

Medication associated delirium risk in patients with and without dementia: A systematic review

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Background / Aims:

Medication has been considered as both a predisposing and precipitating factor for delirium. The same medications that are thought to increase the risk of precipitating delirium, such as Antipsychotics and Hypnotics, are also used as treatment. This study aimed to comprehensively review all available literature on medication associated causes, management and treatment of delirium in adult patients (>18 years) with and without dementia.

Method:

Following Protocol registration (PROSPERO CRD42022366020) a search strategy

was developed with the help of a research librarian at both the Universities of Iceland and Innsbruck. A systematic search across 12 databases was conducted. The SRs were conducted according to the Cochrane best practice standards and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results:

A total of 3867 records were identified across 12 scientific databases of which 106 publications were included in this study (Fig.1). Good quality studies, as well as comprehensive medication related information was, scarce. A total of n=158 individual drugs were identified across 20 different drug classes (Fig.2.). Causative drug related

mechanisms include Neurotransmitter imbalances, Pharmacokinetic changes and Physiological processes. The most serious combinations are those involving Opioid analgesic & Dopamine agonists. Therapeutic alternatives and specific information on drug dosage and form was almost entirely missing. A risk stratification of Antipsychotics most commonly used in the treatment of delirium is shown in Table 1.

Conclusion:

This research has shown the paucity of specific medication related information and prescribing guidance available in the literature. Further studies will focus on extending the information to include several other patient groups (peri-operative, cancer etc.)

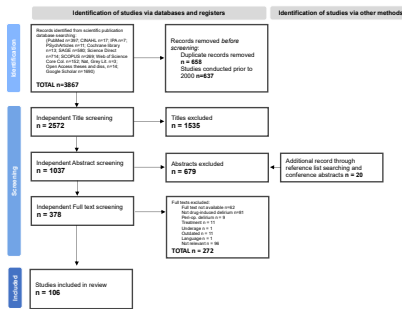


Figure 1: PRISMA flowchart showing the identification, screening and selection of delirium publications across 12 scientific publication databases

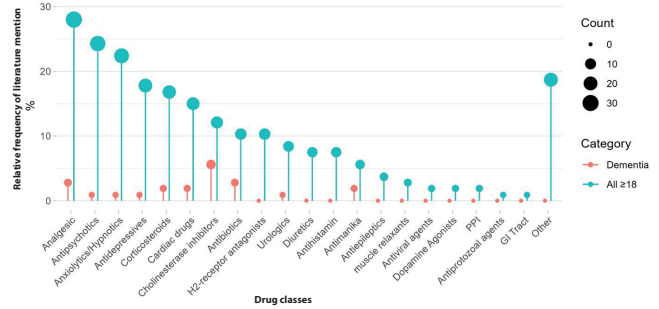


Figure 2.: Reporting frequency of 20 different drug classes associated with an increased risk of delirium with and without dementia across all included publications

Medication	Route of Administration	Typical Dosing Range	Considerations
Ziprasidone	PO, IM and IV	20 – 160mg/day	Moderate D2 blockade Conflicting association with QTc prolongation
Haloperidol	PO, IM and IV	2-30mg/day	Potent D2 blockade Minimal Sedation FDA warning for QTc prolongation for IV form Avoid averssedation Can increase extrapyramidal side effects May have a negative impact on overall survival
Olanzapine	PO, IM and IV	2.5- 30mg/day	Moderate D2 blockade Moderate sedation Metabolic side effects (weight gain, hyperglycaemia) Reduced blood pressure Effective for critically ill patients with delirium Rare association with serotonin syndrome in combination with serotonergic antidepressants It's anticholinergic effects may worsen delirium (rare) CYP1A2 metabolism is concentration and duration of action may be increased substantially in the setting of systemic inflammatory states (eg. sepsis).
Quetiapine	PO	12.5 – 1200mg/day	Minimal D2 blockade Highly sedating Has been reported to induce delirium Off-label for the management of delirium and as a sedation adjunct for ventilated patients in the ICU setting. Reaches a peak plasma concentration 1.5 h after administration and has a half-life of 6 h. Requires dose adjustment in patients with liver disease
Risperidone	PO	0.5 – 16mg/day	High D2 blockade Mildly Sedating oral formulation is available for the management of aggressive or agitated behavior in adults with Alzheimer's disease and other mental health conditions, including delirium.

Table 1.: Risk stratification of Antipsychotic medications used in management of delirium symptoms. Adapted from [84]: Sadlonova M, Beach SR, Funk MC, et al. Risk Stratification of QTc Prolongation in Critically Ill Patients Receiving Antipsychotics for the Management of Delirium Symptoms. Journal of Intensive Care Medicine. 2023;0(0). doi:10.1177/08850666231222470

