Drugs and falls in older people: a systematic review and meta-analysis. I. Psychotropic drugs

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Authors' objectives
To evaluate critically the evidence linking psychotropic drugs with falls in older patients.

Searching
A search was conducted for English language studies in MEDLINE from 1966 to March 1996 using the following key terms: "accidents"; "accidental falls"; and "aged or age factors". Reference lists of retrieved papers were reviewed. Authors of included studies were contacted and experts were consulted. No unpublished studies were included.

Study selection
Study designs of evaluations included in the review
Cohort, case-control, and cross-section designs were included if the association between sedative/hypnotic, antidepressant, neuroleptic or psychotropic drug usage and falls were evaluated. Studies were subsequently excluded for the following reasons: incomplete fall ascertainment; insufficient reporting of data not remediable to contact with the authors; duplication of data; and the inclusion of a contaminated control group.

Specific interventions included in the review
Drugs in the following classes were studied: psychotropics; antidepressants (mainly tricyclics); neuroleptics (mostly phenothiazines and butyrophenones); and sedatives/hypnotics (mainly benzodiazepines both long and short acting, barbiturates, chloral hydrate and hydroxyzine). Ascertainment of medication was done at the time of the fall, at baseline, or at interview.

Participants included in the review
The following groups of people aged 60 years of age and older were studied: community living; long term care; hospital; rehabilitation; acute medical; psychiatric; stroke; and recent medical hospitalization. The mean age of participants across studies ranged from 67 years to 89 years.

Outcomes assessed in the review
Falls were assessed with the definition (in 70% of studies) being that of non-syncopal events not attributable to sustaining a violent blow, loss of consciousness, stroke, or epileptic seizure (Kellogg definition). The other studies did not define falls. Fallers were defined as having one or more falls and recurrent fallers as having two or more falls. Methods of ascertainment of falls included prospective, incident report, recall and baseline.

How were decisions on the relevance of primary studies made?
Article titles, indexing terms and abstracts (where available) were assessed according to the inclusion criteria by one author with the original authors being contacted for clarification.

Assessment of study quality
Studies that ascertained medications at the time of the fall and documented fall occurrence either prospectively or from incident reports were considered as having 'good' medication/falls ascertainment. All others were classified as 'poor'. The authors do not state how the papers were assessed for validity, or how many of the authors performed the validity assessment.

Data extraction
Two investigators independently extracted the following data using a structured data collection form: study design; inclusion and exclusion criteria; setting; subjects; study duration; years of data collection; sample size; response rate; mean age; method of medication verification and fall ascertainment; fall definition; and number of fallers and non-
fallers taking benzodiazepines, antidepressants, neuroleptics, hypnotics or sedatives, or any psychotropic drug.

**Methods of synthesis**

How were the studies combined?
The pooled odds ratio (OR) with 95% confidence interval from cohort studies was estimated using the Mantel-Haenszel fixed-effect method. Pooled OR and pooled relative risks (RR) were compared to assess the extent of overestimate in the OR.

How were differences between studies investigated?
Heterogeneity was assessed statistically. No details are given of the method used.

Pooling of the ORs was done for the following 8 drug classes: psychotropics; antidepressants; tricyclic antidepressants; neuroleptics; sedative/hypnotics; benzodiazepines; and long and short-acting benzodiazepines. For each drug class, sub-group analysis was conducted according to population type (community, long-term care, or other), study type (case-control, cohort, or cross-section), and temporal relationship between medication and fall ascertainment and the index fall. Pooled crude and adjusted OR were calculated for subsets of studies. OR were calculated for >= 2 versus 0 falls; and for >= 1 fall versus 0 falls. OR were compared for mean subject age < or >= 75 years and for communities with < or >= 35% fallers. The relationship between calendar years of data collection and strength of the association between drug use and falls was assessed.

**Results of the review**

Forty studies were included.

No randomised controlled trials were included. Only one published study has addressed the RR of falls for patients taking newer antidepressants. Areas of difference between studies included settings; sample size; characteristics of population; years of data collection; study design; medication ascertainment; and temporal relationship between medication ascertainment, fall ascertainment, and the index fall. 30% of studies did not provide a definition of a fall.

For community-dwelling older people (7 prospective studies) the annual incidence of falls averaged 36% (range 29% to 53%) with psychotropics being prescribed to 34% of subjects (range 28% to 52%).

For one or more falls:
- Any psychotropic use, drugs not specified (19 studies): OR = 1.73 (95%CI: 1.52, 1.97), heterogeneity P = 0.001;
- Neuroleptic use (22 studies) OR = 1.50 (95%CI: 1.25, 1.79), heterogeneity P = 0.01.
- Sedative/hypnotic (22 studies) OR = 1.54 (95%CI: 1.40, 1.70), heterogeneity P = 0.01. Any antidepressant (27 studies) OR = 1.66 (95%CI: 1.41, 1.95), heterogeneity P = 0.55.
- Tricyclic anti-depressants (12 studies) OR = 1.51 (95%CI: 1.14, 2.00), heterogeneity P = 0.62.
- Any benzodiazepine (13 studies) OR = 1.48 (95%CI: 1.23, 1.77), heterogeneity P = 0.60.
- Short-acting benzodiazepine (9 studies) OR = 1.44 (95%CI: 1.09, 1.90), heterogeneity P = 0.10.
- Long-acting benzodiazepine (9 studies) OR = 1.32 (95%CI: 0.98, 1.77), heterogeneity P = 0.84.

Psychiatrically hospitalized patients with neuroleptic use OR = 0.41 (95%CI: 0.21, 0.82); recently discharged patients, community dwelling subjects and long-term care subjects with neuroleptic use OR = 1.66 (95%CI: 1.38, 2.00), heterogeneity P = 0.21. Few studies adjusted for confounders. Pooled crude OR for antidepressants: 1.67 (95%CI: 1.15, 2.40) with adjusted OR = 1.85 (95%CI: 1.20, 2.85); crude OR for psychotropics = 1.95 (95%CI: 1.55, 2.46) with adjusted OR = 1.69 (95%CI: 1.25, 2.27).

Apart from psychiatrically hospitalized patients with neuroleptic use, no effect on OR was noted after stratification for...
the following factors: subject residence in the community or an institution; percentage of fallsers 35% or greater in community studies; mean age of subjects 75 years or over; ascertainment of medications and falls at the time of the fall; and study design. None of the weighted correlation coefficients between size of OR and either the mean age of subjects or the initial year of data collection were statistically significant. Trend for psychotropics towards reduction in size of OR over time $9 = -0.40, P = 0.09$).

Psychotropics $RR = 1.35$ vs $OR = 1.66$; Antidepressants $RR = 1.27$ vs $OR = 1.62$; Neuroleptics $RR = 1.31$ vs $OR = 1.90$; Sedatives/ hypnotics $RR = 1.12$ vs $OR = 1.25$; Benzodiazepines $RR = 1.2$ vs $OR 1.4$; Tricyclic antidepressants $RR = 1.16$ vs $OR = 1.40$. Increased falls occurred in patients taking more than one psychotropic drug.

Authors’ conclusions
There is a small but consistent association between the use of most classes of psychotropic drugs and falls. The evidence to date is based solely on observational data with minimal adjustment for confounders, dosage or duration of therapy.

CRD commentary
The aims and inclusion criteria are clearly stated. Details are given of methods used to select primary studies and extract data. Validity and heterogeneity were assessed and investigation of heterogeneity was undertaken. Results are presented in graphical format. The discussion includes consideration of the following factors: use of a search strategy that would not have retrieved any randomised controlled trials that evaluated falls as one of many adverse outcomes; the weak evidence of causal association provided by observational studies; likelihood of publication bias; overestimate of risk due to use of OR rather than RR because of OR being the only effect size calculable for all studies; inability to assess confounding by indication due to lack of evaluation of mental impairment in any study close to the time of the fall; data being collected over a twenty year period during which time new psychotropic agents were introduced, changes made in dosage recommendations and indications, plus a heightened awareness of the potential hazards associated with use of these medications in older people; inability to examine the effect of dosage due to lack of available data; lack of differentiation in the primary studies between injurious and non- injurious injuries; and use of variable definitions and ascertainment of fall injuries.

By limiting the literature search to published studies in the English language, some relevant studies may have been omitted. No details were given of the statistical tests used to assess heterogeneity or factors for which adjustments were made.

The authors conclusions are supported by the evidence presented.

Implications of the review for practice and research
Practice: The authors do not state any clinical implications.

Research: The authors consider that large randomised controlled trials of any medication in older persons should measure falls prospectively as an adverse outcome.

Bibliographic details

PubMedID
9920227

Other publications of related interest

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Accidental Falls /statistics & numerical data; Age Distribution; Age Factors; Aged /statistics & numerical data; Confounding Factors (Epidemiology); Humans; Incidence; Odds Ratio; Psychotropic Drugs /adverse effects /classification; Research Design; Risk Factors; Time Factors

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