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REDUCING THE RISK OF MEDICATION ERRORS WITH INTRAVENOUS MAGNESIUM SULFATE

This bulletin has been developed by Wessex Academic Health Science Network on behalf of the Thames Valley and Wessex Chief Pharmacists Network



Reducing the Risk of Medication Errors with IV Magnesium Sulfate

To Note: This paper refers mainly to the obstetric management of pregnant women but many of the risks and issues highlighted also relate to other clinical areas.

This bulletin has been developed by Wessex Academic Health Science Network on behalf of the Chief Pharmacists in the Wessex and Thames Valley areas and is endorsed by the Wessex Maternity, Children and Young People Strategic Clinical Network.

Executive Summary

Intravenous magnesium sulfate has the potential to cause serious harm or death when used incorrectly.

Evidence both nationally and locally indicates that patients are being exposed to significant risk when magnesium sulfate injections/infusions are being prepared in clinical areas.

Because of the very serious risks associated with overdose, Trusts are advised NOT to have policies that require the dilution of 50% magnesium sulfate. Diluting 50% magnesium sulfate for injection is complicated and calculation errors are common.

It is safer, easier and potentially more efficient to use ready-made 10% or 20% magnesium sulfate preparations.

Trusts should now review their protocols and procurement arrangements to ensure that clinical areas are aware of the risks; that ready-to-use preparations are made available and staff using the preparations are supported in their safe use.

Whilst the risks described above cannot be eliminated, standardising the doses and strengths used in each clinical area and working with clinicians to make them aware of the risks, including how to perform the calculation accurately, are deemed to be a minimum requirement.

It has been agreed across the regional network of Chief Pharmacists and the Wessex SCN for Maternity Children and Young People, that this initiative should be started in obstetric units initially. Obstetrics is the obvious setting to start this work because of the fixed loading and maintenance doses. (Please see BNF).

Actions to Reduce the Risks of Errors with Magnesium Sulfate

Safer prescribing and administration of magnesium sulfate injection for eclampsia

Trusts should review protocols to ensure that the dose and administration are clearly specified for the treatment and prevention of seizures in the management of eclampsia and foetal neuroprotection for pre term deliveries.

Trusts should ensure prescribing of standard concentrations of solution for administration where possible e.g. 20%

Trusts should ensure that the protocol for the management of eclampsia and foetal neuroprotection (and associated prescribing) relates to the product supplied by Pharmacy.

The 50% solution should never be used neat. Diluting magnesium sulfate is difficult and errors are frequently made when calculating dilutions.

The BNF states that for intravenous injection the concentration of magnesium sulfate should not exceed 20% (200mg/mL or 0.8 mmol/mL)

Magnesium sulfate injection and pre-prepared infusion strengths should be expressed in mmol and grams in all electronic dispensing systems to reduce confusion in magnesium dosing.

Safer procurement of magnesium sulfate injection for eclampsia

Trusts should now review their protocols for the treatment of eclampsia and Pharmacy

should supply magnesium sulfate injection at a concentration that does not require further dilution before administration i.e. 20%w/v or less.

If the Pharmacy cannot purchase a licensed product of magnesium sulfate injection at a concentration that does not require further dilution, then an unlicensed product should be purchased from a specials manufacturer e.g. an NHS Manufacturing unit.

The Oxford Pharmacy Store will stock unlicensed 20% magnesium sulfate injection if it is unavailable as a licensed product.

Where pre-prepared magnesium sulfate infusions are not available, calculation of the volume of magnesium sulfate solution required to prepare the IV infusion should be carried out extremely carefully. See table in Appendix 1 of supporting information.

N.B It is very rare that 'more than 3' vials/ ampoules of magnesium sulfate injection would be required to prepare an infusion, even at the higher doses. For this reason it is imperative that all calculations are independently second checked by another member of medical/nursing/pharmacy staff.

The Medication Safety Officer (MSO) should lead the review of practice in collaboration with the relevant medical, nursing, clinical pharmacists and procurement pharmacists.

At the time of printing, there are no licensed 20% preparations. However, if the whole region moves to purchase this product to reduce the risk to patients, it is more likely to encourage the licensing of such a product. Wessex AHSN will work with other regions and NHS England to support the development of a nationally licensed product.

Steps to making the change in your Trust

1. Trusts are advised to take this bulletin to their local Drug and Therapeutics Committee or equivalent and discuss the implication for obstetric departments in the first instance. Discussions should include costs, training and procurement issues as well as any incidents that have occurred in the trust recently.
2. Trusts should consider immediate cessation of purchasing the 50% products and agree protocols that use the 20% product.
3. Trust should display the magnesium sulfate poster in all clinical areas where magnesium sulfate is used.
4. Drawing from numerous vials should act as a 'red flag' that an excessive dose is potentially being prepared.

Supporting Information

Background

A number of regional projects have been carried out to reduce the risk of injectable medicines to patients, in response to the National Patient Safety Agency Patient Safety Alert 20 <http://www.nrls.npsa.nhs.uk/resources/?entryid45=59812>

Many of the projects have been well received by local trusts. However, the work on magnesium sulfate has proved harder to secure engagement with and, to date, there has been little progress in standardising prescribing, standardising doses or purchasing for safety.

1. Why is IV magnesium sulfate a high risk to patients?

Intravenous (IV) magnesium sulfate is widely used to treat a number of indications such as arrhythmias, asthma, hypomagnesaemia, eclampsia and neuroprotection of the fetus in the management of preterm labour. It is very effective when used safely however, it has the potential to cause serious harm or death when used incorrectly.

It has been classified as a high-risk medicine with a score of 6 according to Medusa - The Injectable Medicines Guide. See below.

DRUG NAME	FORM	Bag (B) Syringe (S) / Infusor (I)	Therapeutic risk	Use of concentration	Complex calculation	Complex preparation	Reconstitute vial	Part/multiple container	Use of Infusion pump/driver	Non standard infusion set	Total risk factors (NPSA 20)	NPSA20 RISK LEVEL
Magnesium sulphate (eclampsia)	IV infusion	S	Y	Y	Y	Y		Y	Y		6	HIGH

Extract from Medusa – The Injectable Medicines Guide. Consensus guide on identification of potential high risk injectable medicines. (Update on “Examples of risk assessments of injectable medicine products prepared in clinical areas” published by the Joint NHS pharmacy technical services groups in 2007) December 2011

2. What can go wrong? (In all clinical setting, not just in the emergency treatment of eclampsia in obstetric units.)

Different ways of expressing the same dose

In addition to problems or confusion around the dose to give to patients for the various different indications, a number of problems are caused by the way that the dose of magnesium sulfate is expressed. The dose of magnesium sulfate can be expressed in grams (g), milligrams (mg), millimoles (mmol) or percentage weight in volume of magnesium (%w/v) (2).

Each 1g of magnesium sulfate (as heptahydrate) is equivalent to approximately 4 mmol magnesium (Mg^{2+}) (2, 8).

Wrong dose

Magnesium sulfate has been identified as a high-risk medication (1). It is vital to administer the correct dose of magnesium sulfate intravenous injection or infusion to avoid underdosing or overdosing. An overdose of magnesium sulfate leads to the development of hypermagnesaemia with adverse effects such as nausea, vomiting, hypotension, confusion, muscle weakness, respiratory depression, loss of tendon reflexes, cardiac arrhythmias, and cardiac arrest (2-6).

Limited range of presentations at the required concentration

According to the BNF magnesium sulfate injection should be available as a 10% w/v, 20% w/v, or 50% w/v licensed preparation (3,4,5,6). However, these licensed preparations are not always available to purchase. Despite the warnings that magnesium sulfate injection should never be given IV at a concentration greater than 20%, the only licensed presentation that has been consistently available in the UK is the 50% solution. Therefore, Trusts have supplied 50% solution to clinical areas, as it was the only product that was available. Unlicensed preparations of 10% and 20% have been available from NHS Manufacturing Units but very few Trusts have purchased these and this may be due to a lack of awareness of availability and clinical risk associated with the higher concentration and/or cost.

Calculation and administration errors

The presentation of the dose in different ways and the different strengths available, often in the same clinical areas can, and does, lead to calculation errors and the administration of an incorrect dose (7). Not all healthcare professionals are familiar with percentage expressions of the concentration and may not be confident in subsequent dosage calculations (9).

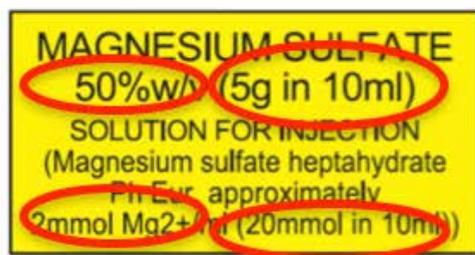
Errors in administration can also occur, for example, if it is incorrectly assumed that a whole vial needs to be given in a single dose, particularly where labeling states 'single dose vial'.

Evidence from Cambridge showed that inadequate mixing of solutions can lead to high concentrations of medicines being administered at the start of infusions and patients have been harmed as a result (13).

An example of a typical calculation that would have to be performed, often in a pressured environment, is available in Appendix 3.

Magnesium sulfate injection should normally be available as a 10% w/v, or 20% w/v, or 50% w/v licensed preparation (3,4,5,6). The abbreviation "w/v" means "percentage weight in volume". This will be in grams per 100ml, so for example 10% w/v means that there is 10g of magnesium sulfate in 100ml of solution. The total amount of grams of magnesium sulfate in the ampoule or vial may also be stated and sometimes a concentration of magnesium in millimoles per ml (3). See picture below.

The picture below shows all of the different ways of presenting the same strength of magnesium sulfate solution for IV injection on a product label.



3. What has happened to patients?

In England, there have been case reports of fatalities caused by patients receiving the wrong dose of Magnesium Sulfate. Between 1st January 2010 and 19th December 2012, 1025 incidents relating to “magnesium” (all preparations) were identified. Five, all related to injectable magnesium were found to be reported as death or severe harm (11).

Following a Serious Adverse Incident involving IV magnesium sulfate and with an awareness of other related incidents, the Northern Ireland Medicines Governance Team undertook a Failure Modes and Effects Analysis (FMEA) into the use of IV magnesium sulfate in an attempt to identify the major risks involved in its use, and to develop recommendations that might reduce the likelihood of future medication incidents (12).

One audit has reported a wide variation in the concentration of magnesium sulfate infusions prepared on an intensive care unit, with 6 out

of 30 syringes containing approximately 4-5 times too much magnesium (Mg²⁺). The authors suggest that this may have been due to confusion about the expression of concentration on the magnesium sulfate injection packaging in relation to the dose prescribed (10).

The majority of IV magnesium associated incidents reported to the NRLS relate to errors in the setting up of the infusion rate. Other themes identified may be viewed as not specific to the use of magnesium but arising from the general context of practice with injectable medicines. There is some evidence of wrong dose error that may be reduced with the introduction of ready to use preparations (11).

NPSA Patient Safety Alert 20 <http://www.nrls.npsa.nhs.uk/resources/?entryid45=59812> advised all trusts to conduct risk assessments for all of their injectable medicines in all clinical areas. It also highlighted purchasing for safety initiatives as having the potential to reduce risks.

4. What is happening locally and how can we reduce the risks?

Assessment of progress with Magnesium Sulfate across the region revealed the following;

- It was identified as a high risk product in 2012 by a regional work group focusing on NPSA alert 20, and there is still significant confusion about the calculations.
- That prescribing is not standardised so a mixture of mmol, grams, % w/v are all used across local trusts.
- The standard treatment for eclampsia is 4g as a loading dose (administered as 20ml of a 20% solution over one hour) followed by 1g/hour as a maintenance dose (administered as 5ml/hour for 24 hours as a 20% solution in a 50ml syringe).
- The only trust in the Wessex and Thames Valley area that supplies magnesium to its clinical area in a ready to use 20% solution (for use in eclampsia) is Oxford University Hospital.

At the time of writing this report all other trusts purchase and supply 50% solution to obstetric units which then requires dilution before administration.

- That dilution from 50% to 20% (or less) occurs frequently in clinical areas, often in emergency/urgent situations e.g. the management of eclampsia in obstetrics and in ITU.
- That magnesium sulfate is being added to IV fluid bags.
- That pharmacists are often not being made aware of what is being done in clinical practice.

It is reasonable to conclude that patients are being exposed to avoidable risks, which could be reduced by trusts adopting the recommendations cited next.

5. Recommendations

Whilst the risks described above cannot be eliminated, standardising the doses and strengths used in each clinical area, and working with clinicians to make them aware of the risks and how to perform the calculation accurately are deemed to be a minimum requirement.

It has been agreed across the regional network of Chief Pharmacists and the Wessex SCN for Maternity Children and Young People, that this initiative should be started in Obstetric units initially. Obstetrics is the obvious setting to start this work because of the fixed loading and maintenance doses. (See BNF).

6. Actions to reduce the risks from errors with magnesium sulfate

6.1 Safer prescribing and administration of magnesium sulfate injection for eclampsia

- Trusts should review protocols, monographs and SOPs to ensure that the dose and administration are clearly specified for the treatment and prevention of seizures in the management of eclampsia, and foetal neuroprotection.
- Trusts should ensure prescribing of standard concentrations of solution for administration where possible e.g. 20%.
- Trusts should ensure that the protocol for the management of eclampsia (and associated prescribing) relates to the product supplied by pharmacy.
- The 50% solution should never be used neat. Diluting magnesium sulfate is difficult and errors are frequently made when calculating dilutions.
- Magnesium sulfate injection and pre-prepared infusion strengths should be expressed in mmol and grams in all electronic dispensing systems to reduce confusion in magnesium dosing.

6.2 Safer procurement of magnesium sulfate injection for eclampsia

Trusts should now review their protocols for the treatment of eclampsia and pharmacy should supply magnesium sulfate injection at a concentration that does not require further dilution before administration i.e. 20%w/v or less.

If the Pharmacy cannot purchase a licensed product of magnesium sulfate injection at a concentration that does not require further dilution, then an unlicensed product should be purchased from a specials manufacturer e.g. an NHS Manufacturing unit. The Oxford Pharmacy Store will stock unlicensed 20% magnesium sulfate injection if it is unavailable as a licensed product.

Where pre-prepared magnesium sulfate infusions are not available, calculation of the volume of magnesium sulfate solution required to prepare the IV infusion should be carried out extremely carefully. See table Appendix 1

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At the time of printing, there are no licensed 20% preparations. However, if the whole region moves to purchase this product to reduce the risk to patients, it is more likely to encourage the licensing of such a product. Wessex AHSN will work with other regions and NHS England to support and encourage the development of a nationally licensed product.

7. Steps to making the change in your Trust

1. Trusts are advised to take this bulletin to their local Drug and Therapeutics Committee or equivalent and discuss the implication for obstetric departments in the first instance. Discussions should include costs, training and procurement issues as well as any incidents that have occurred in the trust recently.
2. Trusts should consider immediate cessation of purchasing the 50% products and agree protocols that use the 20% product.
3. Trusts should display the magnesium sulfate poster in all clinical areas where magnesium sulfate is used.
4. Drawing from numerous vials should act as a 'red flag' that an excessive dose is potentially being prepared (7).

8. An example of a Trust locally that have addressed this problem

Oxford University Hospital supply two magnesium sulfate 20% products to the Obstetric Unit

1. 4g in 20 ml for the loading dose
2. 10g in 50 ml for the maintenance dose (please note that more than one syringe would be required for a 24 hour period)

Date of preparation 23rd April 2015

References

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- (3) Summary of Product Characteristics and Product Specifications - Magnesium Sulfate 50% w/v for injection or infusion. South Devon Healthcare, Torbay PMU. Date of preparation of text March 2012.
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- (9) *Wheeler DW, Degnan BA, Sehmi JS et al. Variability in the concentrations of intravenous drug infusions prepared in a critical care unit. *Intensive Care Med* 2008;34:1441-1447.
- (10) NRLS data mini-scope - Summary of incidents relating to wrong dose magnesium administered Jan 2012. Available from NSH England Patient safety)
- (11) Q&A 210.4 Magnesium sulfate injection: converting between millimoles, milligrams and percentage w/v. Prepared by UK Medicines Information (UKMI) pharmacists for NHS healthcare professionals
- (12) A Failure Modes and Effects Analysis (FMEA) of the use of Magnesium Sulphate injection Northern Ireland Medicines Governance Team August 2013
- (13) Thomas M Donaldson, Vaithianadan Mani Daniel W Wheeler Factors affecting the concentration of electrolyte infusions prepared from stock solutions *Postgrad Med J* 2011;87:83e88. doi:10.1136/pgmj.2010.102830 83

Appendix 1

The table below provides the equivalents.

- In terms of dose units, each 1g of magnesium sulfate (as heptahydrate) is equivalent to approximately 4 mmol magnesium (Mg²⁺)
- The various ways of expressing units of concentration of magnesium sulfate injection are summarised in the table.

Concentrations of magnesium sulfate injection

Magnesium sulfate heptahydrate concentration (percentage w/v)	Magnesium ions equivalence (approximate) (millimoles magnesium (Mg ²⁺) per ml)	Magnesium sulfate heptahydrate concentration(mg/ml) equivalence
10% w/v	0.4 mmol/ml	100mg/ml
20% w/v	0.8 mmol/ml	200mg/ml
50% w/v *Warning* this strength does not mix well in clinical setting and its use increases the chance of dosage errors	2mmol/ml	500mg/ml

Source: Q&A 210.4 Magnesium sulfate injection: converting between millimoles, milligrams and percentage w/v. Prepared by UK Medicines Information (UKMi) pharmacists for NHS healthcare professionals. Before using this Q&A, read the disclaimer at www.ukmi.nhs.uk/activities/medicinesQAs/default.asp Date prepared: 22nd January 2013

Appendix 2

An example of product held in Oxford Pharmacy Stores manufactured by Ipswich

<p>Magnesium Sulfate BP 20% w/v (10g in 50ml)</p> <p>FOR SLOW INTRAVENOUS INJECTION or INTRAVENOUS INFUSION via a syringe driver</p> <p>Contains Magnesium Sulfate BP 1g in 5ml Contains approximately 0.8mmol / ml of Magnesium (40mmol in 50ml)</p> <p>PHARMACY MANUFACTURING UNIT THE IPSWICH HOSPITAL NHS TRUST IP4 5PD</p>	<p>Store below 25°C</p> <p>If only part used discard remainder</p> <p>Keep out of the reach and sight of children</p> <p>MS 13269</p> <p>BN X00000 Use before 28.11.14</p> <p>366.1</p>
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Available Products.

At time of going to print the following presentations of magnesium are available as ready to use solutions that do not require further dilution prior to administration.

Strength of magnesium inj	Volume	No of gram per vial	Supplier	Price
10% (0.4mmol/ml)	10ml	1g in 10ml	See CMU NHS catalogue for the contract line	See CMU catalogue
20% (0.8mmol/ml)	20ml	4g in 20ml	Available unlicensed from NHS Pharmacy Manufacturing Units e.g. Huddersfield	Contact Units direct
20% (0.8mmol/ml)	50ml	10g in 50ml	Available unlicensed from Oxford Pharmacy Store and NHS Pharmacy Manufacturing Units e.g. Huddersfield and Ipswich	Contact Units direct or check the OPS catalogue

Appendix 3

Test your ability to perform this calculation.

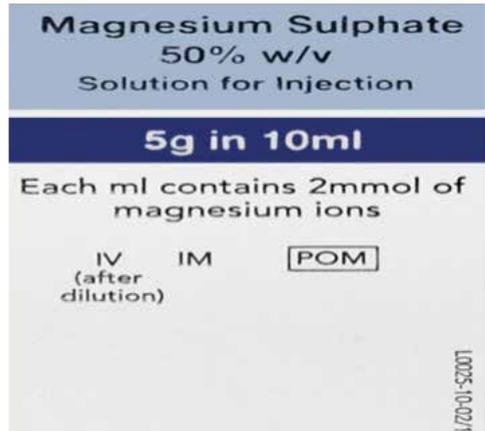
The Eclampsia Protocol for magnesium at an acute trust is:

- 1) Loading dose of 4g over 5-10 minutes, followed by
- 2) 1 g/hour maintenance dose for 24 hours

Given as

Loading: 20% magnesium sulphate as slow bolus over 5-10 minutes and

Maintenance: 50 ml of 20% magnesium sulphate via a syringe driver at 5 ml per hour for 24 hours.



Questions

How would the nurse draw up the doses in a syringe?

Loading dose

..... ml of 50% magnesium sulphate saline Final volume

Maintenance dose

..... ml of 50% magnesium sulphate saline Final volume

GIVING IV MAGNESIUM SULFATE?



BE AWARE IV MAGNESIUM SULFATE IS A HIGH RISK MEDICINE

Overdose can cause respiratory and neurological suppression which can be fatal

50% Magnesium sulfate should **NEVER** be used undiluted
20% is the maximum strength for IV use

A ready to use 20% preparation is preferable
as no dilution is required

Stop diluting and use **ready made products**
Simpler, Faster, SAFER



CHECK The strength of preparation



CHECK You are NOT using multiple vials



CHECK Get your calculation checked by a colleague

CALCULATIONS

are complicated due to %w/v, mmol, and mg, all being used in preparations

MAGNESIUM SULFATE
50%w/v (5g in 10ml)
SOLUTION FOR INJECTION
(Magnesium sulfate heptahydrate
Ph Eur, approximately
2mmol Mg²⁺/ml (20mmol in 10ml))

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