

11. MAGNESIUM RELIEVES PAIN IN POSTHERPETIC NEURALGIA

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Post herpetic neuralgia (PHN) is a complication of acute herpes zoster infection (HZ), characterized by severe constant pain and disturbances of the sensory nervous system in the skin area initially affected by the infection.

In this double-blind, placebo controlled, cross-over study, magnesium sulphate administered intravenously, reduced pain, compared with placebo, in a statistically highly significant manner.

Post herpetic neuralgia is a neuropathic pain condition, which represents an increasing clinical problem in the elderly population. PHN can reach the incidence of up to 75% in patients over 70 years, who have experienced an HZ infection(1). This distressing complication is the consequence of the extensive peripheral nerve and spinal cord damage caused by the reactivation of the dormant virus (2). The typical features of PHN are burning, aching or itching, continuous pain, with additional sharp and shooting components, as well as pathological changes of the sensory pathway, often expressed as mechanical and thermal allodynia.

The N-methyl-D-aspartate (NMDA) receptor plays an important role in the mechanisms underlying central sensitization in the spinal cord, which is critically important for the establishment of several chronic neuropathic pain states(3). In its inactive state the NMDA receptor is blocked by the presence of a centrally positioned magnesium ion. Experimental systemic and intrathecal injection of magnesium suppressed neuropathic pain responses via a spinal site of action in the rat with chronic constriction injury of the sciatic and saphenous nerves (4). In man, an intravenous infusion of magnesium sulphate reduced the intra and postoperative analgesic consumption in a recent clinical study (5).

In the present double blind, placebo-controlled study, seven patients with PHN were randomly assigned to receive magnesium or placebo in a crossover design with a wash-out period of one week in between. The study protocol was approved by the Hospital Ethical Committee and by the Medicine Control Agency of the United Kingdom. Patients above 18 years of age with PHN lasting for more than three months and showing a pain score of >4 on a numerical visual analogue scale (VAS) were recruited and randomly assigned to receive either an intravenous (i.v.) infusion of 0.9% saline (100ml) or magnesium sulphate 30mg/kg over 30 minutes. One week later, the other solution was infused. Patients with cardiac failure (New York Heart Association grade III or IV), atrio-ventricular conduction blockade (grade II or III), serum creatinine in excess of 110 mol/l and severe liver disease were excluded from the study. The severity of pain was recorded using a numeric VAS at baseline, prior to the start, and at 10, 20 and 30 minutes during the infusion.

The Wilcoxon signed rank test with an approximation to the Normal distribution (test statistic denoted by z) was used to establish if pain scores were similar within individuals for the two treatments at 10, 20 and 30 minutes. All reported p-values are two-tailed. The critical level of significance was $p < 0.05$. The Bonferroni method was subsequently applied to adjust for multiple testing and the new critical significance level was $p = 0.017$.

The mean pain score was reduced from the initial value of 6.7 prior to the infusion to 1.9 after 30 minutes. The difference in pain between placebo and magnesium within individuals was significant at 20 ($z = 2.39$; $p = 0.016$) and 30 minutes ($z = 2.39$; $p = 0.016$). Apart from a mild feeling of warmth at the site of the injection no adverse events were reported.

It is likely that the intravenous magnesium infusion increased the Mg^{++} concentration gradient between the extracellular fluid and the cell membranes, causing block of the NMDA-receptor and subsequent pain relief. This beneficial effect may result from the physiological action of magnesium as a non-competitive antagonist of the NMDA-receptor.

Our data provide strong evidence that magnesium sulphate produces pain relief in patients with PHN, a neuropathic pain condition. The present new results provide strong evidence that magnesium produces effective pain relief in an insufficiently controlled neuropathic pain condition. The NMDA receptor antagonist action exhibited by magnesium could be similarly used in other neuropathic pain syndromes.

In conclusion, the intravenous infusion of magnesium sulphate was safe, well-tolerated and effective in relieving PHN pain.

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