

NSAIDs Double Bleeding Risk with Anticoagulants for DVT/PE

In the past, treatment for a headache or musculoskeletal injury consisted of aspirin or acetaminophen. However, since the overuse of acetaminophen is related to hepatotoxicity and aspirin is a known antiplatelet agent which can increase the risk of bleeding, more patients are self-treating with over-the-counter NSAIDs such as Ibuprofen. Earlier work has shown that atrial fibrillation patients who are prescribed an anticoagulant such as warfarin, along with aspirin, have an increased risk of bleeding. However, until recently the bleeding risk in patients receiving an anticoagulant for DVT or PE who take an NSAID or aspirin is poorly documented.

An prospective observational analysis study was published by *JAMA Internal Medicine* on April 14, 2014, concluded that patients receiving anticoagulation for DVT or PE who take NSAIDs or aspirin for pain or headache are at a higher risk for a major bleed. There were two main trials examined in the observational analysis published in JAMA: the EINSTEIN-DVT and EINSTEIN-PE trials, which were conducted by Janssen Pharmaceuticals, the manufacturer of Xarelto (rivaroxaban). Investigators for the JAMA study examined the data from the EINSTEIN trials to assess the bleeding risk from the use of aspirin and/or NSAIDs in a total of 8246 patients randomized to take either enoxaparin bridged with VKAs, or rivaroxaban alone for the treatment of a DVT/PE. The JAMA study examined the risk of clinically relevant bleeding: non-major bleeding, and major bleeding, defined as fatal, occurring at a critical site, or requiring a major transfusion. The trials showed that about one-quarter of patients took aspirin or an NSAID during anticoagulation. Compared to those who avoided NSAIDs and aspirin throughout treatment, patients had a 2.4-fold higher risk of a major bleed if taking an NSAID, and a 1.5-fold higher risk if taking aspirin. Also, patients taking NSAIDs or aspirin were at a 1.77-fold higher risk of having a clinically relevant bleed than those not taking either drug.

Taking the data from the JAMA article, patients should be warned to not take an NSAID for acute pain or headache relief and to only take aspirin for coronary artery disease if indicated. Patients should be instructed to take acetaminophen for pain, discomfort or fever if needed, keeping in mind the limit of 4g in 24-hours to prevent hepatotoxicity. Pharmacists are the healthcare professionals on the front-lines of patient self-care strategies and have an important role in educating patients on the dangers of taking NSAIDs and aspirin with anticoagulants. Efforts should be taken to direct anticoagulated patients towards the use of acetaminophen instead of NSAIDs and aspirin for acute pain and discomfort.

References:

- Busko M. NSAIDs Double Bleeding Risk with Anticoagulants for DVT/PE. Medscape. Available at: <http://www.medscape.com/viewarticle/823628>.
- Davidson BL, Verheijen S, Lensing AWA, et al. Bleeding risk of patients with acute VTE taking NSAIDs or aspirin. *JAMA Intern Med* 2014
- The EINSTEIN Investigators. Oral Rivaroxaban for Symptomatic Venous Thromboembolism. *N Engl J Med*. 2010;363:2499-2510.
- The EINSTEIN-PE Investigators. Oral Rivaroxaban for the Treatment of Symptomatic Pulmonary Embolism. *N Engl J Med*. 2012;366:1287-1297.

Prepared by: Grant A Shaddix, Doctor of Pharmacy Candidate