Bleeding related to oral anticoagulant drugs as cause of emergency department admission: analysis of data from the Tuscan MEREAFaPS Network

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The introduction of novel oral anticoagulants (NOAs: dabigatran, rivaroxaban, apixaban) into the clinical practice was expected to reduce the incidence and mortality for bleeding associated with traditional oral anticoagulants (Goette, 2013). The present investigation was performed to assess the trend of the contribution of admissions to Emergency Department (ED) for adverse drug reactions (ADRs) attributable to bleeding in patients receiving oral anticoagulants after the marketing authorization of NOAs. The analysis was performed using data collected in Tuscany over a period of 3 years, from January 2012 to December 2014, during the implementation of MEREAFaPS, an observational study aimed at investigating drug-related admissions to EDs in Italy. Dabigatran, rivaroxaban and apixaban were introduced in Italy in 2008, 2009 and 2012, respectively, with the indication 'prevention of venous thromboembolism'; they were then approved for the indication 'prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation' in 2013. Notably, in 2012 no record of bleeding events associated with NOAs was recorded in the MEREAFaPS database. Cases were identified as patients with a report of bleeding (MedDRA preferred term) associated with an oral anticoagulant therapy (both traditional and NOA). The rate of overall and serious bleeding over the study period was weighed by the number of ADR reports and by the total number of admissions recorded in the Tuscan MEREAFaPS Network during each year. The analysis included 1,017,034 ED admissions, of which 6,254 were related to ADRs (0.61%) and 443 (231 males and 212 females) were bleedings associated with the use of oral anticoagulants (0.044%). Among these, 186 cases were classified as serious ADRs. The most frequently recorded serious bleeding ADRs included: melena (16.7%); epistaxis (12.9%); rectal bleeding (11.8%); hematemesis (8.6%); cerebral hemorrhage (8.6%); hematuria (8.1%). The prevalences of drugs associated with bleeding-related admissions were: warfarin (92.1%); acenocoumarol (1.8%); dabigatran (4.1%); rivaroxaban (2.0%) and apixaban (0%). The annual incidences rates of overall bleeding associated with anticoagulants were 27, 17 and 34 cases per 100 admissions due to any ADR per 1,000,000 admissions/year in 2012, 2013 and 2014, respectively. When only serious bleedings were considered, the incidence rates were 9, 7 and 16 cases of bleeding per 100 admissions due to any ADR per 1,000,000 admissions/year in 2012, 2013 and 2014, respectively. In conclusion, although NOAs have been expected to reduce the frequency of serious bleeding (Goette, 2013), our preliminary analysis suggests that their introduction into the clinical practice has not reduced the proportion of ADRs attributable to anticoagulant-related bleeding among the overall number of ADRs that cause drug-related admission to ED. In this setting, the use of NOAs is likely too limited to account for a reduction of this trend. Further studies are warranted to investigate on this topic in the future.

Goette (2013).*Trends Cardiovasc Med*. 4:128-34.