Pharmacotherapy. 2008 Apr;28(4):540-8.

Potential glucosamine-warfarin interaction resulting in increased international normalized ratio: case report and review of the literature and MedWatch database.

Knudsen JF, Sokol GH.

Source : Division of Neurology and Psychiatry Drug Products, Office of Drug Evaluation I, United States Food and Drug Administration, Silver Spring, MD 20993-0002, USA.

Abstract

We describe a 71-year-old man who had received warfarin 7.5 mg/day for 5 years for atrial fibrillation, which had maintained his international normalized ratio (INR) within a narrow range of 2.5-3.2. During this 5-year period, he had also been treating himself with the supplement glucosamine hydrochloride 500 mg-chondroitin sulfate 400 mg twice/day for arthritis. The patient then increased his dosage of glucosamine to 1500 mg and chondroitin to 1200 mg twice/day; his INR previous to this change was 2.3. Approximately 3 weeks later, his INR increased to 3.9. His supplement dosage was reduced to glucosamine 750 mg-chondroitin 600 mg/day; a repeat INR done 16 days later was 4.7. The supplement was then stopped, and his warfarin schedule was changed to 7.5 mg every other day alternating with 3.75 mg every other day. Sixteen days later, his INR was 2.6. This case report suggests that a potential interaction exists between warfarin and glucosamine that is associated with an increase in the INR. We therefore performed a pharmacovigilance survey of spontaneously reported adverse events in warfarin-treated patients concomitantly exposed to glucosamine, glucosamine-chondroitin sulfate, or chondroitin sulfate and present a literature review of this apparent drug-drug interaction. Using the United States Food and Drug Administration (FDA) MedWatch database, 20 reports of glucosamine or glucosamine-chondroitin sulfate use with warfarin associated with altered coagulation (manifested by increased INR, or increased bleeding or bruising) were identified. In some cases, a decrease in the supplement dosage was followed by a return of the INR to the previous therapeutic range. Similarly, a decrease in warfarin dosage was followed by a decrease in INR in one patient who received long-term warfarin therapy. One report described an intraventricular bleed and subdural hematoma, which resulted in a persistent vegetative state. The World Health Organization (WHO) adverse drug reactions database documented 21 spontaneous reports of increased INR associated with glucosamine use, 17 of which resolved when glucosamine was stopped. We located one published case report of concomitant use of glucosamine-chondroitin sulfate potentiating the effect of warfarin. In aggregate, the reports from the FDA and WHO, the published case report, and our case report suggest that the use of warfarin and glucosamine may lead to an increased INR. Patients should be advised that the use of the two products may cause an increase in INR, and they should inform their health care provider if they consume glucosamine. More information is necessary to define this interaction.