Scottish Executive Health Department Chief Scientist Office

FOCUS ON RESEARCH

MAGNESIUM IN ACUTE LACUNAR STROKE PATIENTS: PRELIMINARY STUDIES FOR CONSIDERING A PROTOCOL FOR A RANDOMISED CLINICAL TRIAL

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Aim

The recent Intravenous Magnesium Efficacy in Stroke (IMAGES) trial found significant benefit from treatment with magnesium (Mg) in patients with non-cortical stroke but not in all patients. Further analysis indicated that this effect was seen especially in patients with small deeply placed strokes called lacunar clinical syndromes (LACS). Whilst we considered that magnesium may deserve to be tested further, we first needed to consider three issues:
I. to examine whether the effect observed in LACS could be explained by baseline differences amongst patients that would independently improve outcome.
II. to examine other clinical trials in stroke to see if other treatments selectively influence lacunar stroke.
III. to review the literature related to lacunar stroke prognostic models, trial inclusion and exclusion criteria and outcome measures.

Project Outline/Methodology

We performed analyses that examined whether the benefit from Mg treatment was still significant when other factors were examined to answer question I. We undertook a systematic review of the literature according to a prespecified protocol to answer question II. We collected information along the way to inform our conclusions on optimal trial design under point III.

Key Results

The Mg and placebo groups of LACS patients were well matched on baseline factors. Benefit from Mg treatment was confirmed in LACS but also seen in patients with younger age, higher baseline diastolic blood pressure, higher mean blood pressure and without ischaemic heart disease. Even when we made allowance for these other factors, the benefit of magnesium in LACS patients remained statistically significant. In the LACS subgroup, Mg led to improvement of standard measures of disability.
From literature, subgroup data from 9 trials were obtained, totalling 2071 patients. Here, a significant overall benefit of various treatments was found, but mostly due to IMAGES, which was both the largest and only trial with an independent effect in LACS.

Conclusions

The positive treatment effect of Mg in lacunar stroke syndromes cannot be discounted due to general issues of severity, time to treatment, blood pressure or other baseline factors: equally, this finding may be due to chance. A large trial of magnesium treatment in lacunar stroke appears justified.
Failure of researchers to consider lacunar stroke separately from other stroke types when designing or reporting previous trials leaves uncertainty over the potential for benefits of other treatment approaches in this lacunar stroke.
Finally, our literature review has shown that doctors use a variety of methods to identify LACS, possibly limiting reliability of their reports. Until MRI scanning is universally available, we need to agree upon a simple reliable bedside method to identify LACS.

What does this study add to the field?

The hints of benefit for lacunar stroke seen in the IMAGES trial cannot easily be discounted as chance findings: a second trial is now justified. We find that doctors may have missed other opportunities to consider lacunar stroke patients separately from other stroke patients when seeking best treatments.

Implications for Practice or Policy

Acute stroke is the third leading cause of mortality in the western world, and the largest single cause of disability. Lacunar strokes constitute about 16% of all ischaemic strokes. Mg is inexpensive and is widely available. Confirmation of a positive effect of Mg could have major public health significance. We have built a strong case to proceed to a clinical trial in LACS and have the information needed to design it.

Where to next?

We will seek funding to conduct a trial of magesium in patients with lacunar stroke.

Further details from:

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