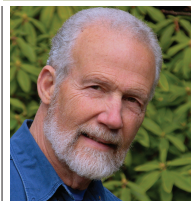


Hyperkalemia from Drug Interactions: New Data

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Hyperkalemia resulting from various combinations of drugs has become an important issue for pharmacists due to the high frequency of drug-drug interaction (DDI) alerts and the potential for life-threatening outcomes. While we know some of the risk factors that increase the risk of hyperkalemia in patients receiving these drug combinations, a new paper has substantially improved our knowledge of these risk factors.

The Study

The researchers looked at the risk factors and the clinical outcomes of 8413 incidents of “potentially severe” potassium-increasing DDIs in patients hospitalized in University Hospital in Zurich, Switzerland.¹ They considered the following drugs to be potassium increasing: angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers, direct renin inhibitors (aliskiren), calcineurin inhibitor immunosuppressives (cyclosporine, tacrolimus), potassium-sparing diuretics, and trimethoprim. The researchers looked at risk factors such as age,

gender, duration of therapy, renal function, diabetes, and other comorbidities. They also looked at physician-related factors that might affect risk, such as serum potassium monitoring.

Results

The highest risk of hyperkalemia occurred in patients who had received lung transplants, with a relative risk (RR) of 5.1, probably due to the number of potassium-increasing drugs they received (eg, immunosuppressants, ACE inhibitors, trimethoprim). Impaired renal function (creatinine clearance <60 mL/min) also substantially increased risk (RR: 2.7), as did diabetes (RR: 1.6) and female gender (RR: 1.5). Not surprisingly, the risk of hyperkalemia was higher in patients receiving more potassium-increasing drugs, and with greater duration of therapy with such drugs. Also as expected, physician-related risk factors for hyperkalemia were lack of serum potassium determinations or elevated serum potassium before potassium-increasing drugs were started, and infrequent monitoring (interval: >48 hours) of serum potassium after the drugs were started. Interestingly, older age was not found to be a risk factor in this study (Table 1).

TABLE 1: RISK FACTORS FOR HYPERKALEMIA DRUG-DRUG INTERACTIONS

Lung transplant
Impaired renal function
Diabetes mellitus
Female gender
Number of potassium-increasing drugs taken
Duration of drug-drug interaction exposure
Inadequate serum potassium monitoring

Implications for Pharmacy

Although this study involved hospitalized patients, it has been shown that increasing numbers of outpatients taking combinations of potassium-increasing drugs have been hospitalized for severe hyperkalemia.^{2,3} Many of these outpatients had been taking ACE inhibitors plus potassium-sparing diuretics, but as the Swiss study showed, many other drugs can increase the risk of hyperkalemia (Table 2).

TABLE 2: DRUGS THAT CAN INCREASE THE POTASSIUM LEVEL

Angiotensin-converting enzyme inhibitors
Angiotensin-receptor blockers
Drosiprenone (Yasmin)
Heparin
Immunosuppressants (eg, cyclosporine, tacrolimus)
Nonsteroidal anti-inflammatory drugs
Potassium-containing salt substitutes
Potassium-sparing diuretics
Potassium supplements
Succinylcholine
Trimethoprim (in cotrimoxazole)

Taken together, the studies show that risk factors are important in assessing the likelihood of hyperkalemia in patients receiving potassium-increasing DDIs. By taking these factors into consideration, we can focus our attention on patients at higher risk of hyperkalemia. ■

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