Treatment of severe mania with intravenous magnesium sulphate as a supplementary therapy

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Abstract

Ten patients with severe, therapy-resistant manic agitation received magnesium sulphate infusions with a continuous magnesium (Mg) flow of approximately 200 mg/h (4353 ± 836 mg/day; daily monitored Mg plasma level: 2.44 ± 0.34 mmol/l) for periods ranging from 7 to 23 days. Concomitant psychotropic treatment consisted of lithium (\(n=10\)), haloperidol (\(n=5\)) and clonazepam (\(n=10\)). During i.v. Mg treatment the mean values of the maximum dosages of neuroleptics in chlorpromazine equivalents and benzodiazepines in diazepam equivalents were significantly lower than during the last day of pretreatment (= baseline). Seven patients showed a marked improvement in the Clinical Global Impression scale. In case of bradycardia detected by the ECG monitor (\(n=5\)), Mg flow was reduced and bradycardia disappeared promptly. Mg i.v. may be a useful supplementary therapy for the clinical management of severe manic agitation. This open study needs double-blind confirmation. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Magnesium; Calcium; Lithium; Agitation; Sedation; Psychiatric intensive care unit

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1. Introduction

Manic patients with severe agitation are often treated with high doses of various neuroleptics. Most conventional antipsychotics have extrapyramidal, anticholinergic (e.g. delirium, ischuria) and antiadrenergic (e.g. orthostatic hypotension) side effects. Sometimes changes in liver function occur. The use of high doses of various neuroleptics should be limited because they sometimes cause confusion and persistent excitement despite heavy sedation and respiratory dyskinesia that may lead to aspiration pneumonia (Kruk et al., 1995; Casey, 1997).

We were trying to find a better tolerated treatment for patients with severe mania when our attention was drawn to the muscle-relaxing and sedative effects of intravenous magnesium. Hypermagnesemia is considered to act as a central nervous system depressant, and its sedative effects have proved to be useful in anesthesia (James, 1992; Tramer et al., 1996). Furthermore, i.v. treatment with Mg salts has been found to be effective in disorders presenting with neuromuscular hyperexcitability such as pre-eclampsia and delirium tremens (Meignan, 1992; Frakes and Richardson, 1997). Oral Mg aspartate was reported to be effective in the treatment of rapid cyclers (Chouinard et al., 1990).

Mg activates approximately 300 enzyme systems, including most of the enzymes involved in energy metabolism (Durlach, 1992a). Although the role of Mg in neuronal function is not completely understood, it has been shown that Mg can block calcium (Ca) influx and, in particular, non-competitively antagonize the N-methyl-D-aspartate (NMDA) channels (Ascher and Nowak, 1987; Lipton and Rosenberg, 1994). Intracellular Ca$^{2+}$ ions play a fundamental role in the release of neurotransmitters and in the functioning of receptors involved in mood disorders (Dubovsky et al., 1992). The mood stabilizers lithium and carbamazepine have Ca antagonistic properties (Dubovsky and Franks, 1983; Messing et al., 1985), and Ca channel blocking drugs like verapamil have been introduced as antimanic drugs (Dubovsky, 1995). Magnesium, which has been called ‘nature’s physiological Ca channel blocker’ (Iseri and French, 1984), might also play a role in the treatment of manic excitement.

The recent interest in the sedative and muscle-relaxing effects of Mg prompted us to examine the efficacy and tolerability of Mg sulphate i.v. as a supplementary therapy in the clinical management of therapy-resistant manic agitation in a pilot study. We hypothesized that i.v. Mg would bring about a reduction in the dosages of antipsychotics and tranquilizers.

2. Methods

2.1. Patients

Ten patients with a mean age of 33.8 ± 5.8 years suffering from severe, therapy-resistant manic agitation (Table 1) received Mg infusions. They were transferred from other psychiatric facilities to the psychiatric intensive care unit of the Department of General Psychiatry in Vienna. Pretreatment with neuroleptics and benzodiazepines (assessed in equivalents of chlorpromazine and diazepam, respectively) is specified in Table 1 (= baseline). We used the following formula for chlorpromazine equivalence: 2 mg of haloperidol, 2 mg of fluphenazine, 25 mg of zuclopenthixol, 25 mg of dixyrazin, 50 mg of clozapine, 100 mg of chlorprothixen, 100 mg of levomepromazine or 100 mg of thioridazine are equivalent to 100 mg of chlorpromazine (World Health Organisation, 1998). It is impossible to establish benzodiazepine equivalents precisely, because half-lives may differ considerably (Higgitt et al., 1985). We used the following formula for diazepam equivalence: 2 mg lorazepam or 50 mg oxazepam are equivalent to 10 mg diazepam (Geiselmam and Linden, 1991). In our study we considered 2 mg of clonazepam equivalent to 10 mg diazepam.

Each patient underwent an internal medical evaluation, electrocardiogram, routine laboratory analyses (including thyroid function) and a neurological evaluation, and each was found to be free of major medical illness. The use of Mg i.v. for sedation and muscle relaxation was approved by
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