Oral Anticoagulants and NSAIDs, SSRIs, or SNRIs

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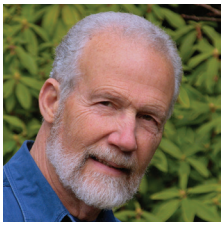

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PREVIOUS COLUMNS HAVE SUMMARIZED the potential pharmacokinetic interactions between oral anticoagulants (OACs) (eg, warfarin, apixaban, betrixaban, dabigatran, edoxaban, and rivaroxaban) and drugs that alter their elimination. OACs are also susceptible to pharmacodynamic interactions with drugs that alter their pharmacologic response. The co-administration of other anticoagulants, such as heparin or drugs designed to inhibit platelet aggregation (eg, clopidogrel, prasugrel, and low-dose aspirin), is known to increase the risk of clinically significant bleeding episodes. Combining OACs and drugs that have antiplatelet activity (eg, nonsteroidal anti-inflammatory drugs [NSAIDs], selective serotonin reuptake inhibitors [SSRIs], and serotonin and norepinephrine inhibitors [SNRIs]) as an adverse effect has also been shown to increase the risk of bleeding. These interactions are summarized below.

NONSTEROIDAL ANTI-INFLAMMATORY DRUGS

In addition to their anti-inflammatory and analgesic activity, NSAIDs that inhibit cyclooxygenase-1 reversibly inhibit platelet aggregation and reduce the ability of the stomach lining to prevent ulceration. If bleeding in the gastrointestinal (GI) tract or elsewhere in the body occurs in a patient taking an OAC, it may be more severe in patients who are also taking drugs that inhibit platelet aggregation. One of the first reports of the effect of NSAIDs on bleeding risk with OACs noted a 3.7-fold increased risk of GI bleeding.[1] Others have reported a similar increased risk of GI bleeding associated with NSAIDs.[2-4] The risk of bleeding in patients simultaneously taking OACs and NSAIDs has been noted to increase if additional drugs associated with GI bleeding (eg, systemic corticosteroids, aldosterone antagonists, and SSRIs) are co-administered.[3,5] Conversely, the co-administration of gastric acid suppressants, such as proton pump inhibitors, is associated with a reduced risk of GI bleeding.[2]

The management of patients receiving NSAIDs and OACs depends on several risk-modifying factors. As noted above, the co-administration of other drugs can increase or decrease the risk of GI bleeding. In addition, patients with a prior history of GI bleeding are likely to be at increased risk, as are chronically ill patients who take NSAIDs, compared with those using NSAIDs as needed. The use of topical NSAIDs is not considered to increase the risk of bleeding. The risk of combining OACs plus NSAIDs should be discussed with all patients; however, those with additional risk factors should be counseled in more detail.

SELECTIVE SEROTONIN REUPTAKE INHIBITORS AND SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS

Antidepressants belonging to the SSRI and SNRI classes inhibit platelet aggregation by decreasing the uptake of serotonin by platelets. They are not associated with an increased risk of GI ulceration. The administration of SSRIs and SNRIs with OACs increases the risk of bleeding by 2- to 3-fold.[2-4] There are insufficient data to discern the relative risk for bleeding episodes between these classes. Factors similar to those noted above for NSAID–OAC interactions increase the risk of bleeding in patients taking OACs and these antidepressants.[3,5-7] Unlike bleeds associated with NSAIDs and OACs, however, antidepressant-OAC bleeds are not excessively GI related.

Because antidepressants tend to be administered on a long-term basis and gastro-protective drugs are unlikely to reduce the risk of bleeding, it is difficult to identify a subset of patients who are at lower risk of bleeding. Antidepressants that do not affect serotonin reuptake do not appear to increase the risk of bleeding with OACs and could be considered as alternatives.

SUMMARY

Although most of the data on bleeding risk with OACs are on warfarin, one should assume similar risks are associated with nonvitamin K antagonist anticoagulants. Knowledge of factors that increase or mitigate the risk of an interaction is important when evaluating patients. Pharmacists should be particularly watchful for patients with risk factors who should be considered for alternative therapy. Patients who are exposed to NSAIDs, SSRIs, or SNRIs in addition to OACs should be counseled to report any evidence of bleeding to their health care practitioners. ◆