

# Exposure and clinical consequences of interactions with Non-Steroidal Anti Inflammatory Drugs in elderly poly-treated patients

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**Background.** Poly-pharmacy is very frequent in elderly patients and may cause drug–drug interactions with adverse clinical consequences. Interactions often involve NSAIDs (Non-Steroidal-Anti-Inflammatory-Drugs), which are at high risk of inappropriate prescription.

**Aim.** Our aim was to investigate the risk of kidney injury and bleeding following various NSAIDs interactions in elderly poly-treated patients.

**Methods.** A historic cohort study based on administrative databases of the Local Health Authority of Bologna (866,000 inhabitants) was performed. Patients with at least a NSAID prescription in the first semester of 2012 were selected among elderly ( $\geq 65$  years) poly-treated ( $>4$  different drugs) subjects. Co-prescriptions of NSAIDs with (A) ACE-Inhibitors (or sartans), diuretics, ACE-Inhibitors (or sartans) and diuretics (triple whammy), metformin; and (B) SSRIs, corticosteroids, warfarin were considered at risk of clinically relevant interactions. Hospitalisations for kidney injury and bleeding represented the study outcomes for (A) and (B) interactions, respectively. Incidence Rate Ratios (IRRs) of kidney injury or bleeding, following the exposure to each interaction, were estimated. For those interactions with a statistically significant IRR, the Cox regression model was performed to calculate the relevant Hazard Ratio (HR), with 95% Confidence Interval (95CI), after adjustment for gender, age, concomitant drugs and substances with a known risk for considered outcomes.

**Results.** Out of 34,353 elderly poly-treated patients, 7,420 subjects received NSAIDs (60.8% female, 76.9 average age). Among these, 85.7% were exposed to NSAIDs + ACE-Inhibitors (or sartans), 69.9% to NSAIDs + diuretics, 32.8% to the 'triple whammy' association, 21.6% to NSAIDs + metformin, 20.1% to NSAIDs + SSRIs, 17.1% to NSAIDs + corticosteroids and 8.2% to NSAIDs + warfarin. A significant IRR of kidney injury was found for NSAIDs + diuretics (IRR: 1.32; 95CI: 1.09-1.59) and for the 'triple whammy' association (IRR: 1.88; 95CI:1.58-2.23); significant IRR of bleeding was found for NSAIDs + warfarin (IRR: 3.66; 95CI: 1.67-8.02). After time adjustment by using Cox regression, a significant risk of kidney injury was found only for triple whammy (adjHR: 1.33; 95CI: 1.12-1.59). The risk of bleeding following exposure to NSAIDs + warfarin was statistically significant also after time adjustment (adjHR: 2.84; 95CI: 1.29-6.29).

**Conclusions.** In elderly poly-treated patients, concomitant prescriptions of NSAIDs + ACE-Inhibitors (or sartans) + diuretics or NSAIDs + warfarin have caused hospital admission for kidney injury and bleeding, respectively. Other NSAID interactions did not show impact on expected clinical outcomes. Therefore, physicians should carefully evaluate individual risk-benefit profile before prescribing NSAIDs to elderly poly-treated patients, when they receive other specific concomitant therapies.