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Calculation of Doses of Drugs in Solution

Are Medical Students Confused by Different Means of Expressing Drug Concentrations?

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Abstract

Introduction: Our hypothesis was that clinical medical students find the different means of expressing the concentration of drugs in solution confusing. We are concerned that lack of formal teaching on this topic may make students liable to make drug dosing errors after they have qualified. Administering the wrong volume of a drug may have serious consequences for patient safety.

Study design and participant group: Web-based electronic multiple-choice examination of clinical medical students.

Methods: We asked clinical medical students at our university three multiple-choice questions concerning the concentration of lidocaine (lignocaine) and epinephrine (adrenaline) in solution and the maximal recommended dose of lidocaine. The incorrect options were wrong by factors of between 4 and 1000.

Results: One hundred and sixty-eight clinical students out of 350 contacted responded to an invitation to participate (response rate 48%). Twenty-seven percent answered every question incorrectly and 10% answered all three correctly. The mean score for all students was only 1.24 out of 3 (standard error 0.96). However, final-year students performed significantly better ($p = 0.016$), implying that some knowledge had been acquired informally. Their higher mean score resulted from correctly identifying the amount of epinephrine ($p = 0.005$) and lidocaine ($p = 0.018$) more frequently. Only 27% knew the maximal recommended dose of lidocaine, with no difference between years ($p = 0.724$).

Conclusions: A substantial majority of medical students are unable to calculate the mass of a drug in solution correctly. There is evidence that some students are picking up this skill during the course, because final-year students performed significantly better than first-year students. Modern medical student pharmacology teaching is highly sophisticated, encompassing genomics, molecular and cell biology. The ability to calculate drug doses safely appears to have been overlooked. Students should be familiar with these concepts, so as to avoid dose errors and associated morbidity, mortality and cost when they begin prescribing. To

simplify calculations, drug packaging should express the concentration of drugs in solution solely as mass per unit volume, e.g. milligrams per millilitre.

Introduction

The objective of this study was to assess the ability of clinical medical students in a UK university to correctly calculate doses of drugs in solution. We hypothesised that they would be confused by different means of expressing drug concentration, which is not taught formally as part of their curriculum. Such confusion would be highly likely to contribute towards future drug administration errors.

The definitions of an adverse drug event (ADE) and the different types of error that might occur during the process of prescribing, preparing and administering a drug are summarised in table I.[1-3] Many patients experience an ADE during their hospital admission. The exact proportion is not clear, as previous research has used different definitions of ADE and been conducted in different environments. For example, an ADE is thought to occur during 0.7–6.5% of hospital admissions in the US, 1.5% in the UK, and 1.8% in Australia.[4-7] The substantial morbidity and mortality caused by ADEs is in no doubt. In-hospital ADEs are associated with longer hospital stays, greater cost of hospitalisation and increased risk of death.[8,9] ADEs are thought to account for approximately 4% of hospital admissions.[10] Not all ADEs result in a malpractice claim, but those that do are expensive. In the US in 2002, the mean cost of defending malpractice claims was as high as $US376 500 for preventable inpatient ADEs.[11]

The proportion of ADEs that are administration errors is also not clear, again due to the difficulty of studying different healthcare environments and using different means of defining ADE and data collection. The frequency of drug administration errors has previously been reported as being as high as 19% of all drug administration episodes, and of these 17% were dose errors.[12] These figures were derived by direct observation of drug rounds on busy wards in 36 US hospitals, but used a reasonably broad definition of drug administration error that included incorrect timing of administration. A dose error may be made because a drug is incorrectly prescribed on a chart: a prospective examination of over 36 000 prescription charts in a UK teaching hospital over a 4-week period identified an error in 1.5% of prescriptions, 54% of which were associated with the wrong dose.[13] In this study, errors were corrected before administration so it is unclear how many patients would have actually received the wrong dose. The same investigators also studied causes of prescription error in the same hospital by interviewing those who had made prescribing mistakes.[14] Theories of human error were then used to identify the causative factors, which were found to include lack of knowledge and inadequate training.

Table I. Definitions of different types of errors, reactions or events as used in this study

Term	Definition	References
Adverse drug event	An injury related to the use of a drug	1
Medication error	An error in the process of prescribing, dispensing, or administering a drug, whether there are adverse consequences or not	1-3
Drug administration error	Misinterpretation of correctly written prescription, leading to: administration of the wrong drug and/or administration of the wrong dose and/or administration of the wrong formulation and/or administration by the wrong route and/or administration to the wrong patient	1-3
Dose error	Administration of the wrong dose of a drug	2,3
Adverse drug reaction	Any response to a drug which is noxious and unintended that occurs in doses normally used in man	1

A dose error may arise from a correctly written prescription. When the act of administering intravenous drugs was observed in a UK children's hospital, an error was made 98% of the time, but only 2% involved the wrong dose.[15] The contribution of different means of expressing the concentration of drugs in solution to dose error has never been assessed, although it is known that hospital doctors struggle with the calculations.[16] Analysis of a database of reported drug errors compiled by the US Pharmacopeial Convention and the Institute for Safe Medication Practices revealed that the drugs most commonly involved in errors were heparin, lidocaine (lignocaine), epinephrine (adrenaline) and potassium chloride; lidocaine was implicated in the largest number of fatalities.[17] It may be no coincidence that these drugs are all presented in solution.

When a drug in solution is administered, the correct volume must be calculated. The steps in this calculation require an understanding of the many different ways that the concentration of a drug in solution may be expressed. Some of these may be confusing. For instance, the concentration of bleomycin, a chemotherapeutic agent, has been expressed in milligrams (by potency), milligrams (by weight), International Units or US Pharmacopeia Units. The potential for dose error resulting from this variety of expressions of drug concentration have already been highlighted.[18]

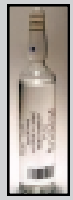
The concentration of drugs in solution may also be expressed as mass per unit volume (e.g. milligrams or millimoles per millilitre), ratios (e.g. 1 in 1000), or percentages. As the metric system is based on thousands whilst percentages are based on hundreds, even these simpler means of expressing drug concentration can cause confusion. Calculating the safe volume of drug mixtures is even more difficult, for example the mixture of 1% lidocaine and 1 in 200 000 epinephrine that is often infiltrated into surgical sites.[19]

In this study we used a web-based survey to assess clinical medical students' awareness of the active drug concentration in a solution of epinephrine (normally expressed as a ratio) and lidocaine (expressed as a percentage), and the maximal recommended dose of lidocaine.

Q1.
The first picture shows a vial of epinephrine.
It contains 1mL of 1 in 1000 epinephrine.
How much epinephrine is there in the vial?

A. 10 micrograms
B. 100 micrograms
C. 10 milligrams
D. 1 milligram
E. 1000 milligrams

Q2.
The second picture shows a vial of lidocaine.
It contains 10mL of 1% w/v lidocaine.
How much lidocaine is there in the vial?



A. 0.1 milligams
B. 1 milligram
C. 10 milligrams
D. 100 milligrams
E. 1000 milligrams

Q3.
What is the maximal recommended dose of plain lidocaine?

A. 1 mg.kg^{-1}
B. 2 mg.kg^{-1}
C. 3 mg.kg^{-1}
D. 8 mg.kg^{-1}
E. 16 mg.kg^{-1}

Fig. 1. The multiple-choice questions used in the survey (correct answers in bold).

Study Design and Methods

In our university, medical students study preclinical medicine for 3 years, learning basic sciences such as anatomy, physiology and pharmacology. They then spend 2.5 years in a University Teaching Hospital, gaining clinical experience. Clinical pharmacology teaching spans all clinical years; anaesthesia teaching is confined to the final year.

Every clinical medical student in our university was e-mailed using the University 'Educational Resources Web' with information about the survey. Those choosing to participate were directed to a web page and were asked to answer three multiple-choice questions under timed conditions (figure 1). The questions were devised to test knowledge of drugs used in many specialties that should be famil-

Table II. Results of multiple-choice questionnaire broken down by student seniority

No. of years of clinical training	Question 1			Question 2			Question 3		
	no. answering correctly	no. attempting question	% answering correctly	no. answering correctly	no. attempting question	% answering correctly	no. answering correctly	no. attempting question	% answering correctly
1	29	58	50.0	14	57	24.6	19	57	33.3
2	37	61	60.7	23	58	39.7	17	56	30.4
3	35	43	81.4	22	42	52.4	10	39	25.6
Total (all years)	**101**	**162**	**62.3**	**59**	**157**	**37.6**	**46**	**152**	**30.3**

iar to all students. Students were thought to be more likely to complete the survey if it was brief.[20] Although answers were submitted anonymously, students collaborating could be detected and excluded by software which analyses the timing of each student's answers and the Internet Protocol (IP) address of their computer to identify students sitting together in information technology facilities.[21] The examination structure could not eliminate the use of calculators or formularies. Time taken to answer each question and seniority of the student (first-year, second-year or final [third] clinical year) were also recorded. The survey was conducted for 3 weeks in November 2001, just prior to the third-year students' final examinations. The correct answers were e-mailed to all participants a week later. The web page may be viewed at http://axis.cbcu.cam.ac.uk/dosesurvey/, although answers are no longer recorded.

Statistical Analysis

Data were analysed using Kruskal Wallis non-parametric tests (Statview™, SAS Institute Inc., Cary, North Carolina, USA), stated p-values are corrected for ties.

Main Outcome Measures and Results

Results are summarised in table II. One hundred and sixty-eight clinical students took part in the survey, a response rate of 48%. None were found to have collaborated or were excluded, but some students did not answer every question. Response rate was not significantly different between year groups ($p = 0.079$). The mean score for all students was 1.24 out of three ($n = 168$, range = 0–3, standard error [SE] 0.96). Mean score improved with student seniority (figure 2); first-year students scored 1.00 (SE 0.11), second-years 1.27 (SE 0.13) and third-years 1.56 (SE 0.14). The percentage answering questions 1 and 2 correctly showed the same improvement (table II, figure 3). In all these areas, there were significant differences between each year group's performance (mean score $p = 0.016$; question 1 $p = 0.005$; question 2 $p = 0.018$). The percentage correctly answering question 3, concerning the

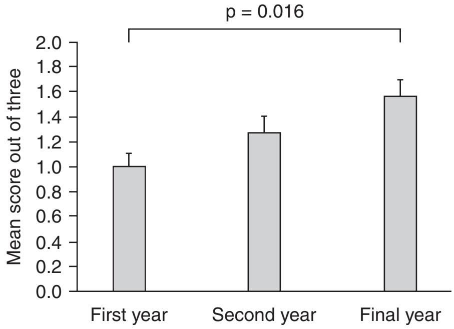


Fig. 2. Mean score out of three against number of years of clinical training completed. Error bars ± 1 standard error (n = 168).

maximal recommended dose of lidocaine, was much lower (table II, figure 3). The apparent decline in proportion answering correctly with student seniority is not statistically significant (p = 0.724). Combining year groups, 45 (27%) students got all three questions wrong, and only 17 (10%) answered all three correctly. Time taken to answer, whether correctly or incorrectly, did not differ significantly between year groups (p = 0.949, figure 4). The effect of guessing was not taken into account.

Conclusion

The mean score (1.24 out of 3), and the fact that only 10% of clinical students answered all three questions correctly, are disappointing but perhaps not surprising. The relatively simple skills of drug prescribing and preparation are not taught formally at many medical schools. The better mean scores of the final-year students imply that some students are acquiring these skills informally during the course. However, knowledge of the maximal recommended dose of lidocaine was uniformly poor. This question had been chosen to test an observation – and confirmed our suspicions – that many students are unaware that there is a limit to the amount of lidocaine that can be administered safely, and because this knowledge forms the next step when calculating a safe dose for a patient.

The ability of medical students to perform the arithmetical calculations required to identify the correct volume of a drug in solution has not been investigated previously. Conclusions drawn from questionnaire-based studies are limited by the problem of how non-responders might have performed. Even if all the non-responders had answered correctly, this study demonstrates that a substantial proportion of medical students cannot calculate the concentration of familiar drugs in solution, and even fewer are aware of the maximal recommended dose of lidocaine. It has been suggested that to reduce prescribing errors, hospitals should train junior doctors in the principles of drug prescribing.[17] Our findings demonstrate that even correctly and clearly written prescriptions are open to misinterpretation and dose error. These findings add weight to the argument that medical schools should also teach dose calculation skills as part of the undergraduate and clinical pharmacology curricula.[22]

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 ADEs.[23] 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

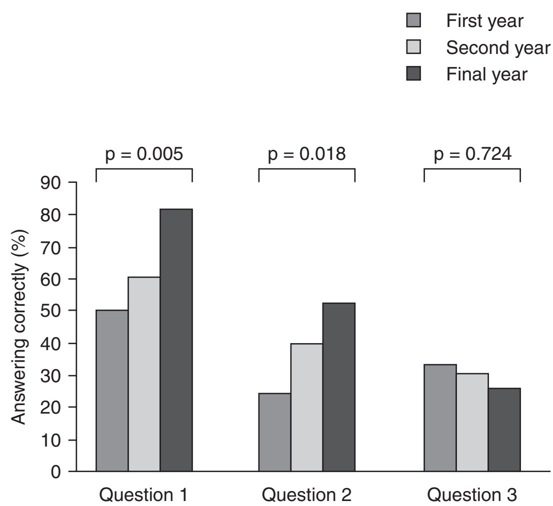


Fig. 3. Percentage of students answering each question correctly against number of years of clinical training completed (n = 168).

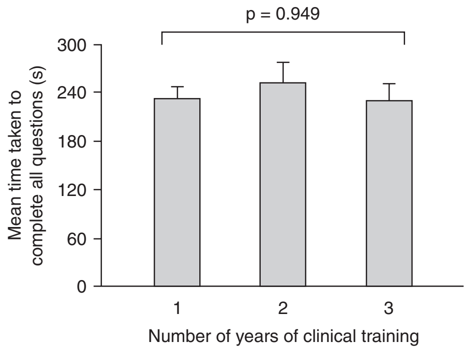


Fig. 4. Mean time taken to complete the questions against number of years of clinical training completed. Error bars ± 1 standard error (n = 168).

tired, then there is potential for serious error and patient harm. Pharmaceutical companies are beginning to package new drugs with concentration expressed as mass per unit volume. Local anaesthetics are traditionally labelled with concentration expressed as a percentage; however, the concentration of levobupivacaine, a new stereoisomer of bupivacaine, is expressed as 2.5 or 5 mg/mL. We believe that this is the first step in the right direction to improve patient safety. We recommend that the concentration of all drugs in solution should be compulsorily expressed as the mass of active drug per unit volume. Rather than teaching a confusing system, should the system not be changed?

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