Reporting units for therapeutic drug monitoring: a correctable source of potential clinical error

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ABSTRACT

- Variation between laboratories and reference sources in the units used for reporting pathology results raises the possibility of medical error.
- Data submitted to the RCPA Quality Assurance Programs demonstrate wide variation in the units used for reporting therapeutic drug concentrations.
- This potential source of medical error needs to be addressed by all parties involved in communicating drug concentrations and providing support information.

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The space industry is known for avoiding risk and placing the highest priority on safe practices, but a mismatch in reporting units in the software developed for the Mars orbiter led to the loss of the US$125 million spacecraft in 1999.[1] We should aim to avoid this type of error in medical practice by adopting standardised measurement units. In most areas of pathology reporting, this is established; examples include the ubiquitous use of molar units (mmol/L) for electrolyte concentration and mass units (g/L) for albumin concentration.

However, an area of pathology testing which has varying units in common use is the measurement of serum drug concentrations for therapeutic or toxicological assessment. The use of different units creates obvious potential for error; for example, if a serum paracetamol result in μmol/L is interpreted against a nomogram in mg/L, then a wrong action may result. An anecdotal example of such an error with salicylates has been described.[2] While pathology laboratories are required to report test results accompanied by measurement units,[3] it is not uncommon for pathology results to be communicated without units in verbal and handwritten communications. This separation of a pathology result from its units may lead to errors in interpretation and clinical decision making if different units are used in different locations.

To assess the variability in units used for reporting drug concentrations in Australia, I examined results submitted in 2007 for therapeutic drugs in the General Serum Chemistry and the Special Therapeutic Drugs programs run by the Chemical Pathology office of the RCPA Quality Assurance Programs Pty Ltd. Laboratories may choose between mass and molar units when submitting results for most drug measurements in these programs, and, while the units used for this reporting are not necessarily the same as those used for reporting patient results, it is likely that they are the same. The results are shown in the Box, together with the units used in common reference material, such as the *Monthly index of medical specialties* (MIMS),[4] the *Australian medicines handbook*[5] and *Therapeutic guidelines*.[6]

For many drugs, there was considerable variation in the units in use, and there was no overall consensus about the use of molar or mass units. Some drugs were consistently reported in molar units, others almost entirely in mass units, and most in a mix of the two types of units. This variability in drug units is accommodated in commonly available guidelines, which express therapeutic intervals in both mass and molar units, although only mass units were available for some entries in MIMS. The supporting material was also not consistent, with both litres and millilitres used as the denominator for reporting mass concentrations.

The International System of Units (SI) for measurements was adopted in Australia in 1960, with the aim of ensuring clarity of communication with regard to all measured quantities. SI is enforced for medical laboratories by compulsory accreditation against Australian Standard 4633–2004, which states that results must be reported in SI units or units traceable to SI units.[7] While molar units are often considered the preferred SI unit, an alternative view is that both mass and molar units are acceptable under SI,[8] which is a reasonable position given that the kilogram and the mole are both fundamental SI units. Even where SI units are specifically delineated, there are many laboratory tests where alternate units are universally accepted in Australia. Examples include mmHg for blood gases (the SI unit for pressure is the pascal) and units per litre for liver enzymes (katal).

In an attempt to provide clear guidance during the introduction of SI units into pathology testing, the Royal College of Pathologists of Australasia (RCPA) recommended in 1986 that molar units (eg, μmol/L) be used for reporting drug concentrations.[9] While the RCPA document has succeeded in providing uniformity in many areas, its recommendations have not been universally adopted for drug measurements. For successful adoption of uniform reporting, it must be supported by all interested parties. With regard to drug concentrations, MIMS reports preferentially in mass units, research literature reports almost universally in mass units, and the Australian Standard for the related area of urine toxicology uses mass units (ng/mL).[10] A recent review of digoxin published in this Journal discussed serum concentrations using mass units.[11]

The priority for avoiding clinical errors is uniformity in reporting, which requires acceptance by all relevant organisations, rather than slavish enforcement of a particular unit type. Indeed, a recent guideline published in this Journal, supported by pathology and clinical groups, recommended use of the non-SI unit of mL/min for glomerular filtration rate, rather than mL/s, to align laboratories with other local and overseas sources of clinical information.[12]

I believe uncritical universal adoption of either molar or mass units by laboratories would not be the best way forward. A competent collaborative authority with representation from clinical, pharmacy, pathology and publishing organisations is required to provide clear guidance on the units to be used for drug concentrations. A proposal in the United Kingdom for the use of mass units, with certain specified exceptions, provides a model for a mixed mass and molar system for toxicology,[13] and this has recently been extended to therapeutic drugs.[14] For new drugs brought into clinical use in Australia, there should be a clear statement of the units to be used for measuring concentrations. For drug measurements already in use, the key stakeholders should address the issue, bearing in mind the current spread of units in

Units used for therapeutic drug monitoring by pathology laboratories reporting to the RCPA Chemical Pathology Quality Assurance Program in 2007 and in online supporting material (data accessed 16–19 February 2007)

Drug	Data source	Total number of laboratories	Mass units		Molar units		Units used in supporting material		
			Unit	% of laboratories	Unit	% of laboratories	MIMS	AMH	*Therapeutic guidelines*
Methotrexate	STD	24	mg/L	0	µmol/L	100%	10^{-6}, 10^{-7}, 10^{-8} M	na	na
Lithium	GSC	163	mg/dL	0	mmol/L	100%	mmol/L	mmol/L	mmol/L
Digoxin	GSC	256	µg/L	28%	nmol/L	72%	ng/mL, nmol/L*	µg/L, ng/mL	na
Phenytoin	GSC	144	mg/L	32%	µmol/L	68%	µg/mL, µmol/L*	mg/L, µmol/L	µmol/L, mg/L
Valproate	GSC	131	mg/L	32%	µmol/L	68%	µg/mL, mmol/L*	mg/L, µmol/L	µmol/L, mg/L
Carbamazepine	GSC	132	mg/L	33%	µmol/L	67%	µg/mL, µmol/L*	mg/L, µmol/L	µmol/L, mg/L
Paracetamol	GSC	245	mg/L	37%	µmol/L	63%	µg/mL†	na	na
Phenobarbitone	GSC	55	mg/L	38%	µmol/L	62%	µg/mL, µmol/L*	mg/L, µmol/L	µmol/L, mg/L
Theophylline	GSC	77	mg/L	39%	µmol/L	61%	µg/mL, µmol/L*	mg/L, µmol/L	µmol/L, µg/mL
Salicylate	GSC	96	mg/L	45%	mmol/L	55%	µg/mL‡	na	na
Lignocaine	STD	6	mg/L	50%	µmol/L	50%	µmol/L, µg/mL	na	na
Quinidine	STD	5	mg/L	60%	µmol/L	40%	na	mg/L, µmol/L	na
Tricyclic antidepressants	STD	11	µg/L	64%	nmol/L	36%	na	na	na
Amiodarone	STD	9	mg/L	67%	µmol/L	33%	µg/mL	mg/L	na
Amikacin	STD	20	mg/L	90%	µmol/L	10%	µg/mL	mg/L	mg/L
Vancomycin	GSC	159	mg/L	96%	µmol/L	4%	mg/L, µg/mL§	mg/L	na
Tobramycin	STD	47	mg/L	96%	µmol/L	4%	µg/mL	mg/L	mg/L
Gentamicin	GSC	224	mg/L	98%	µmol/L	2%	µg/mL	mg/L	mg/L

*Molar units were not provided with all data. † Serum concentrations supplied only for indicating metabolism in slow release preparations. ‡ Data for Asasantin SR (ng/mL and µg/mL), Solprin (µg/mL) and Cardiprin (µg/mL) only. § Vancomycin hydrochloride for injection (µg/mL) and Vancocin (mg/L). MIMS = *Monthly index of medical specialties.* AMH = *Australian medicines handbook.* STD = Special Therapeutic Drug program. na = no reference to serum concentrations available. GSC = General Serum Chemistry program. ◆

use, the units used in available supporting information, and the risks associated with a transition period. Of course, until this issue is resolved, care must be taken by all parties providing or receiving therapeutic drug concentration results to ensure they are interpreted using the correct units.

Competing interests

None identified.

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