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Editorial

Dose calculation and medication error – why are we still weakened by strengths?

In 1995 Rolfe and Harper showed that there is substantial confusion about the different means by which the concentration of drugs in solution are expressed [1]. They conducted a survey of 150 doctors in a UK University teaching hospital, and demonstrated that barely half could correctly identify the mass of drug in a solution when its concentration was expressed as a ratio. There were also problems with percentages: less than half could convert the concentration of lidocaine from a percentage to mass concentration, and only one-third knew how many millimoles of sodium bicarbonate are in 100 mL of an 8.4% solution. Less than a third could work out the mass of epinephrine in 10 mL of the mixture of 0.25% bupivacaine with 1 : 200 000 epinephrine used in infiltration anaesthesia. Anaesthesiologists performed substantially better than physicians and surgeons. The authors recommended that the expression of drug concentration should be standardized to mass concentration for all solutions (e.g. milligrams per millilitre). It seems a compelling argument as it involves little or no cost and should only reduce the likelihood of dosing errors. They pointed out that other researchers had been making similar calls since the early 1980s to no avail [2,3].

The correspondence generated by this study debated whether it was desirable, sensible or possible to make these changes. Some argued that not all drugs were suited to having their concentration expressed as mass concentration, for example vaccines [4]. A senior executive in the medicines sourcing department of the National Health Service (NHS) Executive who had also previously called for a universal labelling standard of mass concentration [5] then reported that wider discussion of the proposed changes had identified potential hazards, although these were not specified [4]. Another correspondent highlighted the importance of education and experience, suggesting that students should be drilled rigorously in calculating doses of important emergency drugs [6].

Still, little has changed. In the UK, solutions of drugs are presented in packaging with concentrations expressed in a variety of ways. Epinephrine and norepinephrine are still presented as 1 : 1000 or 1 : 10 000 solutions. Local anaesthetics are still typically presented as percentage solutions, with the notable recent exception of levobupivicaine (Chirocaine™; Abbot Laboratories, Queenborough, UK).

Having previously shown that medical students are just as confused by ampoule labels [7], Wheeler and colleagues recently conducted a novel survey of doctors in the UK using the Internet [8]. They posed six multiple-choice questions concerning the mass of drug contained in solutions of epinephrine, lidocaine and atropine. Additionally, three common clinical scenarios were presented and participants were asked to calculate the correct volume of each drug to give. Almost 3000 doctors took part. Only 85% and 65% correctly identified the mass of drug in the epinephrine and lidocaine solutions, respectively. However, 93% identified the correct concentration of atropine. More would have administered the correct volume of epinephrine and lidocaine in clinical scenarios (89% and 81%, respectively) but only 65% identified the correct volume of atropine. Again there were clear differences between the specialties; anaesthesiologists performed amongst the best. The authors argued that these findings further strengthen the case for standardized labelling of drug solutions as mass concentration, and highlighted an unexpected finding. Less than two-thirds of participants had correctly calculated the volume of atropine to be given in the clinical scenario, even though its concentration is expressed as milligrams per millilitre and the vast majority had calculated its concentration correctly. Atropine may be less familiar than epinephrine or lidocaine, but the clinical scenario – a patient with a symptomatic bradycardia – was not overly esoteric. It did, however, involve a conversion from micrograms to milligrams so it seems likely that the problem was

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one of arithmetic. The potential for ten-fold errors (or worse) under these circumstances has already been widely reported [9–12].

Questionnaire-based research is frequently criticized as inaccurate, but it is ideally suited to investigate this hypothesis. Four surveys conducted over more than 30 yr have now yielded the same result, and it is not acceptable to delay simple changes to drug labelling that would increase patient safety on the basis of criticisms of research techniques. Wheeler and colleagues' use of the Internet allowed them to reach doctors working in the community, those with little patient contact, and those who administer drug solutions rarely – exactly those for whom volume calculation should be as simple as possible. The price they paid for such access was a response rate of 24.6%. However, using online questionnaires for clinical research is relatively novel and it is not yet clear what an 'adequate' response rate might be. Theirs' compares very favourably with similarly constructed published studies [13] and yielded a group of participants that was highly representative of the population of doctors in the UK. Observation of drug administration in the workplace is now seen as the 'gold standard' research technique for detecting and quantifying medication error [14], but it is narrow-minded to dismiss research that uses a different technique. Nearly 1000 of Wheeler and colleagues' participants were primary care physicians. The scale and cost of an observational study of 1000 primary care doctors' administration of drugs in solution is unimaginable.

There is no international standard for the labelling of drugs. The World Health Organization states that the packaging should state the name, strength, quantity and physical description or identification of the medicinal product, that the labels should permit the identification of each active ingredient, and give the dosage form [15]. It defers responsibility for the exact means of expressing this information to national regulatory bodies. In March 1991 the National Pharmaceutical Supply Group devised an NHS specification for ampoule labels [16]. It specified that units should be SI and 'the amount/concentration [be] expressed as the amount "*x*" or the concentration "*x*" in "*y*" mL, where "*y*" is the total volume of the ampoule' but with the option of certain drugs (specifically local anaesthetics) retaining their traditional labelling. Legislation in the UK is now developing in parallel with the European Union [17], which gives more explicit advice on labelling. Directive 92/27/EEC states that an ampoule label should include a statement of the active ingredients expressed qualitatively and quantitatively, the pharmaceutical form, and the contents by weight, by volume or by number of doses [18]. It does not mention percentages or ratios.

Calculating safe doses should be simple. The safe dose of many drugs is determined by a patient's weight, especially in paediatric practice where incorrect administration of intravenous drugs has been shown to be one of the most important factors contributing to potential adverse drug events [19]. Additional steps are required when calculating the suitable dose for a patient by their weight when the concentration of a drug in solution is expressed as a ratio or percentage. These steps may appear simple, but if doctors are unfamiliar with these concepts, or are hurrying or tired, then there is potential for serious error and patient harm.

So what should be done? Should labels in the UK be changed? We firmly believe that they should – but labelling every drug in solution as milligrams per millilitre is not the answer. There are some circumstances where this might heighten confusion, for example in the prescription and administration of electrolytes, hormones or biological materials such as potassium, insulin and heparin when mass is more conveniently expressed in millimoles or international units. Another example would be potent drugs given by the microgram, such as digoxin and liothyronine sodium. However, when formularies express the dose of a drug in mass per kilogram body weight, its ampoule should be labelled with the concentration of the contents in mass per unit volume using the same units for mass – especially if that drug is frequently used in emergencies.

Those against argue that the process of changing from a familiar system to an unfamiliar one might itself cause confusion and endanger patients, in effect causing the next accident by preventing the last one. Some have argued for a transitional period of dual labelling, although squeezing any extra information onto small ampoules presents problems of its own. There may be lessons to learn from the recent changes in syringe labelling practice in the UK, where a variety of colour-coded pre-written syringe labels for drugs drawn up in critical care areas have been replaced by an internationally recognized system [20,21]. Problems were anticipated during the transition but the long-term benefits were thought to outweigh any short-term problems. Whether this view was justified remains to be seen. Current incident reporting systems probably lack the sensitivity to detect any effects, but reports of problems have appeared in the literature [22–24]. Clearly it would be sensible to have an international standard for ampoule labelling, especially now that increasing numbers of doctors and nurses are moving between countries to pursue their practice.

Anaesthesiologists prepare and administer more drugs than doctors from any other specialty and work in environments where medication errors are most

common and most likely to result in harm to patients [25,26]. We have an important role to play in arguing for improvements in drug labelling and must continue to research novel ways of reducing medication error and improving patient safety. Bearing in mind the contribution of arithmetical error to dosing errors, we must ensure that drug administration is taught properly to medical students and doctors alike.

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