

NSAIDs utilization in a large cohort of Italian elderly in secondary prevention for cerebro/cardiovascular disease

1)Roberto G. 2)Bartolini C. 3)Rea F. 4)Onder G. 5)Vitale C. 6)Trifirò G. 7)Kirchmayer U. 8)Chinellato A. 9)Lucenteforte E. 10)Corrao G. 11)Mugelli A. 12)Lapi F. 13)Gini R.

Regional agency for healthcare services of Tuscany Pharmacoepidemiology unit

Background

Due to the potential hypertensive and prothrombotic effect, the use of non-steroidal anti-inflammatory drugs (NSAIDs) is not recommended in elderly patients with history of cerebro/cardiovascular (CCV) disease. For these patients, current guidelines (Schmidt et al. 2016) strongly discourage the use of coxibs and diclofenac that, among NSAIDs, are associated to the highest thrombotic risk. Nevertheless, little is known on the real world use of NSAIDs in such a special population. Our aim was to describe the real world NSAID utilization in the Italian elderly population in secondary CCV prevention, also providing an estimate of the fraction of major CCV events observed in the study population that are attributable to the exposure to coxibs and diclofenac, respectively.

Methods

Administrative data collected between January 2008 and December 2012 from five Italian geographic areas, i.e. Caserta (South), Lazio, Toscana (Center), Lombardia and Treviso (North), were used. Patients hospitalized for CCV events between January 2008 and December 2011 (cohort entry) were selected. Patients aged <65 and with <2 years of look-back at cohort entry were excluded. During one year after cohort entry we observed: prevalence of use (patients with ≥ 1 dispensing); amount of NSAIDs dispensed to users, measured by Defined Daily Doses (DDD)/1000*user*day; distribution of the Received Daily Dose (RDD) among patients with ≥ 2 dispensings (RDD= between first and last dispensings:[dispensed DDD]/[days of follow-up]. Among new users (no NSAID dispensing during two years before cohort entry), the first dispensed NSAID was also observed. Using estimates from literature of the Relative Risk of major CCV events in patients respectively exposed to diclofenac and coxibs versus placebo (Bhala et al. 2013), we calculated the population attributable fraction (PAF) by applying the following formula (Rockhill et al 1998): $PAF=(\text{proportion of cases exposed}) \times (\text{attributable proportion of cases in the exposed})$. Major CCV cases observed during the first year of follow-up in the total study cohort were considered exposed if the duration of the last dispensing (dispensing date+dispensed DDD) of the drug of interest overlapped the 30-days time-window preceding the event date.

Results

Overall, 511.989 patients were selected. Prevalence of NSAID use ranged from 48% in Caserta to 21% in Treviso. Overall prevalence of use decreased from 34% in 2008 to 27% in 2011. Amount of dispensed NSAIDs ranged from 30 DDD/1000*users*day in Treviso to 67 in Lazio. Overall amount of dispensed NSAIDs increased from 45 to 75 DDD/1000*users*day between 2008 and 2011.

Nimesulide and diclofenac had the highest prevalence of use, 12 and 9% respectively. The highest amount of dispensed DDDs was observed for nimesulide and coxibs, i.e. 10 and 9 DDD/1000*user*day respectively. Around 10% of patients had an RDD \geq 1. In 2011, 35% of new users received diclofenac or coxib as the first NSAID prescription. On a total of 23.527 major CCV events observed during one year of follow-up, PAF was 0.3 (95%CI=0.1-0.5) for coxibs and 0.5 for diclofenac (95%CI=0.2-1.8), with point estimates corresponding to 78 and 124 major CCV cases respectively.

Conclusions

This study highlighted the existence of remarkable variations with respect to the use of NSAIDs across the different geographic areas considered. One in ten users with \geq 2 dispensings during follow-up received high doses of NSAID. Coxibs and diclofenac were among the most used NSAIDs molecules, even as first choice in new users. PAF estimates revealed that a considerable number of hospitalizations for major CCV events occurred in the study population could be potentially prevented if the exposure to diclofenac or coxibs was avoided. Based on this evidence, interventions to improve appropriateness of NSAIDs use are warranted.

Schmidt et al. (2016) Eur Heart J Cardiovasc Pharmacother 2:108-18.

Bhala et al (2013) Lancet 382:769-79.

Rockhill (1998) Am J Public Health 88:16-19