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Case Report

Regression of vasomotor disorders under intrathecal baclofen in a case of spastic paraplegia

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Continuous intrathecal baclofen infusion via a subcutaneously implanted programmable pump has been used in the treatment of severe spasticity. Improvement classically concerns the neurological (hypertonia, spasms, hyperreflexia), urological (bladder function) and other clinically relevant outcomes, such as functional status of daily living. This short note reports on another effect of intrathecal baclofen on vasomotor disorders and cyanosis in the lower limbs, described in a patient with spastic paraplegia.

Keywords: spinal cord; spasticity; intrathecal baclofen; vasodilatation; autonomic dysfunction; substantia gelatinosa; GABA(B)

Introduction

Baclofen (β-4-chlorophenyl γ-amino-butyric acid) is a derivative of the inhibitory neurotransmitter γ-amino-butyric acid (GABA). Its mode of action is not fully understood. It interferes with the release of excitatory neurotransmitters and inhibits monosynaptic and polysynaptic transmission at the spinal level. It may also act at supraspinal sites producing CNS depression. Baclofen is used in the treatment of spasticity, decreases muscle spasms, pain and urinary-tract disorders especially in case of spinal cord lesions.[1,2] In patients with severe spasticity, baclofen can be given intrathecally when medical treatment, including oral baclofen administration, diazepam or sodium dantrolene has failed or adverse effects limit increases in dosage.[3] Here we report the improvement of vasomotor disorders with intrathecal administration of baclofen, in a patient with a severe disabilitating spasticity secondary to spinal cord lesion.

History

The patient was a 39-year-old male who had a car accident in 1972. He initially was comatose for 5 days, and had a compressive fracture of the 3rd and 4th thoracic vertebrae with complete paraplegia. The vertebral fractures were treated by an orthopaedic treatment. No neurological recovery had occurred. After rehabilitation, the patient was independent for daily life activities in a wheelchair. Fifteen years later, he developed increasing spasticity with severe muscular hypertonia, frequent spontaneous spasms and increasing reflexes. He also showed an urge incontinence consecutive to a severe hyperactive bladder with frequent unvoluntary contractions.

Examination

Neurological examination revealed a complete spastic paraplegia below the T4 level and a severe spasticity with muscular hypertonia, spasms and hyperreflexia (Table 1). Urodynamic evaluation showed a hyperactivity with detrusor hyper-reflexia and a detrusor sphincter dyssynergia (Table 1). Radiographic visualization of the bladder during storage and voiding showed a spastic bladder of small size with trabeculations and diverticuli. As verified on MRI, this clinical worsening did not result form a post-traumatic centromedullary cavity.

Moreover, the patient showed vasomotor disorders in his two lower limbs, with marked cyanosis and reduction of the superficial temperature, although the different arterial pulses were present at examination. Thermography examination revealed an important decrease of the superficial temperature in his two lower limbs (Figure 1a).

Treatment

The patient's spasticity was refractory to orally administered baclofen. Spasticity was reduced by a

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Table 1 Improvement of symptoms of spasticity under intrathecal baclofen (180 μg/day) in a case of spastic paraplegia

	Before treatment	*After treatment*
Ashworth Scale	4	2
Rating scale for Spasms	3	2
Rating scale for Reflexes	3	1
Urodynamic evaluation		
Uninhibited detrusor contractions	frequent	reduced
Hyperactivity with detrusor hyperreflexia	severe	reduced
Detrusor sphincter dyssynergia	severe	reduced
Bladder capacity	75cc	200cc

Efficacy measurements consisted to evaluate rigidity, spasms and reflexes using three different scales: (i) The five-point Ashworth scale[5] for measuring muscle tone (1 = No increase in tone; 2 = Slight increase in tone, giving a 'catch' when affected part is moved in flexion or extension; 3 = More marked increase in tone, but affected part easily flexed; 4 = Considerable increase in tone; passive movement difficult; 5 = Affected part rigid in flexion or extension), (ii) A five-point scale for spasms (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 ten times per hour) and (iii) A five-point scale for reflexes (0 = Absent; 1 = Hyporeflexive; 2 = Normoreflexive; 3 = Mild hyperreflexive; 4 = 3–4 beats clonus; 5 = Clonus). Urinary tract disorders were assessed by urodynamic exploration and cystography[6]

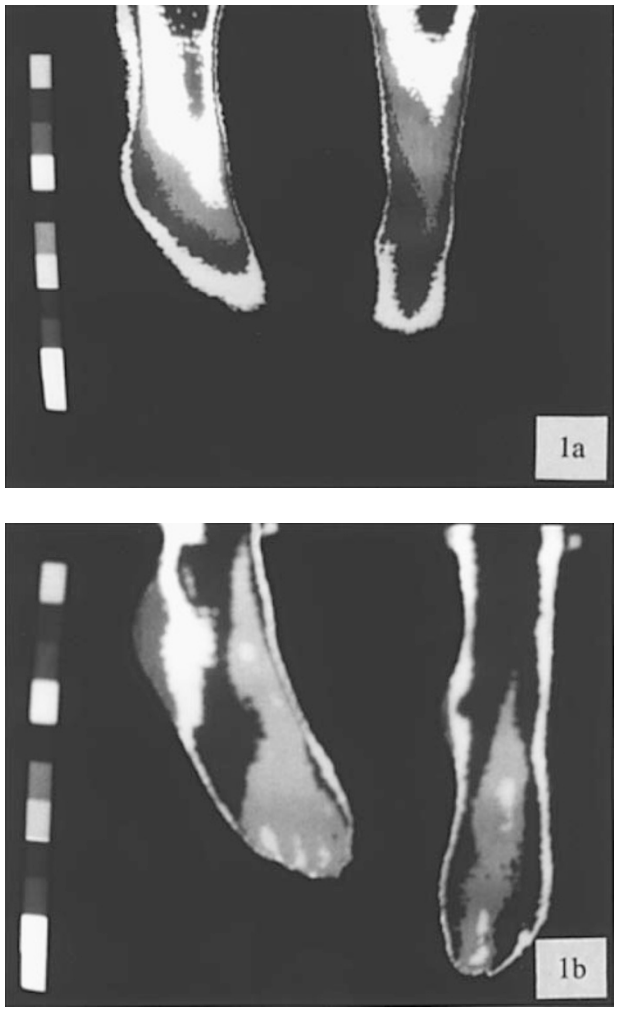

Figure 1 Thermography examination of the lower limbs before (**a**) and after intrathecal baclofen (180 μg/day) (**b**) in a case of spasticity paraplegia. Before treatment, the superficial temperature was included between 22.5 and 23°C. After treatment, the superficial temperature was increased and between 29 and 30°C. Examination did not show difference between the two limbs

trial bolus of 100 μg of intrathecal baclofen. Criteria for inclusion and exclusion to intrathecal baclofen therapy by an implanted pump, proposed by Penn were respected: age was between 18 and 65 years; severe chronic spasticity was due to a spinal cord trauma; the patient had adequate CSF flow as determined by myelogram; prior to implantation of a pump, the patient had responded to a single dose of 100 μg of intrathecal baclofen and the patient had voluntarily signed the informed consent form after its contents had been fully explained.[4] A programmable pump (SynchroMed^{TM}, Medtronic, Minneapolis, USA) was implanted in the abdominal wall and connected to a lumbar subarachnoid catheter introduced under fluoroscopic control in October 1992. The effective daily dose was 180 μg.

After implantation, an improvement of spasticity was noted: reduction of increase in muscle tone and normal reflexes. Bladder capacity was increasing as proved by cystography (200 cc) and urodynamic evaluation showed a reduction of the detrusor hyperreflexia (Table 1). Moreover, a regression of vasomotor disorders was dramatically observed through intrathecal baclofen. The cyanosis had disappeared and the thermography examination showed an increase of the superficial temperature (+7°C) and no difference between the two limbs (Figure 1b). This improvement was long-lasting.

In this case, intrathecal baclofen improved different symptoms of spasticity: muscular hypertonia, muscle spasms, hyper-reflexia and urinary-tract disorders. These positive effects were comparable to those previously reported.[7–10] In this case, a supplementary effect of intrathecal baclofen on vasomotor disorders and cyanosis in the two lower limbs was reported. Two explanations may be proposed to explain this effect: firstly, the regression of vasomotor disorders and cyanosis may be due to the muscle tone reduction which disturbed the blood circulation in the lower limbs. Secondly, intrathecal baclofen may have a direct vasomotor effect.

A complete peripheral vasodilatation has already been described in two cases following an overdose of baclofen.[11,12] The two patients were totally comatose and flaccid, and showed also a collapse and a bradycardia. In these two cases, the overdose of baclofen was respectively 500 and 900 mg of baclofen per os. The clinical and pharmacological status of our patient was different. The vasomotor effect was induced by high level of intrathecal baclofen without peripheral effect. This effect might be consecutive to a selection action of baclofen on autonomic innervation with the spinal cord.

Baclofen interferes with the release of excitatory neurotransmitters and inhibits monosynaptic and polysynaptic transmissions at the spinal level. Within the spinal cord, the receptors for baclofen, gamma-aminobutyric acid (GABA)B receptors, have been shown to have greatest density in the substantia gelatinosa (lamina II) of the spinal cord in both rats and humans.[13,14] The substantia gelatinosa is the central site of termination of most primary afferent fibres excited by painful stimuli and contains many interneurones which form a network that plays a role in modulating the primary afferent signals.[15,16] The exact role of the substantia gelatinosa remains to be determined. The vasomotor effect induced by intrathecal baclofen may be linked to this neuronal circuitry of the substania gelatinosa. In an animal, experimental studies moreover showed that baclofen has a powerful sympatho-inhibitory effect on sympathetic preganglionic neurones and that the baclofen-sensitive receptors in the spinal cord could be involved in regulating sympathetic output in pathways to the vessels and/or to the heart.[17,18] These findings support the clinical effect observed in this human pathological case. Finally, it is interesting to note that this result, with no equivalent found in the literature, was observed 15 years after paraplegia and in long-standing vasomotor disorders which were initially considered permanent and probably irreversible.

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