

Adequacy of Supporting Evidence for Recommendations on Drug Dose Adjustment in Renal Impairment

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Introduction:

The kidney plays a major role in the metabolism and excretion of many drugs and their metabolites, and impaired kidney function is a major cause of adverse drug reactions. This is especially so in the elderly who have a high prevalence of kidney impairment often in association with dysfunction of other organ systems. Dose adjustment of drugs according to the level of kidney function is essential in such settings. There are diverse methods available for measuring and estimating kidney function. We examined the methods used, as stated in the product literature, for a number of commonly used drugs for which dose adjustment according to kidney function, has been recommended.

Method:

We selected drugs for which dose adjustment in kidney failure has been recommended according to the Renal Drug Handbook. The product literature (Summary of Product Characteristics - SmPC) of all of the proprietary preparations of the selected drugs was consulted and information extracted relating to the measurement/estimation method upon which the recommendation was based. Drugs used in Oncology practice were excluded.

Results:

Two hundred and thirty six drugs were identified, for which there were 738 proprietary preparations. The main classes of drugs were antimicrobial (31%), analgesics and anti-inflammatory (13%), those acting on nervous system (19%), those acting on cardiovascular system (17%), antidiabetic (4%) and others (16%). Kidney function parameters were referred to in the SmPC in terms of serum creatinine alone for 1.9% of preparations, and in creatinine clearance in units of ml/min in 42.5%, in units of ml/min/1.73m² in 5.4%, and in other units in 1.4%. Others used glomerular filtration rate (ml/min) in 4.9% and eGFR in 0.4% (as either ml/min or ml/min/1.73m²). In some cases advice concerning different preparations of the same drug was couched in terms of different renal parameters. Where renal function was referred to in terms of clearance, only 5.7% of the SmPCs referred to the method of measurement/estimation. This was the Cockcroft-Gault method in 5.4% and "an equation similar to Cockcroft-Gault" in the remainder. In the vast majority (94.6%) the method was not specified.

Conclusions:

There is great diversity in the ways in which renal function is expressed in product literature in relation to recommendations for drug dose adjustment. In the vast majority of cases the method of measurement/estimation is not specified. There is a risk of these parameters being used interchangeably, posing risks particularly in the frail elderly.

