Originals

Oral magnesium reduces ventricular ectopy in digitalised patients with chronic atrial fibrillation

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Summary. We have examined the effects of magnesium replacement therapy upon post-exercise heart rate and incidence of ventricular premature beats (VPB) in digitalised patients with AF. In 11 such patients, all of whom had serum magnesium concentrations of less than 0.85 mmol/l, treatment with magnesium glycerophosphate was associated with a significant reduction in number of VPBs (982 v. 416 VPB/24 h). Five patients had a high prevalence of ventricular ectopy (> 300 VPB/24 h) and these subjects showed particularly marked decreases in VPBs during magnesium treatment (1998 v. 690 VPB/24 h). Three patients had slightly increased QTc intervals but these did not change during magnesium replacement. No significant changes were seen in the mean post-exercise heart rate although 2 subjects did show falls of 25% or more during magnesium replacement.

We conclude that treatment with magnesium glycerophosphate may be associated with a decreased prevalence of ventricular ectopy in some digitalised patients with chronic AF and mild-moderate hypomagnesaemia.

Key words: magnesium, ventricular ectopy, atrial fibrillation; digitalised patients

Atrial fibrillation (AF) is a common cardiac arrhythmia which is particularly prevalent amongst the elderly [1]. Many patients with chronic AF take long term treatment with digoxin and diuretics and there is some evidence to suggest that both may predispose to magnesium depletion [2-4]. One study has shown that 20% of patients with AF had hypomagnesaemia [5], although serum magnesium concentrations are not a reliable predictor of magnesium status [6]. Magnesium depletion may have two important consequences in patients with AF. Firstly, magnesium deficiency is known to attenuate the pharmacological effects of digoxin, leading to impaired control of the ventricular response rate [5, 7]. Secondly, hypomagnesaemia may predispose to cardiac arrhythmia [8], particularly in digitalised patients [9], and we have previously found a high prevalence of ventricular ectopy among patients with chronic AF [10]. The importance of ventricular ectopy is debatable, although it has been suggested that frequent VPBs (> 400/24 h) may be a poor prognostic sign in patients with cardiac failure or severe ischaemic heart disease [11]. The aim of the present study was to examine the effects of oral magnesium replacement therapy upon control of the ventricular response rate and ventricular ectopy in digitalised patients with chronic AF.

Subjects and Methods

Patients

Patients with chronic stable atrial fibrillation and mild-moderate hypomagnesaemia (serum magnesium concentration < 0.85 mmol/l) were eligible for entry into the study, as long as there was no evidence of renal impairment (serum creatinine > 150 mmol/l), potassium deficiency (serum potassium < 3.5 mmol/l), digoxin toxicity (serum digoxin concentration > 2.6 mmol/l (6-8 h after dosing) or recent myocardial infarction (within the preceding 3 months). Frequent VPBs were not an entry requirement for the study. Patients who were taking a potassium-sparing diuretic were excluded as there is evidence to suggest that drugs such as triameterene, amiloride and spironolactone may promote magnesium retention [3]. Twelve patients (mean age 57 y, range 48-78 y, 6 females) fulfilled these criteria and entered the study. In 7 patients the AF was thought to be secondary to ischaemic heart disease; 4 had rheumatic heart disease and one had treated thyrotoxicosis. One patient with rheumatic heart disease did not complete the study. All of the patients had good exercise tolerance (NYHA class I or II) and none had uncontrolled cardiac failure. All had been taking digoxin (median dose 0.25 mg/day) for at least one year and had a mean serum digoxin concentration of 1.7 (range 1.3 to 2.4) mmol/l. Five patients were taking a diuretic and three were on warfarin. Potassium concentrations at entry ranged from 3.8 to 5.2 (mean 4.1) mmol/l.
Methods

Each patient made two preliminary visits during the course of a 14 day run-in period. At the first visit an exercise test was undertaken to assess maximum effort tolerance. This was carried out using a treadmill, according to a modified Bruce protocol, and patients were simply asked to keep walking for as long as they felt able to. At all subsequent visits patients exercised to a fixed workload which corresponded to approximately 80% of the level achieved during the initial test. At the second baseline visit, a submaximal exercise test was performed and the post-exercise heart rate was determined from 10 consecutive R-R intervals recorded immediately after cessation of exercise. Following this, 24 h ambulatory ECG monitoring was undertaken using Marquette 2 channel ECG recorders. Tapes were analysed independently for numbers of VPBs and for the mean, minimum and maximum heart rate. Printouts of abnormal rhythm were subsequently examined in detail to differentiate between true ectopy and aberrancy using standard criteria [12], and to confirm the validity of the automated counts.

Following the run-in period, patients entered a randomised, double-blind crossover study comprising two treatment periods, each of four weeks duration. Each patient took either magnesium glycerophosphate (6 x 95 mg/day providing 23.4 mmol of elemental magnesium) followed by matching placebo, or the same drugs in the inverse order. Patients were reviewed at two-weekly intervals throughout the study so that two sets of data were obtained during each treatment period. At each visit a standard 12 lead ECG was recorded and QT intervals were measured over 10 complexes. The resting heart rate and blood pressure were recorded and the submaximal effort test was repeated to obtain the post-exercise heart rate. Venous blood was withdrawn for estimation of serum electrolytes, digoxin and magnesium concentrations. All samples were taken after a period of ten minutes supine rest and without using a tourniquet. Finally, repeat 24 h ambulatory ECG monitoring was undertaken.

The results were examined in several ways. In those patients who took placebo as their first treatment, numbers of VPBs recorded during the baseline and placebo periods were compared to assess the reproducibility of the results. In those subjects who took magnesium first, data obtained during the following placebo period was examined for a possible carry-over effect. Using data derived from all patients, numbers of VPBs recorded at the baseline visit were compared with numbers of VPBs seen during magnesium treatment. Finally, "pooled" data was analysed, comparing numbers of VPBs seen on all recordings obtained before magnesium with all data obtained during and after magnesium treatment; the former included all baseline recordings and placebo data for those who took placebo first; the latter included all results obtained during magnesium therapy and placebo data for those who took magnesium as their first treatment.

Results

One patient was withdrawn from the study because of an intercurrent illness which was unrelated to magnesium therapy. No side effects were seen during the course of the study. Among the remaining 11 patients, treatment with magnesium was associated with a modest increase in serum magnesium concentrations (mean 0.15, range 0.08–0.30 mmol/l) (Table 1). There was also a concurrent increase in serum potassium concentrations (mean 0.16; range 0.03–1.10 mmol/l (Table 1).

Ventricular ectopy

Treatment with magnesium was associated with a significant decrease in ventricular ectopy (Fig.1). When compared with baseline, the mean number of VPBs fell from 982 to 416/24 h during magnesium therapy (P < 0.02). Similarly, using pooled data, numbers of VPBs fell from 954 before magnesium to 408/24 h after magnesium (P < 0.05). Five patients had a particularly high prevalence of VPBs (> 300/24 h). These patients showed a substantial decrease in ventricular ectopy during magnesium therapy, the mean number of VPBs falling from 1998 to 690/24 h. Overall, three patients showed a marked decrease (> 200%) in numbers of ectopics and another individual showed a moderate reduction in VPBs. Among the remaining seven patients, there was little change.

In those 6 patients who took placebo as their first treatment, numbers of VPBs were similar during this and the baseline visit (1237 v 1315 VPB/24 h). In those who took magnesium first, the prevalence of ventricular ectopy was similar during this and the following placebo

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<thead>
<tr>
<th>Table 1. Mean serum magnesium and potassium concentrations (mmol/l) seen during magnesium supplementations in 11 patients with chronic atrial fibrillation</th>
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<td>(n = 6)</td>
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