Practice Pointers

Drug Dosing in Chronic Kidney Disease and Dialysis: The Poison Is in the Dose

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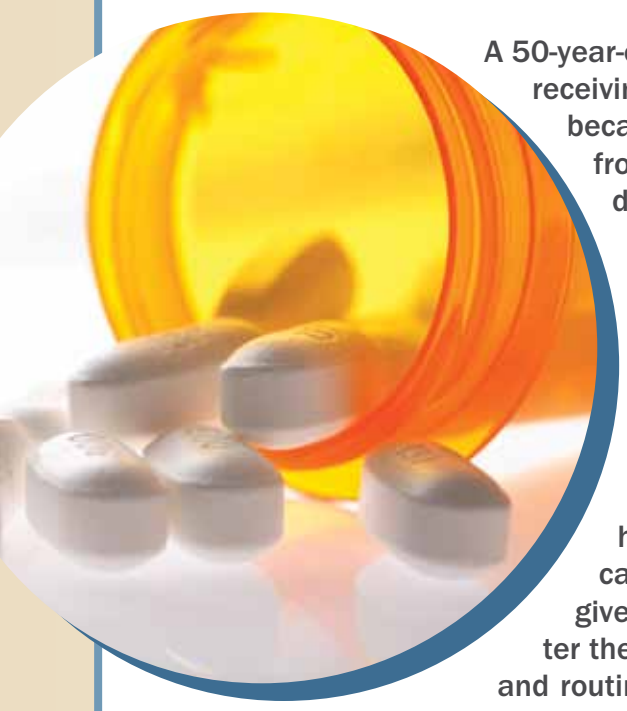

A 50-year-old woman who had been receiving dialysis for many years because of complications from inflammatory bowel disease came to dialysis feeling "not quite right." Her thought processes felt muddled, and her movements were not "right," either. Upon further questioning, she stated that she had a shingles outbreak and had gone to an urgent care facility, where she was given full-dose acyclovir. After the medication was stopped and routine dialysis continued, her symptoms resolved.

When should providers begin to consider modifying drug dosing in patients with chronic kidney disease (CKD) and ESRD?

Once estimated GFR (eGFR) indicates stage 3 or higher CKD (<60 mL/min/1.73 m^2), modification of drug dose, of dosing intervals, or of both should be considered. This is particularly true if the medication has a significant renal clearance. Most laboratories report eGFR as part of the routine blood chemistry results, so identifying patients at risk should not be difficult.

Does this apply to transplant patients?

Drug dose adjustment also applies to transplant patients. The majority of transplant patients do not have a normal eGFR. Renal function often stabilizes at stage 2 to 4, depending on the patient. Drug dosing should follow the same rules as in CKD patients, with special consideration to agents that can alter the metabolism of the immunosuppressant agents.

Do transplant patients have special considerations?

Transplant patients are often taking calcineurin inhibitors. Given that these immunosuppressant agents use the hepatic cytochrome pathways for their metabolism, medications that compete for these pathways may result either in toxicity from a decrease in their rate of metabolism or in low levels of these immunosuppressant agents and a resultant increased risk of rejection caused by an increased rate of their clearance.

What types of symptoms can inappropriate dosing cause in these patients?

Manifestations can include altered mental status, abnormal motor activity, seizures, acute renal failure, acute hepatitis, dermatitis, mucositis, and bone marrow suppression.

Is any class of drugs particularly harmful?

Some examples of class effect include antivirals, anticonvulsants, macrolide antibiotics, nonsteroidal agents, Cox-2 inhibitors, and metformin.

Should any drugs in particular not be used?

Owing to their effects on GFR, Cox-2 inhibitors and nonsteroidal agents should be avoided. Metformin should be avoided if the creatinine determination does not meet the criteria for metformin use. Other drugs can be used if appropriately dose modified or, in the case of transplant recipients, if the immunosuppressant medication levels are measured appropriately.

How can you treat an unintended reaction caused by dosing issues in CKD, ESRD, and transplant patients?

Treatment involves a variety of strategies depending on the situation and can include stopping the medication, giving supportive care, adjusting immunosuppressant medications, or administering dialysis to remove the offending agent.

When does a patient with ESRD need to take certain drugs in relation to hemodialysis or peritoneal dialysis?

Drugs that have significant renal clearance should be taken after hemodialysis. For peritoneal dialysis, when possible, drugs that are renally cleared should be taken after the completion of continuous cycling peritoneal dialysis. Dosing should be for GFR <10 mL/min/1.73 m^2.

Does this apply to hospitalized patients receiving continuous renal-replacement therapy?

Dosing considerations also apply to these patients. Consultation with the hospital pharmacy should occur to ensure that the proper prescription is given to the patient receiving continuous renal replacement therapy.

Where can providers get information on dosing guidelines?

With the advent of the Internet and the multitude of hand-held devices available, information is almost always readily accessible. Useful sites, to name a few, include UpToDate, mobile PDR (Physician's Desk Reference), MPR (Monthly Prescribing Reference), Epocrates, and Medscape.

What would be your general recommendations to make things easier for providers?

Note that eGFR is the first step in making life easier for providers. Providers should do a quick lookup in one of the many available online references when prescribing medications with which they are unfamiliar. Providers should find a reference that they believe is quick and easy to use and have it available on their computer desktops or as an app on their hand-held devices. For children younger than 17, the Schwartz formula should be used to estimate eGFR. It is available online.

Recommended sources

http://www.UpToDate.com
http://www.Medscape.com
http://www.PDR.net
http://www.Epocrates.com
http://www.eMPR.com

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