

Gastrointestinal complications and use of NSAIDs, low—dose aspirin and combination of them: results of spontaneous reporting from a Southern Italian area

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Background: NSAIDs are one of the most prescribed drugs worldwide (1) to treatment of inflammatory and pain, both acute and chronic, conditions. However, gastrointestinal (GI) complications, ranging from mild to severe dyspeptic symptoms, development of gastric or duodenal ulceration, haemorrhage or perforation represent one of the most limiting cause of use of these drugs. In fact, the use of NSAIDs has been associated with a 3- to 5-fold increase in the risk of gastrointestinal complications (2) and the mortality related to these events ranges from 5 to 12% (3). Also, the use of corticosteroids, anticoagulants, selective serotonin reuptake inhibitors (SSRI), antihypertensive drugs and antiplatelet drugs, especially low-dose acetylsalicylic acid (LDA), in combination with NSAIDs could lead to an increase of the risk of developing GI complications. In this scenario we aimed characterize the GI safety profile of NSAIDs and LDA as monotherapy, combination of them and multiple NSAIDs, analyzing the spontaneous adverse drug reactions (ADRs) reported in a southern Italian area (Campania region) from 2007 to 2011. **Methods:** We used all the reports of suspected ADRs occurring in people >18 years old, as registered in the Italian Pharmacovigilance Network (RNF) coming from Campania region during the period January 2007 until December 2011. Associations between specific drugs and GI ADRs were analyzed using the case/non case approach. Moreover, a descriptive analysis of reports of GI events and of non-GI events was performed and suspected ADR reporting odds ratio (ROR) with 95 % confidence intervals was calculated to evaluate the association with GI events (4). Also, we analyzed the associations with GI events for each individual NSAIDs compared to all other reports from the other drugs and, to investigate the effect of a specific NSAIDs, a sensitivity analysis by restricting to the drugs belonging to the same therapeutic class was performed. **Results:** In the study period RNF database collected 2,816 suspected ADR reports in the population aged > 18 years of Campania region. 374 (13.3%) reports concerned GI ADRs and the majority of these were reported in men (62.6%). GI ADRs occurred in older people and were more serious than the other ADRs. The highest number of GI events were reported for LDA use (39.6%), followed by the combination of LDA and NSAIDs (34.1%), the multiple NSAIDs use (30.4%) and for any NSAIDs used alone (27.0%). However, ranked by the strength of the adjusted RORs, the combination NSAIDs showed the highest association, followed by the combination LDA/NSAIDs while the use of NSAIDs as monotherapy and LDA alone showed the lowest association. Among individual NSAIDs, the highest association with GI events was observed for reports related to ketorolac exposure (no. of cases = 45; adj. ROR 28.5, 95% CI: 13.1-62.1), nimesulide (no. of cases = 96; adj. ROR 24.8, 15.1-40.7), diclofenac (no. of cases = 64; adj. ROR 22.4, 95% CI: 11.9-42.2), aspirin (no. of cases = 42; adj. ROR 14.7, 95% CI: 8.0-27.0) and ibuprofen (no. of cases = 13; adj. ROR 7.8, 95% CI: 3.2-18.6). There were mild or null differences among sex in the associations for the most of drugs, except that a trend towards an increase in strength of ROR was observed in women for aspirin and ketorolac. **Conclusion:** The present study has described the highest positive association between multiple NSAIDs use, followed by LDA/NSAIDs combination. Looking at individual NSAID, in line with previous studies, we found the highest association between ketorolac use and GI complication while the lowest one between ibuprofen GI events. In apparent contrast with what has been reported in other studies, our results showed that diclofenac and nimesulide were associated to high ROR of GI complications. Therefore, our data highlight the primary role of the national spontaneous reporting system to bring out potential signals (5-8) which, however, have to be further studied.