Towards standardisation of drug infusion concentrations in UK critical care units

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There is wide variation in infusion practice in UK critical care units. Standardising infusion concentrations may lead to efficiency gains through reduced training burdens, common nomenclature, reductions in error rates and mass production of ready-to-use products by the pharmaceutical industry. A proposed list of standard concentrations for 20 medications given by infusion was produced. Critical care units were surveyed to assess the acceptability of the list for adoption as a national standard; 164 critical care units responded (63% of UK NHS trusts). High acceptance of the list has been shown, with the exception of concentrations of adrenaline, potassium and phosphate where further work is required. The proposed concentrations of the remaining 17 medications should be adopted as a national standard.

Keywords: critical care; intravenous infusions; reference standards; medication errors; clinical governance

Introduction
‘First, do no harm’ (Primum non nocere) is an important maxim of medical practice and yet unintended harm occurs within various health systems, including critical care, with alarming regularity. The National Patient Safety Agency (NPSA) was set up and tasked with monitoring and reducing adverse event rates in the UK. In total, 72,481 medication-related incidents were reported to the NPSA in 2007 from acute Trusts, although under-reporting means that the true figure is likely to be higher. The Institute of Medicine, which is part of the National Academy of Sciences and advises the US government, published the report ‘To Err is Human’ in 2000, which concluded that 98,000 deaths occur annually due to preventable mistakes. This is more than deaths from breast cancer, road traffic accidents or AIDS and yet medical error does not have the same level of public attention.

There are also likely to be cases where errors have occurred but have remained undetected. Medications that require manipulation before administration are prone to these types of errors and studies have demonstrated that a wide variation in administered dose can occur as a result.

One such study analysed samples taken from acetylcysteine infusions prepared in the emergency department for the treatment of paracetamol poisoning. It found that only 61% of doses that had been administered were within 20% of the prescribed dose. Alarmingly, one dose contained no drug, and a further 4% of samples deviated from the expected concentration by 50% or more.

The preparation of controlled drugs in a paediatric critical care population showed that 6% of prepared infusions exhibited a two-fold concentration error or greater. This work has recently been extended, with 118 volunteers from a variety of health professional backgrounds who undertook a series of calculations and prepared morphine syringes which were later analysed. Even here under scrutiny, 8% of 464 morphine infusions prepared were found to have two-fold concentration errors.

In a recent study, discarded syringes containing midazolam, insulin, noradrenaline, dopamine, potassium or magnesium were collected from a UK critical care unit and were analysed. Only midazolam and insulin were within the industry standard for variance in concentration (less than 10%). The mean discrepancies from the expected concentrations in the remaining medications were 144% for magnesium, 20% for potassium, and -12% for dopamine. Box and whisker plots show wide variation in concentrations, which are particularly marked for noradrenaline and potassium. Magnesium and potassium were singled out for further study. The introduction of specific electrolyte charts did reduce the variation in concentration but did not eliminate it.

The US Institute for Safe Medication Practices has long advocated strict functions and constraints to produce a system that should make errors virtually impossible. This is the most powerful tool for preventing errors. Standardisation of practice facilitates this and has been advocated by the UK’s Department of Health and the Audit Commission.

We have previously sought to establish the feasibility of standardising infusion concentrations by ascertaining the extent of variation in practice for a set of medications commonly used in critical care. The aim of this follow-up survey is to assess the acceptability to UK critical care units of a draft list of standard medication concentrations and to identify possible factors that would impede the introduction of such a standard.

Method
A questionnaire was created using the results of the first national survey. The most commonly used concentrations of
all agents examined in the first survey were selected as the basis for standardisation. Participants were asked whether they would be prepared to use the identified products if they were made available from a manufacturer. Those who gave a negative response were asked for alternative concentrations and to provide a rationale as to why the alternative was preferred.

The questionnaire was circulated via the Intensive Care Society Linkman system, the newsgroup services of the United Kingdom Clinical Pharmacy Association Injectable Guide Group, British Association of Critical Care Nurses and The Critical Care Network Managers Group as well as via the website of the Royal College of Anaesthetists.

Data from the questionnaire were entered onto a spreadsheet by a data analyst, with one entry per critical care unit. Duplicate responses were compared and discrepancies queried before being entered onto the database. Entries for each medication were subsequently coded into one of the following categories: ‘Yes, would use,’ ‘No, suitable reason,’ ‘No, unsuitable reason,’ ‘No information given’ and ‘Drug not used’ by two of the authors and the data analyst.

Responses were coded as ‘No, unsuitable reason’ for reasons such as local practice (not further qualified), tradition or consultant preference. Responses were coded as ‘No, suitable reason’ for all other rationales, including easier calculation or where the practice was the result of a specific action point from an incident review.

A sub-analysis for phosphate was carried out to determine the number of responses that indicated the proposed presentation was unacceptable because the use of a phosphate Polyfusor™ was preferred.

A sub-analysis for potassium was carried out to determine the number of responses that indicated the proposed presentation was unacceptable because the use of highly concentrated potassium (1-2 mmol/mL) was preferred.

**Results**

Data from 164 critical care units were received and analysed (representing 63% of UK NHS Trusts). Responses were received from a variety of types of critical care unit (Figure 1) and from all of the home countries (Figure 2).

The results of the survey are shown in Figure 3. Units that gave either no information or stated that they did not use the medication in question are excluded from the results for that medication.

**Discussion**

‘First, hasten to help’ (*Primum succurrere*) is the maxim that we are now presented with after the Darzi review. These results show that of 21 drug concentrations (including two for amiodarone), there was general agreement (with an arbitrary 70% cut-off) with the proposed standard concentrations for 18 drugs, excluding adrenaline, potassium, and phosphate. None of these require large volume dilutions in a critical care setting and as such, it should be relatively easy to find an acceptable recommended infusion concentration.

Potassium and phosphate seem to pose specific problems. While 58% of units would use the proposed phosphate standard if available, 19% would continue to use a phosphate Polyfusor™ formulation, either in full or by delivering part of the Polyfusor, although no overriding rationale for this was established.

Potassium presents an interesting problem that must be resolved. Two specific practices have emerged. The proposed standard supports the administration of potassium on the basis of intermittent dosing of a relatively weak concentration of potassium (20 mmol in 50 mL, although still classified as ‘strong potassium’ by the NPSA) and is supported by 66% of units. The alternative, proposed by 29% of units, is the use of very concentrated potassium (typically 1 or 2 mmol per mL) administered by a continuous sliding scale infusion.

Movement of staff between units with these different practices leads to significant potential for an administration error where either a weak potassium concentration infusion is given slowly (a few mL per minute), or a strong potassium concentration infusion is given rapidly (50-100 mmol over an hour). The co-existence of these practices in the UK is thus potentially extremely dangerous and must be eliminated.

The evidence is now overwhelmingly in favour of standardisation as a simple solution to help avoid errors. This survey demonstrates that there is a considerable amount of acceptance of a proposed list of infusion concentrations. This being the case, should we now be thinking about formally implementing a set of standard UK injectable drug concentrations? This would not only help from a safety standpoint but it would also empower health professionals and the National Health Service to influence the pharmaceutical industry to provide solutions to better meet our needs rather than presentations that are commercially convenient.
Critical care areas have long set the standard for good practice in relation to IV drug administration and the development of standard concentrations could ultimately influence the rest of the organisation helping improve drug administration practice.

A reduction in potential adverse events as highlighted by Wheeler could save considerable monies nationally.

Standardisation would reduce the need for Trust investment in postgraduate IV training which at present is replicated across the UK. Error reduction should also be influenced by lack of variability between drug concentrations in different clinical areas. Product labelling and calculation would be simpler and safer. The production of standard concentrations would allow further development of the national injectable medicines website so that monographs could include example calculations, calculation tables, and drug calculators relevant for drug doses, along with a recommended route of administration based on pH and osmolarity as well as clinical effect. Compatibility information for Y-sites are often concentration-dependant and standardising concentrations facilitates research in the area, giving practical solutions to everyday access problems.

Guidance for drug administration could be simplified and standardisation of monitoring would be possible. Parshuram has specifically shown that a high rate of errors occurs in the calculation and rounding stages when preparing variable strength morphine syringes. Standardisation removes this risk, and although this may feasibly introduce new errors related to the use of infusion rates, this has not been demonstrated.

**Conclusion**

It is now time to bite the bullet and proceed to formal standardisation. The results of this survey have now been shared with the Standards, Safety and Quality Committee of the Intensive Care Society and it is our hope that this will help with the production of a Standards document on intravenous drug concentrations used in critical care.

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**References**


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