

The effect of magnesium oral therapy on spasticity in a patient with multiple sclerosis

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The effects of magnesium glycerophosphate oral therapy on spasticity was studied in a 35-year-old woman with severe spastic paraplegia resulting from multiple sclerosis (MS). We found a significant improvement in the spasticity after only 1 week from the onset of the treatment on the modified Ashworth scale, an improvement in the range of motion and in the measures of angles at resting position in lower limbs. No side-effects were reported and there was no weakness in the arms during the treatment.

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Introduction

Magnesium is the natural physiological antagonist of calcium. For over one century it has been known to be a muscular relaxant agent. In 1891, Sang reported a fatal poisoning in a 35-year-old woman after ingesting 120 g of salts of magnesium and he described a complete flaccid muscular paresis as the main symptom (Sang, 1891). Its first clinical use as a relaxant agent was probably by Blake in 1905, who was able to reduce muscle stiffness in two patients with severe tetanus, by injecting a solution of magnesium sulphate by lumbar puncture (Blake, 1906). In 1954 it was pointed out that an excess of magnesium ions decreases the amount of transmitter liberated at the motor nerve terminals, diminishes the depolarizing action of acetylcholine and depresses the excitability of the muscle fibre membrane (Del Castillo and Engbaek, 1954). Magnesium can compete with calcium for the same sites but without inducing the release of acetylcholine, thereby reducing muscle contractility (Anast and Gardner, 1981).

More recently, it was found that GABA actions were depressed in a dose-dependent reversible manner by a low extracellular concentration of magnesium (El-Beheiry and Puil, 1990). Furthermore, magnesium has a role in regulating a wide variety of enzymatic reactions and phosphorylation-dependent processes, including second messenger systems which are essential for neuronal excitability in the central nervous system (Gurwitz and Sokolovsky, 1980; Grubbs and Maguire, 1987; Stelzer *et al.*, 1988). Finally, magnesium acts by competition with calcium for calcium binding sites on troponin C, by generat-

ing ATP, and therefore allows the sarcoplasmic reticulum to actively transport calcium out of the sarcomere, thus inhibiting contraction and allowing relaxation (Zot and Potter, 1982).

In summary, magnesium is able to produce muscle relaxation by means of several mechanisms. For these reasons and in the light of a case report in 1985, where intravenous magnesium sulphate was able to reverse painful muscle spasms in a paraplegic patient (Clinton *et al.*, 1985), we thought that oral magnesium therapy might reduce the spasticity in a patient with severe spastic paraplegia due to multiple sclerosis (MS).

Case study

A 35-year-old woman with a secondary progressive multiple sclerosis was referred to our rehabilitation service at the end of 1998. This patient had first shown symptoms in 1992 and had been in hospital since October 1997. When she arrived in our service, she presented a right homonymous hemianopia, a third nerve palsy with diplopia and a severe weakness with ataxia in the upper limbs. However, the main clinical feature was a severe spastic paralysis with frequent spasms in the legs. She also had a diminution of the sensation in her lower limbs, cognitive impairments, difficulties in swallowing and she was doubly incontinent. The Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) was 8.5 and the patient was totally dependent with a Barthel (Wade and Collin, 1988) score of 1 out of 20.

The spasticity in her legs was very high, with a score of 4 or 5 in both sides on the modified Ashworth scale (Bohannon and Smith, 1987). At resting position the hips were in slight adduction, the knees in extension and the ankles in inversion with plantar flexion. Neither physiotherapy treatment nor baclofen or tizanidine to the

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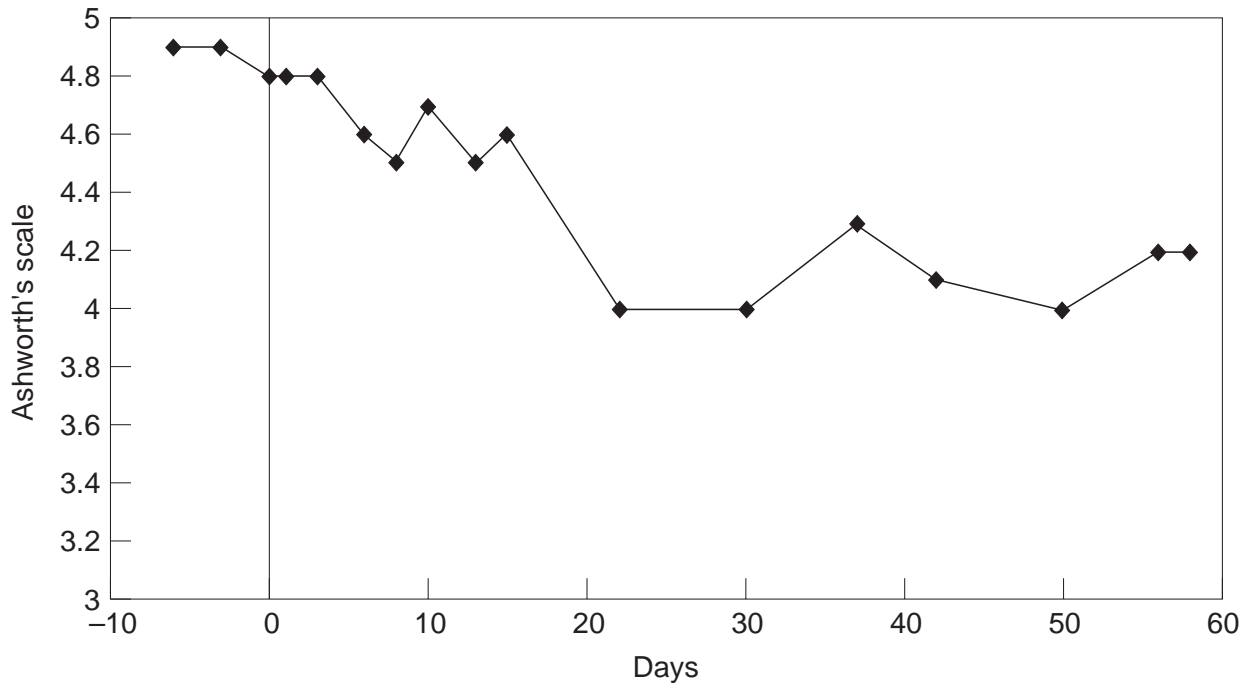


Figure 1 Evolution of the spasticity in the legs measured using the modified Ashworth scale and using an average of 10 measures, during the treatment of magnesium. The treatment started at the day 0 with 100 mg elemental magnesium (no significant change is seen when increasing the dose to 150 mg at the 42nd day).

maximum tolerated doses were able to diminish the spasticity or the spasms in the legs.

Method

Knowing that the normal human diet contains approximately 300–360 mg elemental magnesium (24–30 meq) (Levine and Coburn, 1984), we gave 500 mg b.d. oral magnesium glycerophosphate to our patient, which is equivalent to an additional 100 mg elemental magnesium. After 42 days, we increased the dose to 1500 mg magnesium glycerophosphate.

The spasticity was assessed by the mean of the modified Ashworth scale (Bohannon and Smith, 1987) and the range of motion (Mellin *et al.*, 1994; Watkins *et al.*, 1995) for hip flexion and abduction, knee flexion and ankle dorsiflexion using a goniometer. We also measured the angles at resting position for the hip abduction and for the ankle plantar flexion on both sides. For the modified Ashworth scale, the score is given for hip flexion and abduction, knee flexion and extension and ankle dorsiflexion for each leg; the scores are added and the total divided by 10, to arrive at an average grade. This method has been used for paraplegic patients (Penn and Kroin, 1985; Loubser *et al.*, 1991).

We performed three assessments before the onset of the treatment with magnesium glycerophosphate, followed by assessments every 2 or 3 days for the first 2 weeks and

then once a week for 2 months. No side-effect was reported.

Results

Figure 1 shows the evaluation of the modified Ashworth scale during the treatment. On average, the spasticity was improved by 0.7 points (from 4.9 to 4.2). This improvement occurred within 1 week and reached its maximum after 3 weeks. We did not notice any improvement when we increased the dose at the 42nd day from 100 to 150 mg elemental magnesium. The spasticity was particularly reduced for the movement of the hips and of the knees. There was no change at the ankles.

The modification in the range of motion and in the measures of angles at resting position are summarized in Table 1. We found a highly significant improvement in hip flexion and abduction and in knee flexion bilaterally but there was no change at the ankles. On treatment the position of the hips, which were initially in forced adduction, was improved and after 2 months the resting position of the hips was normal.

Discussion

We noticed a significant improvement in the spasticity in a young woman with severe spastic paraplegia due to advanced multiple sclerosis whilst taking 100 mg elemental

Table 1 Evolution of the range of motion and of the measures at resting position

	Average of 3 measures before treatment	Average of 3 measures at days 8, 10 and 13	Average of 3 measures at days 42, 50 and 56	P-value between measures before treatment and after 2 months
Range of motion (degrees with SD)				
Hip flexion right side	55 (10)	78 (14)	97 (6)	$P < 0.002$
Hip flexion left side	34 (5)	49 (8)	82 (7)	$P < 0.0005$
Hip abduction right side	13 (4)	27 (2)	33 (8)	$P < 0.02$
Hip abduction left side	6 (4)	18 (8)	31 (8)	$P < 0.005$
Knee flexion right side	91 (7)	126 (7)	140 (0)	$P < 0.0002$
Knee flexion left side	56 (6)	109 (14)	134 (3)	$P < 0.0001$
Ankle plantar flexion right side	14 (9)	19 (1)	25 (5)	$P < 0.1$
Ankle plantar flexion left side	20 (2)	21 (9)	21 (5)	$P < 0.5$
Angle at resting position (degrees with SD)				
Hip abduction right side	-11 (1)	-2 (3)	-1 (1)	$P < 0.0005$
Hip abduction left side	-5 (1)	-4 (2)	-1 (1)	$P < 0.005$
Ankle plantar flexion right side	67 (1)	64 (4)	64 (4)	$P < 0.2$
Ankle plantar flexion left side	60 (4)	67 (5)	69 (2)	$P < 0.02$

magnesium oral therapy when other oral anti-spastic agents had failed. During the treatment with magnesium, the patient noted a diminution of the spasms in her legs, that she was able to perform sometimes voluntary movements in her legs, especially knee flexion both sides, and the nurses noticed that it was easier to give care (transfers, dressing and positioning in the wheelchair). There were no noticeable side-effects such as sedation or weakness in the arms.

The muscle relaxant power of magnesium is well reported and has already been used in many clinical situations with muscle hypertonia, such as tetanus (James and Manson, 1985), eclampsia and eclamptic seizure (The Eclampsia Trial Collaborative group, 1995), hyperventilation syndrome (Fehlinger *et al.*, 1988) and painful muscle spasms (Clinton *et al.*, 1985). It also seems useful in restless legs syndrome (Hornyak *et al.*, 1998); we are unaware of whether it has ever been used for spasticity. Because it is safe, cheap, simple to administer and because it has no side-effect at therapeutic dose, magnesium therapy could become an interesting alternative for the treatment of the spasticity. The results obtained in our single case do encourage us to undertake a double-blind placebo controlled trial.

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