



The 3Mg Trial: A randomised trial of intravenous or nebulised magnesium sulphate versus placebo for acute severe asthma

Summary of the project

This is a multicentre pragmatic randomised controlled trial and economic evaluation, to determine whether intravenous (IV) or nebulised magnesium sulphate should be standard first-line treatment for patients with acute severe asthma.

Objectives

We plan to test the following specific hypotheses:

1. IV or nebulised magnesium sulphate will reduce the proportion of patients who require admission at initial presentation or during the following week
2. IV or nebulised magnesium sulphate will improve patient's assessment of their breathlessness over two hours after initiation of treatment

We will also measure the effect of IV or nebulised magnesium sulphate upon:

1. Length of hospital stay and use of high-dependency or intensive care
2. Mortality, adverse events and use of respiratory support
3. Change in peak expiratory flow rate (PEFR) and physiological variables after initial treatment
4. Patient reported health utility
5. Patient satisfaction with care
6. Use of health and social services over the following month
7. Time taken by patients off work
8. Health and social care costs and productivity losses

Study design

Multi-centre, pragmatic, double blind, placebo controlled, three-arm, randomised trial.

Planned interventions

Participants will be randomised using the Sheffield Clinical Trials Research Unit (CTRU) online and phone randomisation system to one of the following three treatment arms:

Treatment arm	Intravenous infusion	Nebulisers
1	Intravenous magnesium sulphate, 8 mmol (2g) in 100ml Water for Injections, adjusted to isotonicity with sodium chloride, given over 20 minutes	7.5ml vial of 0.9% saline, given 3 times 20 minutes apart
2	Intravenous 0.9% saline, 100ml given over 20 minutes	7.5ml vial of 2 mmol (500mg) magnesium sulphate, given 3 times 20 minutes apart
3	Intravenous 0.9% saline, 100ml given over 20 minutes	7.5ml vial of 0.9% saline, given 3 times 20 minutes apart

All three groups will also receive standard therapy, according to BTS/SIGN guidelines, with high flow oxygen and oral prednisolone. Other treatments will be given at the discretion of the attending clinician and recorded on the data collection form, although adherence to BTS/SIGN guidelines will be promoted.



Patient selection

We will recruit adults (age>16) admitted to the emergency department with acute severe asthma as defined by the BTS/SIGN guidelines, i.e. acute asthma with either PEFR < 50% of best or predicted, respiratory rate > 25/min, heart rate > 110/min, or inability to complete sentences in one breath.

We will exclude: 1) Patients with life threatening features (oxygen saturation < 92%, silent chest, cyanosis, poor respiratory effort, bradycardia, arrhythmia, hypotension, exhaustion, coma or confusion); 2) Patients who are unable to provide written or oral consent; 3) Patients with a contraindication to either nebulised or intravenous magnesium sulphate: pregnancy, hepatic or renal failure, heart block or known hypermagnesaemia; 4) Patients who have received IV or nebulised magnesium sulphate in the previous 24 hours prior to admission to the emergency department 5) Previous participants in the 3Mg Trial.

Outcome measures

We will measure two primary outcomes:

1. The proportion of patients who are admitted to hospital, either after emergency department treatment or at any time over the subsequent week.
2. The patient's visual analogue scale (VAS) for breathlessness over two hours after initiation of treatment.

Secondary outcomes will include mortality, adverse events, use of ventilation or respiratory support, length of hospital stay, use of high dependency or intensive care, change in PEFR and physiological variables (oxygen saturation, heart rate, respiratory rate) over two hours, quality of life (EQ-5D) at baseline and one month, number of unscheduled health care contacts over the subsequent month, and satisfaction with care.

Sample size

We plan to recruit 1200 participants divided equally between the three trial arms (400 per arm) over two years at up to 30 hospitals. The study will have 90% power to detect a 10% absolute reduction in the proportion admitted (from 80% to 70%) for any pair of treatment groups compared (two-sided alpha=0.05) and 90% power to detect a 0.8cm difference in a 10cm VAS at two hours after treatment initiation (two-sided alpha=0.05).

Economic evaluation

We will measure health care resource use (including emergency department visits, hospital admission, general practitioner and outpatient visits, tests and treatments), social care resource use and productivity losses over the subsequent month, using case record review and patient self-completion questionnaire.

Patient consent

The Trial will be undertaken in accordance with the Medicine for Human Use (Clinical Trials) Regulations 2004. We will seek consent from the patient as approved by the multicentre research ethics committee. If initially they are unable to provide written consent we will obtain oral consent in the first instance, and obtain written consent before they leave the emergency department.

Project management and funding: The Trial is funded by the NHS Health Technology Assessment Programme and is sponsored by the Sheffield Teaching Hospitals NHS Trust.



Summary of the 3Mg Trial

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