A pilot study of the pharmacokinetics of continuous magnesium infusion in critically ill patients

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Magnesium is vital for numerous biochemical and physiological functions.¹ In clinical practice, serum magnesium is most commonly measured as total magnesium,² with normal values ranging between 0.7 mmol/L and 1.0 mmol/L.¹ Hypomagnesaemia (< 0.7 mmol/L) is a common finding in critically ill patients, may increase the risk of arrhythmias, and is associated with increased mortality.^{2,3} Thus, magnesium supplementation in critically ill patients is common.²

Variability in current clinical intravenous magnesium therapy is evident by differences in quantity, frequency, and mode of delivery. This variability may be due to previous studies only reporting the pharmacokinetic data in specific groups: children,⁴⁻⁶ pregnant women,^{7,8} and cardiac surgery patients.⁹⁻¹¹ No study, however, has described the pharmacokinetic effects of continuous intravenous magnesium therapy on total serum magnesium levels in critically ill patients receiving mechanical ventilation and vasopressor support. These patients may be at particular risk of arrhythmias, especially atrial fibrillation.¹² Moreover, previous small single centre controlled studies have shown that continuous magnesium infusion slows down the ventricular response to atrial fibrillation,¹³ increases its conversion to sinus rhythm¹³ and prevents its development in cardiac surgery patients.¹⁴

Accordingly, we aimed to evaluate the pharmacokinetics of a combined “bolus plus continuous infusion” protocol of intravenous magnesium therapy targeting total serum magnesium levels between 1.5 mmol/L and 2 mmol/L in critically ill, mechanically ventilated, vasopressor-dependent patients. We hypothesised that such intervention would be logistically feasible, provide useful pharmacokinetic data, achieve magnesium target levels, and would not lead to an increase in vasopressor therapy.

Methods

This pharmacokinetic study was approved by Austin Health Human Research Ethics Committee (Reference No. HREC/52758/Austin-2019-177785; ANZCTR.org.au

ABSTRACT

Objective: The pharmacokinetics and haemodynamic effect of continuous magnesium infusion in non-cardiac intensive care unit (ICU) patients are poorly understood. We aimed to measure serum and urine magnesium levels during bolus and continuous infusion in critically ill adults, compare serum levels with those of a control population, and assess its haemodynamic effect.

Design: Pharmacokinetic study.

Setting: A single tertiary adult ICU.

Participants: Mechanically ventilated adults requiring vasopressor support.

Intervention: A 10 mmol bolus of magnesium sulfate followed by 1.5–3 mmol/h infusion for 24 hours.

Main outcome measures: The primary outcome was the change in total serum magnesium concentration. The main secondary outcome was mean arterial pressure (MAP)-adjusted vasopressor dose.

Results: We matched 31 treated patients with 93 controls. Serum total magnesium concentration increased from a median 0.94 mmol/L (interquartile range [IQR], 0.83–1.10 mmol/L) to 1.38 mmol/L (IQR, 1.25–1.69 mmol/L; $P < 0.001$) and stabilised between a median 1.64 mmol/L (IQR, 1.38–1.88 mmol/L) at 7 hours and 1.77 mmol/L (IQR, 1.53–1.85 mmol/L) at 25 hours. This was significantly greater than in the control group ($P < 0.001$). The MAP-adjusted vasopressor dose decreased during magnesium infusion ($P < 0.001$).

Conclusion: In critically ill patients, a magnesium sulfate bolus followed by continuous infusion achieved moderately elevated levels of total serum magnesium with a decrease in MAP-adjusted vasopressor dose.

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Registration No. ACTRN12619000925145). Written consent was provided by the patient's legally responsible person.

Study inclusion criteria

We aimed to study a convenience sample of 30 adult patients admitted to the intensive care unit (ICU) of the Austin Hospital in Melbourne, Australia.

We included patients who:

- had an existing intra-arterial catheter, a central venous catheter, and an indwelling urinary catheter;
- were mechanically ventilated via an endotracheal tube;
- were receiving vasopressor therapy; and
- had a treating clinician who decided that intravenous magnesium replacement was indicated.

We excluded patients who:

- were admitted to the ICU following cardiac surgery;
- had an allergy to magnesium sulfate or one of its excipients;
- were pregnant;
- were already receiving or had received a continuous intravenous magnesium infusion in the previous 24 hours;
- were currently receiving a muscle relaxant infusion;
- had a serum creatinine concentration of $> 200 \mu\text{mol/L}$; or
- were receiving continuous renal replacement therapy.

Basic demographic data, physiological parameters and information relating to ICU and hospital length of stay were collected.

Control group

Using the ICU's electronic admissions database, we retrospectively identified a matched cohort of patients admitted to the ICU in the previous year who were intubated and ventilated and were receiving vasopressor support. They formed a control group for the purpose of comparing magnesium levels in the first 24 hours. Each study patient was matched to three control patients based on age, sex, Acute Physiology and Chronic Health Evaluation (APACHE) III score and admission diagnosis category. We used the ICU's electronic medical records to collect information on basic demographic data, physiological and biochemical parameters along with information relating to ICU and hospital length of stay.

Magnesium infusion

We administered a 10 mmol bolus of magnesium sulfate through a central venous catheter over one hour, followed by a continuous infusion at a rate of between 1.5 mmol/h and 3 mmol/h for 24 hours depending on total serum magnesium levels. The infusion was stopped if there were two consecutive total serum magnesium levels over

2 mmol/L or if urine output was less than 200 mL over 6 hours (Figure 1). Blood and spot urine samples were taken immediately before the bolus infusion and at 6, 12, 18 and 24 hours after the bolus administration was completed. Blood and urine samples were sent immediately to a central pathology department for processing.

Primary and secondary outcomes

The primary study outcome was the change in total serum magnesium levels over a 25-hour period following the commencement of the intervention.

The main secondary outcome was the change in vasopressor dose (in noradrenaline equivalents)¹³ indexed to mean arterial pressure (MAP) over the observation period. Additional outcomes included assessment of the effect of furosemide on magnesium excretion and the comparison of total serum magnesium, sodium and potassium levels with the control population.

The following pharmacokinetic calculations were used:

$$\text{Volume of distribution (VD)} = \frac{\text{dose of bolus drug}}{\text{plasma concentration at end of bolus therapy}}$$

$$\text{Clearance (K)} = \frac{\text{urine concentration} \times \text{urine flow}}{\text{serum concentration}}$$

$$\text{Fractional excretion of magnesium (FE}_{\text{mg}}) = 100 \times \frac{[\text{Mg}]_{\text{urine}} \times [\text{creatinine}]_{\text{serum}}}{[\text{Mg}]_{\text{serum}} \times [\text{creatinine}]_{\text{urine}}}$$

Statistical methods

Statistical analyses were performed using R v3.5.2 (R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were expressed as median with interquartile range (IQR) and categorical variables were expressed as n (%). Baseline variables were compared using the Mann–Whitney U test or Fisher exact test. To compare the difference of magnesium or vasopressors between baseline and each time point, we used a mixed effect model to analyse the time course of each variable, accounting for repeated measurements and treating time as a continuous variable. When time was statistically significant, we performed a post hoc analysis to compare the variables at each time point using a mixed effect model, accounting for repeated measurements and treating time as a categorical variable, adjusted with Tukey test. To compare the intervention group and matched control group at 25 hours, we used the Mann–Whitney U test. For sensitivity analysis, we separated patients into a furosemide use group and a non-furosemide use group during magnesium infusion and applied a mixed effect model. When a group effect or interaction was significant, we compared each time point between the two groups, adjusted with Tukey test. We estimated that a cohort of 30 patients would have a greater than 90% chance of detecting a change from an estimated

Figure 1. Magnesium (Mg) supplementation algorithm

Measure serum and urine Mg at the following times:

- Immediately before the bolus infusion (t = 0 h)
- Immediately after end of bolus infusion (t = 1 h)
- 6 hours after end of bolus infusion (t = 7 h)
- 12 hours after end of bolus infusion (t = 13 h)
- 18 hours after end of bolus infusion (t = 19 h)
- 24 hours after end of bolus infusion (t = 25 h)

Only alter the rate of infusion once results are available

baseline total serum magnesium levels from 0.9 mmol/L to a value of 1.4 mmol/L (with a standard deviation of 0.65 mmol/L in both groups) at $\alpha = 0.05$. A two-sided P value below 0.05 was considered statistically significant.

Results

Patients and intervention characteristics

There were 1442 patients admitted to the study centre between 16 July 2019 and 13 March 2020, of which 31 patients were studied (Figure 2). Ninety-three matched patients from the ICU database were identified to form the control group. The baseline characteristics of the control and intervention groups are outlined in Table 1. During the study period, apart from the intervention, no doses of either enteral or parenteral magnesium sulfate were administered to patients in the intervention group. Historical control group patients received a median of 10 mmol (IQR, 0–20 mmol) magnesium sulfate intravenously during the first 24 hours in the ICU.

In the intervention group, the median baseline creatinine was 74 $\mu\text{mol/L}$ (IQR, 59–117 $\mu\text{mol/L}$). One patient (3%) required a dose reduction, while five (16%) patients had the magnesium infusion ceased — three patients due to consecutive total serum magnesium concentrations greater than 2.0 mmol/L and two due to low urine output. No infusions were ceased due to clinical concern.

Effects on total serum magnesium

At baseline, total serum magnesium concentration was 0.85 mmol/L in the control group compared with 0.94 mmol/L in the intervention group ($P = 0.029$) (Table 1).

In the intervention group, total serum magnesium concentration increased from baseline to 1.38 mmol/L after a 10 mmol bolus of magnesium sulfate administered over one hour, implying a median volume of distribution of 21.28 L or 0.3 L/kg. Thereafter, total serum magnesium concentration increased further to 1.64 mmol/L 7 hours after the start of the intervention and remained stable up to 25 hours when it reached 1.77 mmol/L ($P < 0.001$) (Figure 3, A, and Table 2). There were no instances of total serum magnesium levels greater than 3.0 mmol/L. The corresponding total serum magnesium concentration in the control group, after an equivalent observation period was 0.95 mmol/L, significantly lower than in the intervention group ($P < 0.001$) (Figure 4, A).

Effects on urinary magnesium and clearance

In the intervention group, urine magnesium concentration increased from a median baseline of 4.2 mmol/L to 5.5 mmol/L after the bolus dose. Thereafter, urine magnesium concentrations continually increased to a peak of 29.0 mmol/L at 19 hours after the start of the intervention ($P < 0.001$) (Figure 3, B, and Table 2).

The median magnesium clearance (K_{Mg}) was 4.14 mL/min at baseline, and increased to a peak of 20.98 mL/min at 25 hours after the start of the intervention ($P < 0.001$). The fractional excretion of magnesium (FE_{Mg}) followed a similar trend ($P < 0.001$) (Figure 3, C).

Effects on haemodynamic parameters

There was no statistical difference in heart rate and MAP between the intervention and control groups at baseline or at the end of the intervention period. In the intervention group, over 25 hours, vasopressor requirements (expressed as noradrenaline equivalent doses) decreased from a median of 0.08 $\mu\text{g/kg/min}$ to 0.00 $\mu\text{g/kg/min}$ ($P < 0.001$). Similarly, when the noradrenaline equivalent dose was indexed to

Figure 2. Study flow diagram

Table 1. Baseline characteristics of study patients

	Control	Intervention	P
Total number of patients	93	31	
Demographic characteristics			
Age (years), median (IQR)	60.00 (50.00–70.00)	63.04 (54.84–74.04)	0.174
Sex, female	46 (49.5%)	15 (48.4%)	> 0.99
Weight (kg), median (IQR)	75.00 (66.50–91.50)	75.00 (64.00–85.00)	0.615
Comorbidities			
Hypertension	28 (30.1%)	12 (38.7%)	0.384
Hyperlipidaemia	14 (15.1%)	7 (22.6%)	0.407
Ischaemic heart disease	12 (12.9%)	0 (0.0%)	0.036
Chronic liver disease	29 (31.2%)	2 (6.5%)	0.007
Insulin-dependent diabetes	5 (5.4%)	2 (6.5%)	> 0.99
Paroxysmal atrial fibrillation	10 (10.8%)	1 (3.2%)	0.289
Chronic kidney disease	7 (7.5%)	1 (3.2%)	0.678
Illness severity			
APACHE III, median (IQR)	59.00 (42.00–71.00)	58.00 (50.00–78.00)	0.514
Physiological characteristics			
Heart rate, median (IQR)	80.00 (65.00–95.00)	74.00 (65.00–85.00)	0.254
Mean arterial pressure (mmHg), median (IQR)	75.00 (70.00–85.00)	75.00 (70.00–80.00)	0.945
Central venous pressure (mmHg), median (IQR)	9.00 (7.00–12.00)	10.50 (9.50–12.00)	0.251
Sinus rhythm	93 (100.0%)	31 (100.0%)	na
Respiratory rate, median (IQR)	15.00 (12.00–16.00)	16.00 (14.00–19.50)	0.002
FiO ₂ , median (IQR)	0.40 (0.25–0.50)	0.25 (0.21–0.38)	0.008
SaO ₂ (%), median (IQR)	98.00 (95.00–100.00)	96.00 (95.00–98.00)	0.071
Vasopressor use			
Noradrenaline	85 (91.4%)	31 (100.0%)	0.199
Vasopressin	7 (7.5%)	3 (9.7%)	0.71
Adrenaline	2 (2.2%)	0 (0.0%)	> 0.99
Metaraminol	8 (8.6%)	0 (0.0%)	0.199
Ventilation			0.012
Pressure support ventilation	7 (7.5%)	8 (25.8%)	
SIMV	86 (92.5%)	23 (74.2%)	
Admission diagnosis category			0.049
Cardiovascular	1 (1.1%)	1 (3.2%)	
Gastrointestinal	31 (33.3%)	6 (19.4%)	
Neurological	28 (30.1%)	7 (22.6%)	
Respiratory	12 (12.9%)	3 (9.7%)	
Sepsis	14 (15.1%)	13 (41.9%)	
Trauma	7 (7.5%)	1 (3.2%)	
Serum biochemistry			
Creatinine (μmol/L), median (IQR)	76.00 (61.75–113.50)	74.00 (59.50–117.50)	0.935
Magnesium (mmol/L), median (IQR)	0.85 (0.76–0.96)	0.94 (0.84–1.10)	0.029
Sodium (mmol/L), median (IQR)	139.00 (136.00–142.00)	141.00 (138.00–143.50)	0.05
Potassium (mmol/L), median (IQR)	4.20 (4.00–4.60)	4.10 (4.00–4.45)	0.38

APACHE = Acute Physiology and Chronic Health Evaluation; CVP = central venous pressure; FiO₂ = fraction of inspired oxygen; IQR = interquartile range; na = not applicable; SaO₂ = oxygen saturations; SIMV = synchronous intermittent mechanical ventilation.

MAP, it decreased from a median of 0.001 $\mu\text{g/kg/min/mmHg}$ to 0.000 $\mu\text{g/kg/min/mmHg}$ ($P < 0.001$) (Figure 3, D, and Table 2).

Effects of furosemide

In the intervention group, during the study period, 13 patients (41.9%) received at least one bolus dose of furosemide, and

three patients (9.7%) received a furosemide infusion. There were no observed differences in total serum magnesium levels (group effect $P = 0.96$; interaction $P = 0.54$) (Figure 5, A), urine magnesium levels (group effect $P = 0.99$; interaction $P = 0.19$) (Figure 5, B) or adjusted vasopressor indexed to MAP (group effect $P = 0.29$; interaction $P = 0.93$) (Figure 5, D) when comparing patients who did and did not

Figure 3. Effects of intervention on (A) total serum magnesium concentrations, (B) urine magnesium concentrations, (C) fractional excretion of magnesium (Fe_{Mg}), and (D) adjusted vasopressor dose indexed to mean arterial pressure (MAP)

Table 2. Outcome of magnesium pharmacokinetics and vasopressor requirements expressed as noradrenaline (NA_{Dr}) equivalents

Variable	Baseline	1 hour	7 hours	13 hours	19 hours	25 hours	P
Serum Mg (mmol/L)	0.94 (0.83–1.10)	1.38 (1.25–1.69)	1.64 (1.38–1.88)	1.83 (1.48–2.05)	1.87 (1.52– 2.14)	1.77 (1.53–1.85)	< 0.001
Urine Mg (mmol/L)	4.21 (1.31–8.23)	5.53 (2.38–12.25)	18.09 (13.95–35.33)	20.78 (13.54–34.95)	29.04 (17.56–42.76)	26.01 (8.97–46.23)	< 0.001
Mg clearance (mL/min)	4.14 (1.61–6.10)	4.01 (1.71–9.32)	15.45 (7.85–32.04)	17.49 (11.09–24.24)	17.30 (9.45–28.51)	20.98 (10.58–29.69)	< 0.001
Fe _{Mg} (%)	4.54 (2.64–9.30)	4.67 (2.05–11.81)	19.55 (17.21–26.95)	22.93 (18.11–32.15)	27.06 (18.97–34.01)	27.02 (22.02–33.22)	< 0.001
NA _{Dr} equivalence (µg/kg/min)	0.08 (0.03–0.12)	0.08 (0.04–0.11)	0.03 (0.02– 0.15)	0.03 (0.00– 0.08)	0.00 (0.00– 0.07)	0.00 (0.00–0.05)	< 0.001
NA _{Dr} equivalent dose/MAP (µg/kg/min/mmHg)	0.0010 (0.0004– 0.0015)	0.0011 (0.0004– 0.0016)	0.0005 (0.0002– 0.0020)	0.0003 (0.0000– 0.0013)	0.000 (0.0000– 0.0008)	0.000 (0.0000– 0.0006)	< 0.001
Serum Na (mmol/L)	141 (138–144)	141 (138–144)	141 (137– 145)	142 (138–145)	143 (139–147)	144 (140–148)	< 0.001
Serum K (mmol/L)	4.1 (4.0–4.5)	4.3 (4.0–4.5)	4.1 (3.9–4.3)	4.1 (4.0–4.3)	4.1 (3.8–4.4)	4.0 (3.8–4.2)	0.003
Serum creatinine (µmol/L)	74 (60–118)	76 (60–119)	75 (60–111)	87 (59–116)	94 (54–110)	80 (57–109)	0.947
Urine creatinine (mmol/L)	7.7 (5.2–11.0)	6.8 (4.5–9.9)	5.8 (3.5–9.3)	5.8 (3.1–7.6)	6.4 (2.4–8.5)	5.2 (2.9–7.2)	0.014
Urine output (mL/h)	55 (30–80)	50 (35–75)	65 (40–150)	60 (40–120)	55 (39–100)	63 (40–100)	0.137

Fe_{Mg} = fractional excretion of magnesium; K = potassium; MAP = mean arterial pressure; Mg = magnesium; Na = sodium. *P* values reflect time effect. All values are expressed as median (interquartile range).

receive furosemide. Furosemide therapy, however, increased the FE_{Mg} (group effect *P* = 0.016) (Figure 5, C).

Effects on serum biochemistry

In the intervention group, serum sodium concentrations increased from a median 141 mmol/L (IQR, 138–143 mmol/L) at baseline to 144 mmol/L (IQR, 140–148 mmol/L; *P* < 0.001) over the observation period. The final serum sodium concentration was significantly different from the median control group's serum sodium of 140 mmol/L (IQR, 137.00–143.00 mmol/L; *P* = 0.002) (Figure 4, B).

A small statistically significant decrease in serum potassium was noted over the observation period in the intervention group, from a median 4.1 mmol/L (IQR, 4.0–4.4 mmol/L) to 4.0 mmol/L (IQR, 3.8–4.2 mmol/L; *P* = 0.003). This value was significantly different from the final control group serum potassium median of 4.2 mmol/L (IQR, 4.0–4.4 mmol/L; *P* = 0.023) (Figure 4, C). There were no statistically different measurements in serum creatinine levels throughout the observation period (Figure 4, D).

Discussion

Key findings

Our study demonstrates that moderate hypermagnesaemia can be safely achieved in mechanically ventilated,

vasopressor-dependent critically ill patients with normal to moderately impaired renal function using a “bolus followed by infusion” protocol of magnesium sulfate. In addition, sustained hypermagnesaemia occurred despite a concomitant increase in urinary excretion of magnesium, even when furosemide was given, and resulted in levels that were within target and clearly different from usual care and baseline. Finally, there were no instances of severe hypermagnesaemia (> 3 mmol/L) and no increase in vasopressor requirements and only small changes in serum sodium and potassium.

Relationship to previous studies

To our knowledge, no study had assessed the pharmacokinetics of intravenous magnesium bolus followed by infusion targeting a total serum magnesium level between 1.5 mmol/L and 2.0 mmol/L in adult, mechanically ventilated, vasopressor-dependent, critically ill patients. However, in 1995, a study used a magnesium bolus and infusion strategy in patients with atrial tachyarrhythmias.¹⁴ The investigators delivered a bolus dose of 0.15 mmol/kg followed by a continuous infusion at 0.1 mmol/kg/h. This approach increased the probability of conversion to sinus rhythm compared with an amiodarone infusion and similarly targeted serum magnesium concentrations between

Figure 5. Effect of the intervention grouped by furosemide use on (A) total serum magnesium (Mg) concentrations, (B) urine Mg concentrations, (C) fractional excretion of Mg (Fe_{Mg}), and (D) adjusted vasopressor dose indexed to mean arterial pressure (MAP)

1.5 mmol/L and 2.0 mmol/L after 24 hours. Regrettably, no pharmacokinetic data such as the volume of distribution or clearance were reported.

With regard to volume of distribution, we found a similar value at 0.3 L/kg as seen in patients after cardiac surgery,⁹⁻¹¹ in women with pre-eclampsia,^{7,8} and in children with asthma.⁴⁻⁶ However, the clearance of magnesium was much greater in pregnant women (80–100 mL/min) and children (> 100 mL/min), highlighting that information obtained in relatively healthy individuals cannot be extrapolated to critically ill patients.

Our findings demonstrate that even when the serum creatinine level is normal, in the presence of vasopressor therapy, renal clearance of magnesium is reduced. As a consequence, 20% of our study population required a reduction in the rate of magnesium infusion, to a greater

degree than that seen in cardiac surgery patients.^{10,11} Thus, an increased degree of vigilance in the form of total serum magnesium monitoring is required in patients receiving vasopressor therapy. Similar to previous studies,^{2,11} magnesium supplementation did not affect the amount of vasopressor used. Finally, although furosemide increased the urinary excretion of magnesium as previously reported,¹⁵⁻¹⁷ it did not alter total serum magnesium levels.

Implications of study findings

Our findings imply that in ICU patients for whom magnesium therapy may be particularly relevant, the volume of distribution is 0.3 L/kg. Therefore, if the target total serum magnesium level is between 1.5 mmol/L and 2.0 mmol/L, in a patient weighing 80 kg, assuming a baseline level of 0.8 mmol/L, rapid achievement of such levels would require a bolus dose of about 24 mmol of magnesium sulfate.

Figure 4. Serum biochemistry of the control and intervention groups, with P values representing statistical significance between the two groups at the end of the intervention period (at 25 hours)

K = potassium; Mg = magnesium; Na = sodium.

Moreover, our findings imply that given the urinary excretion of magnesium in these patients, a continuous infusion of between 1.5 mmol/h and 3 mmol/h is necessary to maintain such levels, provided that caution is applied in the presence of oliguria and deteriorating renal function. Furthermore, they imply that such infusion rate is sufficient even in the presence of furosemide treatment. Finally, they imply that the regimen described in this study is likely to be safe, as no deterioration in vasopressor support was noted and no total serum magnesium level exceeded 3.0 mmol/L.

Strengths and limitations

We report, for the first time, the effect on total serum and urinary magnesium concentrations of a combined bolus and infusion magnesium therapy protocol in non-cardiac ICU patients receiving mechanical ventilation and vasopressor therapy. We have provided key pharmacokinetic

information, which may help clinicians who wish to target similar magnesium levels in this patient population. We have demonstrated that it is possible to maintain a moderate degree of hypermagnesaemia, that the pharmacokinetics differ somewhat from those seen in relatively healthy patients and are not substantially modified by furosemide therapy.

We acknowledge several limitations. The sample size was small, but doing detailed pharmacokinetics studies is logistically very demanding and expensive. In addition, the design was single centre. However, the findings in the population targeted (vasopressor-dependent, mechanically ventilated patients) are likely to apply to similar such patients in other centres. The duration of the intervention was only 24 hours; therefore, we cannot comment on the clinical risks and benefits of such treatment over longer time periods. However, this study was conducted to inform such

future prolonged infusion with the goal of affecting clinical outcomes such as atrial tachyarrhythmias.

Conclusion

In critically ill patients, compared with baseline values and levels in a control population, a magnesium sulfate bolus followed by continuous infusion achieved the target moderately elevated levels of total serum magnesium over 25 hours without ever exceeding a value of 3 mmol/L and was associated with a decrease in MAP-adjusted vasopressor dose. These findings form the pharmacokinetic basis for future randomised controlled trials of a magnesium infusion targeting moderate hypermagnesaemia in this population with the aim of preventing or slowing atrial fibrillation.

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Competing interests

All authors declare that they do not have any potential conflict of interest in relation to this manuscript.

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