Glucocorticoids and Risk of Atrial Arrhythmias

Christiansen CF, Christensen S, Mehnert F, et al. Glucocorticoid use and risk of atrial fibrillation or flutter. A population-based, case-control study. Arch Intern Med 2009; 169:1677–83.

Study Overview

Objective. To examine whether the use of glucocorticoids is associated with increased risk of atrial fibrillation or flutter.

Design. Population-based, case-control study.

Setting and participants. The study was conducted in Northern Denmark. The Danish National Registry of Patients was used to identify 20,011 patients that had an inpatient visit for atrial fibrillation or flutter between 1999 through 2005. The Danish Civil Registration System was used to identify 202,130 population controls that were matched for age and sex. The region's prescription database was used to identify prescription of glucocorticoids. Patients were classified into 4 categories of glucocorticoid users: (1) *current users* (patients who had filled their most recent glucocorticoid prescription within 60 days prior to hospitalization); (2) *new users* (filled first prescription within 60 days prior to hospitalization); (3) *long-term users* (filled first prescription more than 60 days prior to hospitalization); and (4) *never users* (no glucocorticoid prescriptions). Individuals were also assessed for previous diagnosis of cardiovascular, pulmonary, or thyroid disease based on hospital diagnosis indicated by the national registry or use of prescription drugs associated with these conditions.

Main outcome measures. Risk of hospitalization for atrial fibrillation or flutter.

Main results. Among the 20,221 cases of atrial fibrillation or flutter, 6.4% were current users of glucocorticoids and 11.7% were former users. Among the 202,130 controls, 2.6% were current users and 9.9% were former users. The increased risk of atrial fibrillation or flutter was associated with current glucocorticoid use compared with never-use (OR, 1.9 [95% confidence interval {CI}, 1.8–2.1]). There was no association between increased risk and former glucocorticoid use (adjusted OR, 1.0 [95% CI, 1.0–1.1]). The increased risk of atrial fibrillation or flutter hospitalization was greater for older patients (< 50 years: OR, 1.2 [95% CI, 0.6–2.4]; 50–59 years: OR, 1.8 [95% CI, 1.2–2.5]; 60–69 years: OR, 2.2 [95% CI, 1.8–2.6]; 70–79 years: OR, 2.0 [95% CI, 1.7–2.2]; ≥ 80 years: OR, 1.8 [95% CI, 1.6-2.0]). New glucocorticoid users had an adjusted OR of 3.6 (95% CI, 3.1–4.2) and long-term users had an adjusted OR of 1.7 (95% CI, 1.5–1.8). The increased risk of hospitalization was found among both patients with and without pulmonary and cardiovascular diseases.

Conclusion. This large, population-based case-control study found that the risk of hospitalization for atrial fibrillation or flutter nearly doubled among glucocorticoid users.

Commentary

Atrial fibrillation (Afib) is the most common cardiac arrhythmia in the United States and may be present in more than 10% of men over the age of 80 years [1]. The occurrence of Afib is associated with a 3- to 4-fold increased risk of ischemic stroke and high rates of morbidity, mortality, and health care costs [2]. While hypertension and ischemic heart disease are both risk factors for AFib, we know relatively little about other risk factors. Several previous studies have suggested that the use of glucocorticoids, which are known to have deleterious effects on muscle tissue, may be a contributing factor. This study by Christiansen and colleagues adds to the literature by trying to examine, in a large population-based study, whether glucocorticoid use was associated with higher risk of Afib or atrial flutter (Aflutter), a related condition.

There are several strengths of the study that are worth noting. It was conducted among a relatively homogeneous group with excellent follow-up and detailed clinical data. However, at least 2 major limitations of the study significantly affect its interpretability. First and foremost is the choice of "control" patients. In a case-control study, the biggest threat to validity comes from using controls that are dissimilar at baseline. Generally, one should find controls using the same data source as the cases. The study by Christiansen used different databases—one of hospitalized patients to find cases and another of population-based healthy patients to identify controls. It is of little surprise that hospitalized patients are more likely to be current users of glucocorticoids. In fact, the cases were generally sicker and were far more likely to have cardiopulmonary diseases than the controls. The authors attempt to adjust for these baseline differences but such adjustments are imperfect.

Finally, the authors provide a series of subgroup analyses —those with and without each of the cardiopulmonary conditions—but these subgroup analyses are unconvincing. They show that even among patients with and without these conditions (eg, asthma), glucocorticoids are associated with greater rates of Afib or Aflutter. However, it is almost surely true that hospitalized patients with asthma have more severe cases of the condition requiring steroid use. The subgroup analyses make the results uninterpretable.

Applications for Clinical Practice

There are several studies that have suggested that glucocorticoids may be associated with higher risk of development of Afib or Aflutter. The study by Christiansen adds some credence to this notion. However, the poorly chosen control patients limit the utility of the study. Further, given that glucocorticoids are already known to have toxic side effects, it is unlikely that these findings will dissuade clinicians from using these drugs, nor should they.

—Review by Ashish K. Jha, MD, MPH

References

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2. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: The Framingham Study. Stroke 1991;22:983–8.