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Benzodiazepine use in the elderly: factors modifying the associated risk of hip fracture

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Inappropriate medication use, defined as use of medications in which the risk outweighs the benefit, represents a serious problem in the context of drug therapy in older patients. An important drug group classified as potentially inappropriate depending on half-life and the dosage prescribed represent the benzodiazepines. Benzodiazepine use is associated with an increased risk of falls and fractures in the elderly. However, this risk might be modulated by various factors that are likely to modify benzodiazepine exposure or the effect of benzodiazepines. Up to now, little was known particularly about the impact of drug-drug interactions on this risk. The aim of this work was therefore to assess the impact of modifying factors on the risk of hip fracture associated with the use of benzodiazepines and related substances (BDZ) in older adults in order to identify patients at particularly high risk. In a nested case-control study in elderly patients we found that short-acting BDZ were associated with an increased risk of hip fracture. Up to now particularly long-acting substances were classified as inappropriate. The increased risk in patients using short-acting substances might reflect a change in prescribing behaviour over the last years. Hip fracture risk increased with increasing BDZ dose and was highest in doses > 1 defined daily dose (DDD). With regard to duration of BDZ therapy the highest risk was found in those patients who started BDZ therapy within 14 days preceding the index date. Concomitant use of several potentially interacting drugs was associated with an increased risk of hip fracture in patients using BDZ. This is mainly due to the increased risk associated with the use of the potentially interacting drugs themselves, rather than a synergistic effect. However, concomitant use of BDZ and interacting drugs should be avoided where possible.

As a consequence of the findings in this epidemiologic study, the aim of the second project was to assess BDZ prescriptions with regard to drug interactions and dosage with respect to age at discharge from a university hospital.

We found a high percentage of lorazepam and zolpidem users aged 65 years or older concomitantly receiving a potentially interacting drug. Only in case of zolpidem the prevalence of concomitant use of potentially interacting drugs was lower in the elderly as compared to a younger control-group which suggests selective prescribing considering the age of the patients. As co-administration of a BDZ and an interacting drug is associated with an increased risk of hip fracture in elderly patients, there is urgent need to develop a clinical decision support (CDS) module in order to optimise therapy in the elderly at discharge and thereby to increase patient safety.

In terms of dose we found no differences in prescribing with regard to age looking at lorazepam and zolpidem. This finding further stresses the need for the development of a CDS module in order to decrease high dose prescriptions in older patients.