

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

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SSRIs and abnormal bleeding

The first published report of abnormally increased bleeding time associated with Selective Serotonin Reuptake Inhibitor (SSRI) treatment was published in 1990, noting that these antidepressants also have the pharmacological property of diminishing granular storage of serotonin in platelets, suggesting a basis for a drug-induced defect in haemostasis. Other early reports also provided important signals in the form of case reports of abnormal bleeding and bruising; a report of a fatal intracranial haemorrhage associated with an SSRI; and a case where a patient developed a demonstrable and reversible defect in platelet aggregation after the commencement of fluoxetine. Even a cursory examination of the prescribing information for any of the SSRI agents reveals many clues about the knowledge that was to evolve later – adverse effects listed for SSRIs include purpura, petechial rash, ecchymosis, epistaxis, menorrhagia and rectal bleeding, and some are listed as “common”.

Since these early signals, much more information has evolved from large-scale pharmacoepidemiological studies and post-marketing surveillance. Dutch researchers used data collected over an eight year period from more than 64 000 new antidepressant users to examine the association between abnormal bleeding and the use of SSRIs, finding that the risk of hospitalization for abnormal bleeding increased with the use of these drugs. There is now convincing evidence that treatment with SSRIs significantly increases the likelihood of major haemorrhagic events, in particular upper gastrointestinal bleeding.

Moreover, it appears that the risk of upper gastrointestinal bleeding with SSRIs is increased by concurrent treatment with Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or oral anticoagulants, and that the extent of risk may be mitigated to some extent by the intercurrent use of a proton pump inhibitor. This observation has prompted some clinicians to advocate for the routine use of gastro-protective drugs such as proton pump inhibitors in cases where SSRI and NSAIDs are used concomitantly.

Research has demonstrated that the risk of blood transfusion increased almost four-fold amongst patients treated with serotonergic antidepressants who were undergoing orthopaedic surgery, as compared with the non-users. The researchers concluded that treatment with these agents is associated with an increased risk of intra-operative and post-operative bleeding and the subsequent need for blood transfusion in the context orthopaedic surgery. Other research from Denmark suggests a similar finding in relation to post-operative bleeding complications amongst women undergoing surgery for breast cancer.

Interestingly, there is now a developing literature linking venlafaxine and desvenlafaxine (antidepressants with some properties similar to the SSRIs) to abnormal bleeding, and it is possible that with time, a similar picture to that initially observed with the SSRIs may evolve.

This E-Bulletin is based on work by Chris Alderman, Clinical Pharmacist, RGH

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