The GeriJournal

Volume 6, Number 2
February 2011
A publication of GeriatRx Pharmacy

WarfarInteractions

I have been quite preoccupied with warfarin over these past few months. After reading a splendid article in the *Canadian Pharmacists Journal*, I'm afraid I must write about it one more time.

The article contains an invaluable practice tool which details warfarin interactions in a practical way that I have not seen before. The interacting drugs, mechanism, anticipated onset, conclusion or offset and management of the interaction are detailed clearly. The tool was created by a pair of pharmacists working in two major anticoagulation centres in Alberta. It is a blend of their wisdom gleaned from years of clinic work and established recommendations from the medical literature.

I was most interested in the "Suggested Management" column of the chart. When interactions are significant, it shows the percentage by which the warfarin dose should be diminished (or increased). By showing the anticipated onset of the interaction, we can see when the INR testing process should be initiated.

I have included a small selection of commonly used medications from the chart. The entire tool may be viewed at www.cpjournal.ca.

Quinine Cramps Up

A side benefit of the antimalarial drug quinine is its ability to prevent nocturnal leg cramps. Over the years it has been used quite frequently for this indication, but warnings by the FDA in 1994 and 2006 have curtailed its use.

Quinine can cause thrombocytopenia (reduction in platelet levels) which may result in severe bleeding. It may also cause hemolytic-uremic syndrome, a disorder where red blood cells are destroyed and their residue travels to the kidneys, resulting in further damage. The FDA recently issued another warning, because quinine continues to be used and adverse events and deaths are still being reported.

Calf stretching exercises, hydration and correction of electrolyte imbalances will often reduce cramping frequency. It is also important to consider and treat other possible cramp triggers such as restless legs syndrome and vascular insufficiency. Diltiazem and vitamin B complex (with at least 30mg of B6) have also helped some individuals.

WARFARIN DRUG INTERACTIONS

Drug	Direction and severity of effect on INR	Mechanism	Anticipated onset	Anticipated offset ($t_{½}$)	Suggested management
Carbamazepine (CBZ)	↓INR Moderate to severe	Increase in warfarin metabolism (through CYP2C9 induction)	10-35 days	Delayed (14-40 days) ($t_{½}$=12-17 hours)	Monitor INR closely when starting, stopping, or adjusting CBZ; increase in warfarin dose of 50%-100% may be required when initiating CBZ; decrease warfarin dose by ~50% when stopping CBZ
Clarithromycin	↑INR Moderate	Inhibition of warfarin metabolism (through CYP3A4 inhibition)	3-7 days	NR ($t_{½}$=5-7 hours)	Monitor INR more frequently when starting or stopping clarithromycin; AMS considers empiric 15%-25% warfarin dose reduction
Lactulose	↑INR Moderate	Decreased intestinal absorption of vitamin K	1-3 days	Delayed	Monitor INR closely when starting or stopping lactulose
Metronidazole	↑INR Major	Decrease in warfarin metabolism (through CYP2C9 inhibition)	3-5 days	~2 days ($t_{½}$=8 hours)	Monitor INR closely when starting or stopping metronidazole; AMS considers empiric 25%-40% warfarin dose reduction
Rosuvastatin	↑INR Moderate	Unknown	3-7 days	3-7 days ($t_{½}$=19 hours)	Monitor INR closely when starting or stopping rosuvastatin; consider alternative statin (no reports of interaction with warfarin for atorvastatin or pravastatin); AMS empirically reduces warfarin dose by 10%-25% and reassess INR within 1 week
Sulfamethoxazole (with or without trimethoprim)	↑INR Severe	Inhibition of warfarin metabolism and displacement of warfarin from protein-binding sites	2-5 days	2-14 days ($t_{½}$=10 hours)	Monitor INR closely when starting or stopping sulfamethoxazole-containing drug regimens; AMS considers empiric 25% -40% warfarin dose reduction

*AMS: Anticoagulant Management Service

Source: Canadian Pharmacists Journal: Jan 2011, Vol. 144, No. 1, pp21-25.e9

Prepared by Randy Goodman
Certified Geriatric Pharmacist