Drug Monitor

The Link Between Arthritis and Diabetes

Rheumatoid arthritis (RA) and psoriasis both have been linked with diabetes and insulin resistance. Studies have suggested that disease-modifying antirheumatic drugs (DMARDs) that act directly against the inflammatory response, such as tumor necrosis factor (TNF) inhibitors and hydroxychloroquine, improve insulin resistance and reduce the risk of incident diabetes mellitus (DM).

Researchers from Brigham and Women's Hospital in Boston, Massachusetts, conducted a retrospective examination of the relationship between DMARDs and the risk of newly diagnosed DM. Their study involved 13,905 patients with RA or psoriasis. All participants had at least 2 diagnoses and 1 filled prescription for a DMARD before the start of follow-up. The researchers estimated the relative risk of diabetes according to the drug: TNF inhibitors, methotrexate, and hydroxychloroquine, and other nonbiologic DMARDs, such as sulfasalazine, cyclosporine, and azathioprine.

During a mean follow-up of 6 months, the researchers identified 267 newly diagnosed cases of DM: 55 among nonbiologic DMARD users (3,993 treatment episodes); 80 among TNF inhibitor users (4,623 treatment episodes); 82 among methotrexate users (8,195 treatment episodes); and 50 among hydroxychloroquine users (5,682 treatment episodes). Patients who switched to nonbiologic DMARDs had the highest incidence of diabetes, while those using TNF inhibitors or hydroxychloroquine had the lowest rates.

The findings from their epidemiologic study should be considered "hypothesis generating," the researchers conclude. Several prior studies, they note, suggested TNF inhibitors improved insulin metabolism among patients with RA. In the context of those prior findings, the researchers say their study supports the potential role for systemic immunosuppression in preventing and controlling DM.

Source: *JAMA.* 2011;305(24):2525-2531. doi:10.1001/jama.2011.878.

Gauging the Safety of the Tiotropium Mist Inhaler

Tiotropium mist inhalers may put patients with chronic obstructive pulmonary disease (COPD) at risk of death, according to a meta-analysis conducted by researchers from Johns Hopkins University School of Medicine in Baltimore, Maryland; the University of East Anglia in Norwich, United Kingdom; the University of Arizona in Tucson; and Wake Forest University School of Medicine in Winston-Salem, North Carolina. Reviewing data from 5 randomized, controlled trials of 6,522 patients with COPD, they found the tiotropium mist inhaler was associated with a 52% higher risk of all-cause mortality compared with a placebo, possibly due to a dose-response relationship.

Inhaled tiotropium is available in 2 formulations: as a powder (Spiriva) delivered with a Handihaler (Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany) device and in solution as a mist delivered with the Respimat Soft Mist Inhaler (Boehringer Ingelheim Pharma GmbH & Co. KG). According to pharmacokinetic studies, peak plasma concentrations with the mist inhaler at doses of 5 µg and 10 µg were 35% and 3 times higher, respectively, than with tiotropium 18 µg delivered by the Handihaler. In the 5 trials analyzed, 3,686 patients used the tiotropium mist inhaler and 2,836 used a placebo.

Overall, the tiotropium mist inhaler was associated with a significantly increased risk of mortality compared with the placebo (in the 5 trials, 90 of 3,686 vs 47 of 2,836; relative risk 1.52).

Research has found both a higher risk of cardiovascular illness and death among patients with COPD, and a significantly increased risk of major cardiovascular events with inhaled anticholinergics. The FDA raised concerns about the safety of tiotropium in hearings in 2009, although 1 large-scale study that compared tiotropium powder with a placebo did not report any increase in mortality or cardiovascular events. The researchers for the current study, however, say patients receiving the drug via the mist inhaler are potentially exposed to higher concentrations.

An ongoing, 2-year, head-to-head trial of tiotropium mist inhaler at different dosages has been designed to investigate the safety issues. Until the results are known, the researchers advise caution when prescribing a tiotropium mist inhaler, particularly in patients with possible cardiac disease.

Source: *BMJ.* 2011;342:d3215. doi:10.1136/bmj.d3215.

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