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Reducing the risk from medication errors with IV Magnesium Sulfate

To Note: This paper refers mainly to the management of eclampsia in 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 has been rated as complex 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 and that ready-to-use preparations are made available and staff using the preparations should be supported in their safe use.

However, Trusts must be aware of the additional governance issues related to the use of unlicensed preparations and incorporate these into a review of their arrangements for Magnesium Sulfate in line with the Trust’s unlicensed medicines policy.

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 SCN for Maternity 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). Use in other areas should be considered subsequently.

Actions to reduce the risks from 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.

Trusts should ensure prescribing of standard concentrations of solution for administration where possible.

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. Errors are frequently made when calculating dilutions due to incorrect interpretation of the prescription and product because of the multiple ways the strength may be expressed.

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 and prescribing systems to reduce confusion in magnesium dosing.

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.

Safer procurement of Magnesium Sulfate injection for eclampsia

It is imperative that all calculations are independently second checked by another member of medical/nursing/pharmacy staff.

At the time of printing, there are currently no licensed 20% preparations commercially available. 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.

The Medication Safety Officer (MSO) should lead the review of practice in collaboration with the relevant medical, nursing, clinical pharmacists and procurement pharmacists.
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 Obstetrics departments in the first instance. Discussions should include costs, training and procurement issues, considering treating the requirement for protecting patients from avoidable harm as a “special clinical need”, issues and risks related to the use of unlicensed preparations 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 a ready-to-use 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.

5. Trusts should be aware of the additional governance issues related to the use of unlicensed preparations and incorporate this into their review of other use of Magnesium Sulfate and act in concordance with their Trust unlicensed medicines policy.

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 medication 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 (or Syringe) | Serum risk | Therapeutic risk | Use of fixed type (not greater than 0.5ml) | Complex calculation | Complex preparation | Reconstitute, vial preparation | Use of inhaler/tube/tubing/ampoule | Non-standard packaging | Total Risk Factors | NPSA20 SCORE |
|-----------|------|-----------------|------------|-----------------|------------------------------------------|-------------------|---------------------|-----------------------------|------------------------|-----------------|---------------|
| Magnesium sulfate (eclampsia) | IV infusion | S | Y | Y | Y | Y | Y | Y | N | | 6 | HIGH |


2. What can go wrong? (In all clinical settings, 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) (1). Each 1g of magnesium sulfate (as heptahydrate) is equivalent to approximately 4 mmol magnesium (Mg2+) (1,2).

Wrong dose

Magnesium sulfate has been identified as a high-risk medication (3). It is vital to administer the correct dose of magnesium sulfate intravenous injection or infusion to avoid under-dosing 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 (1, 4, 5, 6, 7).

Limited range of presentations at the required concentration

According to the BNF magnesium sulfate injection should be supplied as a 10% w/v, or 50% w/v licensed preparation (2). However, these licensed preparations are not always available to purchase. Despite the warnings that magnesium sulfate injection should never be given intravenously 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 traditionally supplied 50% solution to clinical areas. Unlicensed preparations of 10% and 20% have been available from NHS Manufacturing Units but very few Trusts have purchased them. This could be for a variety of reasons including the advice contained in MHRA Guidance Note 14(8) which states that an unlicensed product should not be used if a licensed one is available.

However, the advice allows exceptions to be made in circumstances judged to meet a “special clinical need”.

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 (9). Not all healthcare professionals are familiar with percentage expressions of the concentration and may not be confident in subsequent dosage calculations (10).

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 labelling states ‘single dose vial’.

Evidence from Cambridge showed that inadequate mixing of solutions can lead to high concentrations of drugs being administered at the start of infusions and patients have been harmed as a result (11). 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 (4, 5, 6, 7). 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 (4). See picture below.

The picture below demonstrates all of the different ways of presenting the same strength of Magnesium Sulfate solution for IV injection.
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 related to “magnesium” (all preparations) were identified. Five, all related to injectable Magnesium were reported as death or severe harm (12).

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 (13).

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 the recommended dose of 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 (14).

The majority of IV Magnesium related 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 (12).

NPSA Patient Safety Alert 20 http://www.nrls.npsa.nhs.uk/resources/?entryid445=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 the situation locally and how can risks be reduced?

In 2012 a South Central Regional work group, focusing on NPSA alert 20, identified magnesium sulfate as a high-risk product and noted there was significant confusion about the calculations, in particular:

- Locally Trusts were using a standard treatment for eclampsia, 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).
- However, prescribing was not standardised and local Trusts were using a mixture of conventions employing mmol, grams, % w/v
- Only one out of seven local Trusts supplied magnesium for use in eclampsia to its clinical areas in a ready to use 20% solution. All other Trusts purchased and supplied 50% solutions to obstetric units, which required further dilution before administration.

It was reasonable to conclude that patients were being exposed to risk of avoidable harm.

In April 2015 the first iteration of this bulletin was published and within a year, five out of the seven local Trusts with maternity units have implemented the recommendations cited below. However, there is still a requirement to consider standardising use in other departments such as critical care to reduce risk.

- Dilution from 50% to 20% or less occurred frequently in clinical areas, and often in emergency/urgent situations e.g. the management of eclampsia in obstetrics and in ITU
- Magnesium sulfate was being added to IV fluid bags, rather than being administered via syringe drivers
- Pharmacists were often not aware of what was being done in clinical practice.

It was reasonable to conclude that patients were being exposed to risk of avoidable harm.

5. Recommendations

- It has been agreed across the regional network of Chief Pharmacists and the SCN for maternity 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). Use in other areas should be considered subsequently.

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 verify protocols that ensure that the dose and administration are clearly specified for the treatment and prevention of seizures in the management of eclampsia.
- Trusts should ensure prescribing of standard concentrations of solution for administration where possible.
- 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. Errors are frequently made when calculating dilutions due to incorrect interpretation of the prescription and product because of the multiple ways the strength may be expressed.
- 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 and prescribing systems to reduce confusion in magnesium dosing.
- 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
- It is imperative that all calculations are independently second checked by another member of medical/nursing/pharmacy staff

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. Due consideration must be given to the advice contained in MHRA Guidance Note 14: carefully weighing up the duty of care to protect patients from avoidable harm as a “special clinical need”, against the additional governance measures needed for using an unlicensed product and compliance with the organisation’s Unlicensed Medicines Policy.

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

- 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 currently 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 Obstetrics departments in the first instance. Discussions should include costs, training and procurement issues, considering the treatment for protecting patients from avoidable harm as a “special clinical need”, issues and risks related to the use of unlicensed preparations 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 a ready-to-use 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.

5. Trusts should be aware of the additional governance issues related to the use of unlicensed preparations and incorporate this into their review of other use of Magnesium Sulfate and act in concordance with their Trust unlicensed medicines policy.

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 finalisation 21st September 2016

References


4) Summary of Product Characteristics and Product Specifications - Magnesium Sulfate 50% w/v for injection or infusion. South Devon Healthcare, Torbay PMU. Date of publication: test March 2012.


6) Personal communication and Summary of Product Characteristics – Magnesium sulphate injection 10% w/v, 20%w/v and 50%w/v. Medical Information, Martindale Pharma. 25th January 2013.


8) MRHA Guidance Note 14 - The Supply of Unlicensed Medicinal Products (2014)


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**

<table>
<thead>
<tr>
<th>Magnesium sulfate heptahydrate concentration (percentage w/v)</th>
<th>Magnesium ions equivalence (approximate) (millimoles magnesium (Mg²⁺) per ml)</th>
<th>Magnesium sulfate heptahydrate concentration (mg/ml) equivalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% w/v</td>
<td>0.4 mmol/ml</td>
<td>100mg/ml</td>
</tr>
<tr>
<td>20% w/v</td>
<td>0.8 mmol/ml</td>
<td>200mg/ml</td>
</tr>
<tr>
<td>50% w/v</td>
<td>2mmol/ml</td>
<td>500mg/ml</td>
</tr>
</tbody>
</table>

*Warning* this strength does not mix well in clinical setting and its use increases the chance of dosage errors


Appendix 2

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

![Magnesium Sulfate BP 20% w/v (10g in 50ml)](image-url)

**FOR SLOW INTRAVENOUS INJECTION or INTRAVENOUS INFUSION via a syringe driver**

Contains Magnesium Sulfate BP 1g in 5ml

Contains approximately 0.66mmol/ml of Magnesium (40mmol in 50ml)

**For use by:**

- Obstetric Unit
- Neonatal Unit

**Store below 25°C**

If only part used discard remainder

Keep out of the reach and sight of children

MS 13269

BN X00000

Use before 28/11/14
Questions

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

Loading dose

\[ \text{ml of 50\% magnesium sulphate} \quad \text{ml of saline} \quad \text{Final volume} \]

Maintenance dose

\[ \text{ml of 50\% magnesium sulphate} \quad \text{ml of saline} \quad \text{Final volume} \]

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.

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.

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

Appendix 3

Test your ability to perform this calculation.

The 50\% Magnesium sulfate solution is

50% Magnesium sulphate

Solution for Injection

5g in 10ml

Each ml contains 2mmol of magnesium ions

\[ IV \quad IM \quad POM \]

Miles Laboratories (Pharma Division) Ltd

STOP 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 Sulphate 50% w/v Solution for Injection

(5g in 10ml)

MAGNESIUM SULFATE

50% w/v (5g in 10ml)

SOLUTION FOR INJECTION

(Magnesium sulfate heptahydrate)

15.2g/100ml (20mmol in 10ml)

Developed by Wessex Academic Health Science Network on behalf of the Thames Valley and Wessex NHS Chief Pharmacists Network. September 2016