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Usage of renal function equations to guide prescribing in general medicine

We recently surveyed doctors working in the Department of General Medicine, Christchurch Hospital/Princess Margaret Hospital (Christchurch, New Zealand) regarding their usage of equations for estimating renal function in the setting of drug dosing. The Department managed 14,000 acute admissions in 2012 (MSS Lee, Christchurch Hospital, NZ, personal communication, 2013).

Estimating an individual's renal function is a key step in the individualisation of the dosage of renally-cleared drugs.[1,2] This is especially important for those drugs with a narrow therapeutic index, such as dabigatran and gentamicin. The Cockcroft-Gault equation[3] has been in use for several decades[4] and is part of the guidance from the Food and Drug Administration for pharmacokinetic studies in the setting of renal impairment.[5] However, values of estimated glomerular filtration rate (eGFR), which are routinely reported by laboratories in association with plasma creatinine concentrations,[6] represent a convenient alternative for clinicians to use.

The laboratory-reported eGFR is typically calculated either using the Modification of Diet in Renal Disease Study (MDRD) equation,[7] or more recently, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[8] The performances of these equations for drug dosing have been debated in the literature, and it is unclear whether any particular equation is superior in all settings.[9] It is also unclear what equation(s) clinicians use during prescribing. Knowledge of this could help guide efforts in improving the use of renal function estimation for dose-adjustment.

An electronic questionnaire (http://www.surveymonkey.com/s/Q2CC359) was sent to all 67 doctors working in the Department in April 2013. There were 34 responses (51% response rate), including 13 specialist general physicians and 21 junior doctors.

When prescribing renally-cleared medications, most doctors (20/34, 59%) reported mainly using the laboratory-reported eGFR to guide dosing (Table 1). Significantly more respondents used the laboratory-reported eGFR for guiding the dosing of dabigatran (71%) compared with gentamicin (35%) (McNemar's $\chi^2(1) = 8.6$, $P = 0.0018$). These results reflect local prescribing guidelines that highlight the use of the Cockcroft-Gault equation when prescribing gentamicin, but not dabigatran.

Table 1. Usage of renal function equations by medication (total n=34 respondents)

Renally-cleared medication	Mainly laboratory eGFR*, n (%)	Mainly Cockcroft-Gault equation, n (%)	Both equally, n (%)	Other, n (%)
Any†	20 (59)	5 (15)	8 (24)	1 (3)‡
Dabigatran	24 (71)	3 (9)	1 (3)	6 (18)§
Gentamicin	12 (35)	16 (47)	2 (6)	4 (12)§

* Estimated glomerular filtration rate; † Examples of commonly prescribed renally-cleared drugs were provided in the survey; ‡ Respondent stated using a combination of creatinine, age, body weight and gender; § Responses consisted of "not prescribed yet" and "pharmacy consultation".

The survey also included a question asking respondents to recall the units of the laboratory-reported eGFR value. A minority (7/34, 21%) correctly stated that these were mL/min per 1.73 m^2. A further 18% (6/34) noted that body surface area (BSA) was part of the eGFR units, whereas the majority (62%, 21/34) made no mention of this aspect. This apparent deficiency is important to identify, as the laboratory-reported eGFR value should be adjusted for the individual patient's BSA when used for drug dosing, especially at the extremes of size.[10]

A BSA of 1.73 m^2 represents an individual with a height and weight of approximately 170 cm and 65 kg, respectively. Thus, using the 'raw' laboratory-reported eGFR value potentially leads to underestimation of renal function and thus under-dosing in the obese patient, and the converse in the underweight patient.

These survey results, of the prescribers in a department that handles a large number of admissions annually, are the first that we are aware of to demonstrate that the laboratory-reported eGFR is more commonly used for drug dosing than the Cockcroft-Gault equation. This reflects the convenience to the clinician of using the former, which is routinely calculated by the laboratory, compared with the latter, which the laboratory does not routinely generate.

Further, we have highlighted the need to inform prescribers that individual patient size should be considered when using the laboratory-reported eGFR values for drug dosing. These results have been presented to the Department, and local prescribing guidelines are being updated to remind prescribers of this aspect of using the laboratory-reported eGFR values.

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References:

1. Doogue MP, Polasek TM. Drug dosing in renal disease. Clin Biochem Rev. 2011;32:69-73.
2. Begg EJ, Chin PK. A unified pharmacokinetic approach to individualized drug dosing. Br J Clin Pharmacol. 2012;73:335-9.
3. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron. 1976;16:31-41.
4. Millar JA. The Cockroft and Gault formula for estimation of creatinine clearance: a friendly deconstruction. N Z Med J. 2012;125:119-22.
5. Lalonde RL, Wagner JA. Drug development perspective on pharmacokinetic studies of new drugs in patients with renal impairment. Clin Pharmacol Ther. 2009;86:557-61.

6. Saleem M, Florkowski C; for the Australasian Creatinine Consensus Working Group. Reporting of estimated glomerular filtration rate (eGFR) in New Zealand—what are the clinical laboratories doing? N Z Med J. 2006;119(1246):U2337. http://journal.nzma.org.nz/journal/119-1246/2337/content.pdf
7. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. Ann Intern Med. 1999;130:461-70.
8. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med. 2009;150:604-12.
9. Chin PKL, Florkowski CM, Begg EJ. The performances of the Cockcroft-Gault, Modification of Diet in Renal Disease Study and Chronic Kidney Disease Epidemiology Collaboration equations in predicting gentamicin clearance. Ann Clin Biochem. 2013 (in press).
10. Jones GR. Estimating renal function for drug dosing decisions. Clin Biochem Rev. 2011;32:81-8.