

ISoP18-1169 The Impact of Sex on the Associations Between Ace Inhibitors and Cough and Angioedema: A Systematic Review and Meta-Analysis

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Background/Introduction: Cough and angioedema are well-known adverse effects of angiotensin-converting enzyme (ACE) inhibitors. Some observational studies in patients using ACE inhibitors have observed that women have a higher incidence of cough and angioedema than men.

Objective/Aim: To evaluate based on randomized controlled trials (RCTs), whether the risks of developing cough and angioedema with ACE inhibitors are modified by sex.

Methods: We searched PubMed and Cochrane databases for all years to August 2016. We included RCTs that contain information about the incidence of cough and angioedema in users of ACE inhibitors and controls (active/placebo) in men and women. We performed meta-analyses using the random effects model. Pooled risk ratios (RRs) for cough and angioedema associated with ACE inhibitors in women and men were estimated and tested for interaction.

Results: We included four RCTs in our analysis (three studies for cough and two studies for angioedema). We found that there was no difference in the RR to develop cough or angioedema for ACE inhibitors versus controls between women and men. For cough in women, the RR was 3.70; 95%CI (2.55–5.35) and for men, 2.61; 95%CI (1.30–5.27) (P value for interaction 0.39). For angioedema, these RRs were 5.56; 95%CI (2.45–12.62) and 6.35; 95%CI (1.81–22.36), respectively (P value for interaction 0.86).

Conclusion: Our meta-analyses show that the risks of developing cough and angioedema associated with ACE inhibitors are not modified by sex. However, these findings should be interpreted cautiously due to limited number of studies involved.

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ISoP18-1170 Abciximab-Induced Delayed Thrombocytopenia: Case Analysis in the French Pharmacovigilance Database

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Background/Introduction: Abciximab (ABX) is a chimeric monoclonal antibody Fab fragment, blocking the platelet receptor glycoprotein IIb/IIIa, used as antithrombotic therapy during percutaneous coronary intervention. The most common adverse effects are bleeding and thrombocytopenia. If most cases of thrombocytopenia occur within a few hours after ABX, delayed thrombocytopenia (3–6 days after ABX

discontinuation) is described in the literature but not in its monography; this may wrongly incriminate others etiologies.

Objective/Aim: Case description of delayed thrombocytopenia with ABX from the French Pharmacovigilance Database (FPVD).

Methods: A query of FPVD was performed with the following criterias: ABX single suspected drug, thrombocytopenia with onset delay over 3 days. Each case was analyzed separately according to the good pharmacovigilance practices.

Results: In the FPVD, among 292 cases of thrombocytopenia with ABX, we extracted 43 cases of delayed thrombocytopenia. Patients studied (32 men and 11 women) were aged 35–87 years (median 58 years). The mean time of onset for thrombocytopenia was 8.2 ± 2.1 days (median 8 days, range 3–15 days) and the mean time of improvement was 5.1 ± 2.7 days (median 5 days, range 1–14 days). Eight cases were not serious and 35 were considered serious (30 hospitalizations, 4 life threatening, 1 medically significant situation). Two patients had hemorrhagic signs (epistaxis and purpura). When the data were known ($n = 27$), 16 of these thrombocytopenia were grade IV (< 25 G/L), 5 grade III (25–49 G/L), 5 grade II (50–74 G/L) and 1 grade I (75–99 G/L). The median platelet nadir was 19 G/L (range 1–78 G/L) and a platelet transfusion was realized only for 5 patients, (median platelet nadir 5 G/L, range 1–11 G/L), regarding the thrombotic risk context. Among the 43 cases, thrombocytopenia recovered totally or partially in 38 patients. For 8 patients, the diagnosis of delayed thrombocytopenia with ABX was made after detection of anti-complex (ABX-platelet) antibodies.

Conclusion: Several cases of ABX-induced delayed thrombocytopenia are reported in the literature [1–6]. The median onset delay is 7 days (range 3–17 days) and the median time of improvement is 4 days (range 2–7 days) which is concordant with our results. In some cases, treatment was initiated with platelet transfusion, infusion of corticosteroids and/or intravenous immunoglobulin, which does not seem to be the majority of our study's cases. More than half of the cases manifested hemorrhagic signs, including 1 fatal outcome with cerebral hemorrhage, while in our study 5% of the cases presented bleeding complications (no death). As in the literature, thrombocytopenias reported in the FPVD were mainly severe (grade III/IV). Anti-complex (ABX-platelet) antibodies were identified in FPVD and in literature. The pharmacological mechanism underlying the occurrence of thrombocytopenia with ABX is not well established, but may be immune-mediated. These anti ABX-platelets antibodies may be specific for murine peptide sequences in ABX [5]. In conclusion, physicians administering ABX should be aware of this severe but reversible complication, which may occur at home, and should monitor a platelet control 1 and 2 weeks after hospital discharge, even if it was well tolerated previously [3]. This study underlines the importance of pharmacovigilance investigations with the realization of the medical history.

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