffering from spinal spasticity and implanted DAD an infection of the subcutaneous pocket or impaired wound healing occurred.

In 4 patients a catheter dislocation (fig. 3) had to be diagnosed by clinically observed dramatically increased spasticity and confirmed by X-ray. In 2 cases a catheter break off and in one case a malfunction secondary to catheter torsion by pump rotation occurred (fig. 4). Mostly the catheter dislocation was connected with a CSF leakage, which could be stopped by catheter reimplantation or autologous blood injection.

This complication occurred especially in patients improving their mobility and consequently increasing physiotherapeutic activities. Therefore in patients expected to gain markedly improved motor performance an additional loop of the catheter, to prevent catheter dislocation by ante- or retroflexion movements, was fixed subcutaneously. Nevertheless even this catheter fixation was not completely successfull.

In contrast to other authors a DAD malfunction was not observed.

In none of the 11 patients treated with intrathecally administered Baclofen via an implanted DAD the signs and symptoms of an intoxi-

cation secondary to Baclofen overdose was diagnosed, which is probably due to the low concentrations used in spinal spasticity.

In patient no. 3 who additionally to his spinal lesions also suffered from a severe brain injury generalized seizure occurred after intrathecal Baclofen application, which may indicate a proepileptic effect of Baclofen [12].

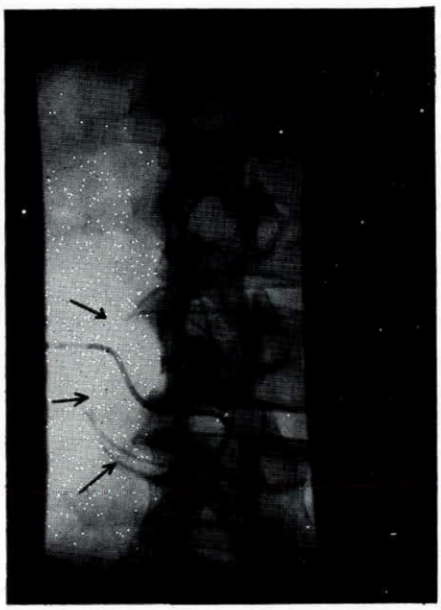

FIG. 3. — X-ray of a typical catheter dislocation.

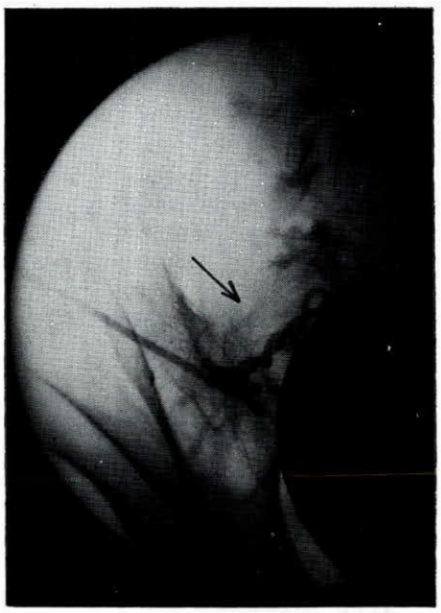

FIG. 4. — X-ray of catheter torsion by multiple pump rotation.

In some cases the reservoir drug concentration of 500 μg/ml was increased to 2000 μg/ml thus to prolonge the refilling intervals. In these cases the tonus increased again for 2-3 days consequently to the reduced pump delivery of the low concentrated substance remaining in the catheter.

DISCUSSION

In our 2 year follow-up study of continuous intrathecal Baclofen application in patients suffering from spinal spasticity we could confirm those reports, which proved the efficiency of this treatment [6, 11, 1]. During this period of time a marked tolerance forcing to dose increase, toxic side effects or local mechanic irritations could not be diagnosed by clinical means in any of our patients.

In all patients spasticity markedly improved and in some cases also an improvement of their motor performance could be noticed. Therefore in spinal spasticity and insufficient response to oral antispastic treatment intrathecal continuous Baclofen administration is indicated.

Nevertheless, prior to the DAD implantation, administration of Baclofen boli seems to be necessary as the patient can assess by himself the benefit of this therapy for decision making.

Intrathecal Baclofen application did not decrease the muscle strength and never severely aggravated spasm induced upright standing, as the fine adjustment of DAD delivered dosages are done telemetrically very precisely.

Bladder function improvement previously reported by several authors was not observed in our patients, except in one with an additional Brindley stimulator.

Catheter dislocation was the most common complication and occurred predominantly in patients with markedly improved mobility.

The DAD seems to be technically well developed as proved during this period of time, whereas the catheter complications point out the necessity of a new catheter design.

Continuous intrathecal Baclofen administration by an implanted DAD seems to be an effective new way of spinal spasticity treatment.

SUMMARY

In 19 patients, who suffered from severe spinal spasticity of different etiologies and did not respond sufficiently to oral antispastic therapy, intrathecal Baclofen test boli were administered.

In 11 patients a DAD (Drug Administration Device) [SynchroMedR Model 8611 H, Medtronic Inc. Minneapolis, USA] was implanted.

Catheter dislocation or torsion was the most common complication to be observed in these 11 patients.

Long term intrathecal Baclofen application was effective in all patients, as reducing spasticity, flexor spasms and spasm induced pain. In some cases the motor performance ameliorated.

RIASSUNTO

In 19 pazienti affetti da una severa spasticità spinale legata a differenti etiologie e non rispondenti in maniera adeguata alla terapia orale antispastica, è stato praticato il test del bolo di Baclofen intratecale. In 11 pazienti è stata impiantata una pompa automatica a lento rilascio (Synchro MedR Model 8611 H Medtronic Inc. Minneapolis USA). La dislocazione del catetere è stata la più comune complicazione osservata in questi 11 pazienti. L'applicazione della pompa al Baclofen in terapia cronica è stata efficace in tutti i pazienti nel ridurre la spasticità. In alcuni casi sono migliorate anche le performances motorie.

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