



PIC QUESTION OF THE WEEK: 07/04/05

Q: Is there an increased risk of gastrointestinal bleeding with selective serotonin reuptake inhibitors (SSRIs)?

A: In addition to its importance as a neurotransmitter in the CNS, serotonin plays a key role in several other physiologic functions including platelet aggregation. Platelets cannot synthesize serotonin and are dependent on a transport protein for its supply. SSRIs inhibit this transport protein resulting in reduced serotonin reuptake by platelets. The decrease in platelet serotonin reuptake and release is thought to be responsible for the increase in bleeding abnormalities associated with SSRIs. There are several case reports describing various bleeding disorders associated with SSRIs. These include epistaxis, hematoma, uterine and vaginal bleeding, etc. Observational studies have identified a greater risk of gastrointestinal (GI) bleeding and some suggest the risk may be similar to that observed with NSAIDs. The potential for GI bleeding is increased several fold in patients receiving SSRIs along with NSAIDs. The use of SSRIs also appears to increase post-operative blood loss, but does not seem to affect the risk of hemorrhagic stroke. These antiplatelet effects of SSRIs may be beneficial in cardiac patients suffering from unstable angina or MI. The risk of bleeding abnormalities with SSRIs is related to the degree of inhibition of serotonin reuptake. Drugs with a high degree of inhibition of reuptake (e.g. fluoxetine, sertraline, clomipramine, and paroxetine) seem to produce these effects more frequently than antidepressants with intermediate activity (e.g. venlafaxine, citalopram, fluvoxamine, etc.). Antidepressants with a low degree of inhibition (e.g. bupropion, doxepin, nefazodone, etc.) have limited potential for increasing the risk of bleeding. Unfortunately, there are no published controlled trials that confirm this suspected complication of SSRIs. Regardless, the elderly, patients receiving NSAIDs, those receiving warfarin or antiplatelet agents, and other high risk groups should be monitored for bleeding complications when SSRIs are prescribed.

References:

- Dalton SO, Johansen C, Mellekjaer L, et al. Use of selective serotonin reuptake inhibitors and risk of upper gastrointestinal tract bleeding: a population based cohort study. *Arch Intern Med* 2003;163:59-64.
- Meijer WE, Heerdink ER, Nolen WA, et al. Association of risk of abnormal bleeding with degree of serotonin reuptake inhibition by antidepressants. *Arch Intern Med* 2004;164:2367-70.

John G. Lech, Pharm.D.