RENAL DECLINE IMPACTS DRUG SELECTION AND DOSING IN THE ELDERLY

Don Bastian

As a Consultant Pharmacist, one of my primary goals is to monitor all residents for renal decline and to recommend when appropriate, alternative drug selection or dose modification to account for reduced renal function. The geriatric population is a fragile age group from a pharmaceutical perspective since renal function declines with the aging process. This is particularly important since most drugs and/or the drug metabolites have a significant renal mode of elimination. Unfortunately, when most drugs are brought to market they are tested on the healthy young adults when determining effective dosing guidelines.

We need to think of the geriatric resident in the same light we think of the neonate when considering drug selection and dosing. This involves looking up the patient weight, age, serum creatinine, using the calculator to determine creatinine clearance and referring to the literature dosing guidelines. This is a time consuming process but important when considering the negative consequences of drug overdose including side effects, additional drug therapy, drug therapy failures, increased costs, additional lab tests, resident falls, hospitalizations, morbidity and mortality.

When determining creatinine clearance, it is best to use the Cockroft-Gault formula since it takes all the key patient specific variables into consideration including gender, age, weight and serum creatinine. Many lab reports of basic and complete metabolic profiles include a rough calculation of creatinine clearance, however, the lab report calculation is not as accurate or reliable since not all the patient specific variables are included in the calculation. Pocket personal computers/smart phone applications are readily available to minimize time constraints by providing quick and easy to use programs that apply the Cockroft-Gault method of determining creatinine clearance and provide easy access to renal dosing guidelines (e.g. Lexi-Comp, Inc. and Clinical Pharmacology). One final point worth mentioning is that the serum creatinine levels can be very misleading in the elderly. For example in a 90 year old female, weight of 98 lbs, and a serum creatinine of 1.0 mg/dl the calculated creatinine clearance is 26.27 ml/min. The decreased muscle mass in the elderly accounts for the misleading conclusions one could make if only looking at serum creatinine. A serum creatinine of 1.0 mg/dl could mean significant renal compromise in the elderly.

I recently conducted a simple retrospective review of all medical records on a 60 bed unit of a long term care facility to determine the percent of drugs typically used in the elderly population that require renal impairment dosing. My review identified 65.9% or 56 of the total 85 drugs in use on the unit have renal dosing guidelines according to two reference sources (Lexi-Comp & Clinical Pharmacology). The percent of drugs that were dose adjusted according to patient specific renal compromise would be interesting to study, but was beyond the scope of this review. Of the 34.1% of the drugs that do not have renal dosing guidelines, in over 50% of these drugs, the literature stated that "Specific guidelines are not available; it appears that no dosage
adjustments are needed” (Clinical Pharmacology). This statement suggests that the majority of drugs without renal dosing guidelines have not been adequately studied or renal dosing information is unknown.

According to the renal dosing literature, drug dosages should by lowered or the dosing interval extended based on a specified range of creatinine clearance. In some cases the drug should be avoided or is contraindicated at certain levels of decreased creatinine clearance. For example, sulfamethoxazole-trimethoprim (Bactrim/Bactrim-DS) dose should be reduced by 50% if CrCl 15—30 ml/min and if CrCl < 15 ml/min, then use is not recommended by the manufacturer (Clinical Pharmacology). Another example of a commonly used antibiotic is nitrofurantoin (Macrobid) which is contraindicated when CrCl <60mL/min. Therapeutic concentrations of nitrofurantoin are not attained in the urine of patients with CrCl <60mL/min (lexi-Comp). This fact will explain many therapeutic failures when nitrofurantoin is used to treat urinary tract infections in residents with significant renal compromise. Metformin (Glucophage) is contraindicated in the presence of renal dysfunction defined as a serum creatinine > 1.5mg/dl in males, or > 1.4mg/dl in females. Clinically, it has been recommended that metformin be avoided in patients with CrCl <60-70mL/min (Lexi-Comp). The manufacturer states; “Use metformin with caution in the elderly; less than 3% of patients in clinical trials were >= 75 years of age. Metformin is substantially excreted by the kidney and the risk of adverse reactions (including lactic acidosis) is greater in patients with reduced renal function. Because aging is associated with renal function decline, care should be taken with dose selection and titration. Monitor renal function regularly. Unless renal function is normal, do not use metformin in those patients >= 80 years of age.” (Manufacturer Package Insert). One of the most commonly used drugs in the elderly is acetaminophen (Tylenol). Acetaminophen is considered a very safe analgesic/antipyretic in the elderly when dosed appropriately. Every pharmacist and physician is well aware that the total daily maximum acetaminophen dose is 4 g from all sources. However, how many health care providers are aware that acetaminophen should be dose adjusted when CrCl 10-50 ml/min: Administer every 6 hours; CrCl <10ml/min: Administer every 8 hours (metabolites accumulate) (Lexi-Comp). This is interesting since almost all routine Tylenol orders in long term care facilities are dosed every 4-6 hours.

The above examples are a small sampling from the literature that demonstrate how renal compromise can significantly impact drug selection, dosing and ultimately patient safety. Even when the serum creatinine is reported to be within “normal limits” and the lab report stated that the projected creatinine clearance is >60 ml/min, use caution, calculate the actual creatinine clearance, check the literature for renal dosing guidelines and monitor the resident for drug efficacy and side effects.

Don Bastian, RPh, MS, CGP, is a Board Certified Geriatric Pharmacist and President, DB Pharmacy Consultants LLC, Wescosville, PA