

Short report

Intrathecal baclofen and the H-reflex

R A L MACDONELL,* A TALALLA,** M SWASH,* D GRUNDY†

From the Department of Neurology, The London Hospital, Whitechapel, London, United Kingdom, Department of Neurosurgery, McMaster University, Hamilton, Ontario, Canada,** Duke of Cornwall Spinal Treatment Centre, Odstock Hospital, Salisbury, United Kingdom†*

SUMMARY Baclofen was given intrathecally to six patients with severe lower limb spasticity due to traumatic spinal cord injury. The effects of the drug on spasticity and the ratio between the maximum amplitude of the H reflex and the M response from the soleus (Hmax/Mmax ratio) were assessed. In each patient, spasticity was reduced following intrathecal baclofen and in four patients there was a reduction in the amplitude of the H reflex and Hmax/Mmax ratio. These results suggest that the Hmax/Mmax ratio may be helpful in establishing optimum drug dosage, particularly when the drug is used on a chronic basis.

Spasticity may be defined as a motor disorder characterised by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperactivity of the stretch reflex.¹ It is beneficial to patients with mild to moderate leg weakness because increased muscle tone in quadriceps may improve walking by stiffening the weak knee.² However, spasticity is of less benefit in patients with more severe degrees of weakness because it reduces the flexibility of flail limbs and makes it more difficult for paraplegic patients to transfer to and from wheelchairs.

The most effective pharmacological agent currently used to reduce spasticity is baclofen, a GABA derivative. Baclofen appears to act primarily at a spinal cord level, since spasticity is reduced as effectively in patients with complete spinal cord transections as in those with incomplete lesions.³ Oral doses should be limited because of side effects such as drowsiness and confusion resulting from the central depressant actions of the drug. These side effects may occur before the dose is sufficient to produce an effective concentration at the spinal cord⁴ and is probably the main reason for the failure to respond to oral administration of the drug in 25 to 35% of

patients.^{5,6} To overcome this problem an intrathecal technique for long term administration has been developed.^{5,7,8} Using this route high local concentrations can be achieved at the spinal cord with small doses, considerably reducing the concentration to which the brain is exposed. Better long term control of spastic symptoms without unwanted central side effects can be achieved by this method.^{7,8}

In assessing the response to such treatment it would be useful if an objective measure of spasticity was available. One technique uses the ratio between the maximum amplitude H-reflex and M response from the soleus muscle, the so called Hmax/Mmax ratio.⁹⁻¹¹ Patients with lower limb spasticity have a mean value of this ratio significantly higher than controls.^{10,11} We have investigated the effects of intrathecal baclofen on the H reflex, on the Hmax/Mmax ratio and on spasticity in functionally complete traumatic spinal cord lesions.

Material and methods

Six patients with post-traumatic spinal cord lesions were studied. All were men ranging from 22-42 years (mean: 30.5 years). In each, there was a complete absence of motor and sensory function below the level of injury (table). The upper level of the deficit varied from C4 to T11 and the time interval from the injury ranged from six months to three years (mean 17.2 months). All had bilateral leg spasticity which considerably interfered with their rehabilitation and most were taking oral antispasticity drugs. All such drugs were withdrawn 24

Correspondence to: Dr M Swash, Department of Neurology, The London Hospital, Whitechapel, London E1 1BB, United Kingdom

Received 7 February 1989 and in revised form 15 May 1989.
Accepted 14 June 1989

Table Effects of intrathecal baclofen on spasticity, the H reflex, M response and Hmax/Mmax ratio in patients rendered paraplegic by traumatic spinal cord injury

Patient	Lesion level	Baclofen (μg)	Pre Baclofen				Post Baclofen			
			Spasticity*	Hamp (μV)	Mamp (μV)	Hmax/Mmax	Spasticity*	Hamp (μV)	Mamp (μV)	Hmax/Mmax
1	T6	25	4	450	1000	0.45	3	0	950	—
2	T11	50	4	280	720	0.39	1	220	1600	0.14
3	T10	100	2	215	380	0.57	1	0	540	—
4	C4	75	3	175	350	0.50	1	0	730	—
5	T10	100	4	1500	3400	0.44	1	1300	5200	0.25
6	T5	75	4	740	3800	0.19	3	80	1300	0.06

*Spasticity was graded according to the Ashworth Scale.¹²

Hamp—maximum amplitude H response, Mamp—maximum amplitude M response, Hmax/Mmax—ratio of maximum amplitude H reflex to maximum amplitude M response.

hours prior to our investigation. All patients gave informed consent.

The H-reflex and M-response from the right soleus muscle were recorded both before and after baclofen was administered intrathecally. Recording electrodes were placed two cms apart in the mid calf region and the posterior tibial nerve was stimulated in the popliteal fossa using a 0.1 msec duration square wave pulse at a frequency of 1 Hz. Stimulus intensity was gradually increased to elicit both H and M responses. The H reflex varied in amplitude. Hmax was selected by increasing stimulus intensity until maximum amplitude H responses were obtained. Ten H responses were recorded at this stimulus intensity and the one of greatest amplitude was chosen as Hmax. Mmax was the amplitude of the M response at supramaximal stimulation. Filter settings were 20–10,000 Hz. The recordings were made using a Medelec 92A electromyograph.

Baclofen was administered into the CSF, under sterile conditions, using an intrathecal catheter inserted at L1. It was given in 25 μg aliquots every 20 minutes until clonus at the ankle was abolished and providing the blood pressure remained stable. Repeat electrophysiological testing was performed 20 minutes after the final dose of baclofen had been given. Leg spasticity was graded before the insertion of the intrathecal catheter and again at the end of the study by the same observer, using the Ashworth scale.¹²

Results

In all patients H reflexes and M responses were present before the baclofen was administered. The mean value of the Hmax/Mmax ratio (0.42) was higher than that reported in previous studies from normal subjects.¹⁰ Following intrathecal baclofen the H-reflex could not be recorded in three of six patients (50%) and in the remaining three patients the Hmax/Mmax ratio was reduced by between 43% and 68% (table). Two of the patients with intact H reflexes after baclofen had been administered had little change in H amplitude. The reduction in Hmax/Mmax ratio was due to an increased size of the M response. There was no change in latency of either response following administration of the drug.

Leg spasticity, judged using a clinical rating scale,¹² was reduced in all patients (table).

Discussion

The reduction of spasticity produced by intrathecal baclofen was accompanied by abolition of the H reflex in three patients (50%), and a marked reduction in the amplitude of the H response and Hmax/Mmax ratio in one other. In the two remaining patients, the reduction in Hmax/Mmax ratio occurred due to an increase in Mmax rather than any change in H reflex amplitude. This reflects differences in configuration of the electrodes pre and post treatment and hence no inference can be made about the effects of intrathecal baclofen on the H reflex in these two patients.

Our findings differ somewhat from previous reports concerned with the effects of baclofen on the H reflex. Ashby and White¹³ reported that oral baclofen had little effect on the H reflex even though spasticity was profoundly reduced. They did comment, however, that some reduction in H reflex was observed with higher oral doses. Birkmayer *et al*⁴ reported that IV baclofen reduced the H reflex and spasticity in most patients, although others have found that IV baclofen reduces the H reflex less predictably.¹⁵

These results suggest that the effects of baclofen on spasticity and on the H reflex may operate by different mechanisms. The H reflex is a monosynaptic reflex⁹ whose activity is increased in spasticity.¹⁶ Although this reflex contributes to spasticity there are a number of other reflexes which also contribute. One of the most important of these is the muscle stretch reflex. This is part of the fusimotor system which relies on both monosynaptic and polysynaptic connections.¹⁷ At low CSF concentrations, such as following oral administration, baclofen may inhibit polysynaptic reflexes in the spinal cord including muscle stretch reflexes, reducing spasticity but may have little effect on monosynaptic reflexes explaining the lack of inhibition of the H reflex. As the CSF and spinal cord

concentration rises following IV or intrathecal administration, monosynaptic reflexes are also suppressed which explains the correlation between Hmax/Mmax and spasticity observed in this series.^{13 18 19}

The response to intrathecal baclofen can vary quite widely as seen in the variability of drug dosage required to abolish clonus in our patients. Our findings suggest that the Hmax/Mmax ratio may be useful in evaluating the clinical response and dosage in patients treated with intrathecal baclofen.

We are grateful to Mr J Benfield, Research Registrar, Duke of Cornwall Spinal Treatment Centre, Odstock Hospital, Salisbury.

References

- 1 Lance JW. In: Feldman RG, Young RR, Koella WP, eds. *Spasticity: disordered motor control*. Chicago, Year Book, 1980:485-94.
- 2 Landau WM. Spasticity: The fable of a neurological demon and the emperor's new therapy. *Arch Neurol* 1974;**31**:217-9.
- 3 Davidoff RA. Antispasticity drugs: mechanisms of action. *Ann Neurol* 1985;**17**:107-16.
- 4 Young RR, Delwaide PJ. Drug Therapy: Spasticity Part 2. *New Eng J Med* 1981;**304**:96-9.
- 5 Muller H, Zierski J, Dralle D, Hoffmann O, Michaelis G. Intrathecal baclofen in spasticity. In: *Local-spinal Therapy of Spasticity*. Muller H, Zierski J, Penn RD, eds. Springer-Verlag, Berlin, 1988. 155-214.
- 6 Corston RN, Johnson F, Godwin-Austin RB. The assessment of drug treatment of spastic gait. *J Neurol Neurosurg Psychiatry* 1981;**44**:1035-9.
- 7 Penn RD, Kroin JS. Continuous intrathecal baclofen for severe spasticity. *Lancet* 1985;**ii**:125-7.
- 8 Penn RD, Kroin JS. Long term intrathecal baclofen infusion for treatment of spasticity. *J Neurosurg* 1987;**66**:181-5.
- 9 Goodgold J, Eberstein A. Electrodiagnosis of Neuromuscular Diseases, 3rd edition. Williams and Wilkins, Baltimore, 1983:263-8.
- 10 Angel RW, Hofmann WW. The H reflex in normal, spastic and rigid subjects. *Arch Neurol* 1963;**8**:591-6.
- 11 Matthews WB. Ratio of maximum H reflex to maximum M response as a measure of spasticity. *J Neurol Neurosurg Psychiatry* 1966;**29**:201-4.
- 12 Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. *Practitioner* 1964;**192**:540-2.
- 13 Ashby P, White CJ, Knowles L. "Presynaptic" inhibition spasticity and the effect of Beta-(4-chlorophenyl)GABA. *J Neurol Sci* 1973;**20**:329-38.
- 14 von Birkmayer W, Danielczyk W, Weiler G. Zur objektivierbarkeit des myotonolytischen effektes eines aminobuttersaurederivates (Ciba 34647-Ba). *Wein med Wschr* 1967;**117**:7-9.
- 15 Pedersen E, Arlien-Soborg P, Mai J. The mode of action of the GABA derivative baclofen in human spasticity. *Acta Neurol Scand* 1974;**50**:665-80.
- 16 Magladery JW, Teasdall RD, Park AM, Languth HW. Electrophysiological studies of reflex activity in patients with lesions of the nervous system. I. A comparison of spinal motoneurone excitability following afferent nerve volleys in normal persons and patients with upper motor neurone lesions. *Bull J Hopkins Hosp* 1952;**91**:219-44.
- 17 Boyd IA. Muscle spindles and stretch reflexes. In: *Scientific basis of Clinical Neurology*, Swash M, Kennard C, eds. Churchill Livingstone; Edinburgh, 1985:74-97.
- 18 Schwartz M, Klockgether T, Turski L, Sontag KH. Intrathecal injection of antispastic drugs in rats: muscle relaxant action of midazolam, baclofen, 2-Aminophosphonoheptanoic acid (AP7) and tizanidine. In: *Local-therapy of Spasticity*, Muller H, Zierski J, Penn RD, eds. Springer-Verlag, Berlin, 1988:65-79.
- 19 Curtis DR, Lodge D, Bornstein JC, Peer MJ. Selective effects of baclofen on spinal transmission in the cat. *Exp Brain Res* 1981;**42**:158-70.