



# Drug Monitor

## Low-dose Aspirin and Diabetes Prevention

Recent data has shown subclinical inflammation to be a risk indicator for obesity-linked inflammatory disorders, such as type 2 diabetes. And some research suggests women may have a higher risk of these types of disorders. Thus, the thinking goes, long-term, low-dose aspirin might help prevent diabetes among women. But researchers from Brigham and Women's Hospital, Harvard Medical School, and the VA Boston Medical Center, all in Boston, MA, say the data don't support that hypothesis.

They evaluated data on 38,716 healthy women aged 45 or older in the Women's Health Study—a 10-year, randomized, placebo-controlled trial of aspirin (100 mg on alternate days) and vitamin E for primary prevention of cardiovascular disease and cancer. Although clinical diabetes was not an endpoint, it was an outcome of interest and was evaluated prospectively throughout the study.

The researchers found no statistically significant difference in the incidence of type 2 diabetes between the aspirin and placebo groups: Of 19,326 women in the aspirin group, 849 developed diabetes, as did 847 of 19,390 women in the placebo group. After considering diminished medication adherence over time, and after excluding cases of diabetes that were diagnosed early in the trial, they still found no significant difference between the two groups. Additionally, aspirin did not significantly reduce the risk of developing diabetes in women who had dyslipidemia, elevated hemoglobin A<sub>1c</sub> values, or high-sensitivity C-reactive protein levels at baseline.

The researchers caution that their findings do not pertain to the salicylate agents currently being evaluated for diabetes treatment or to intermediate or high doses of long-term aspirin. They add, however, that even at the low dose used in this trial, the use of aspirin was associated with a significant increase in clinically important bleeding events.

Source: *Diabetes Care*. 2009;32(1):3–8.  
doi:10.2337/dc08-1206.

## Antipsychotics and Sudden Cardiac Death: Is Newer Safer?

When it comes to the risk of sudden cardiac death (SCD), the atypical antipsychotic agents are no safer than the older, typical antipsychotics, warn researchers from Vanderbilt University School of Medicine and the Nashville VA Medical Center, both in Nashville, TN.

In their retrospective cohort study of data from Tennessee Medicaid, the researchers identified all individuals aged 30 to 74 years who had at least one qualifying day of antipsychotic drug use from January 1990 through December 2005. For each of these antipsychotic drug users, two controls were matched for age, sex, and first day of follow-up. In total, 44,218 users of single typical antipsychotics, 46,089 users of single atypical antipsychotics, and 186,000 nonuser controls were identified.

During more than one million person-years of follow-up, there were 1,870 SCDs, or 18 per 10,000 person-years. The unadjusted rate ranged from 4.7 SCDs per 10,000 person-years for those aged 30 to 34 at baseline to 47.6 per 10,000 person-years

for those aged 70 to 74. The mortality rate was more than twice as high for men as it was for women. The rate of SCD for current typical antipsychotic users was twice that for nonusers and the rate for current atypical antipsychotic users was more than twice that for nonusers, with no significant difference between the typical and atypical groups. The lack of significant differences between the two antipsychotic groups persisted even when the researchers performed several analyses to control for confounding factors. Patients who had used antipsychotics formerly were not at significant risk for SCD.

For both classes of drugs, the risk for current users increased significantly with dosage (which was expressed using approximate equivalents of 100 mg of chlorpromazine). Among users of the typical agents, the incidence-rate ratio rose from 1.31 for patients taking low doses (less than 100 mg) to 2.42 for those taking high doses (300 mg or greater). Among users of atypical drugs, the ratio rose from 1.59 at low doses to 2.86 at high doses.

The researchers found a dose-response trend for SCD risk with each of the six frequently prescribed antipsychotic drugs. The trend was significant in the case of thioridazine (a typical antipsychotic) and of borderline significance in the case of risperidone (an atypical antipsychotic). Current users of high dose thioridazine had the highest risk of SCD. ●

Source: *N Engl J Med*. 2009;360(3):225–235.