Citation: Edge R, Argáez C. Droperidol for Agitation in Acute Care [Internet]. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2021 Jan.

Background: In 2001, a black box warning was issued by the US FDA for the use of droperidol based on post-marketing surveillance data. The black box warning emphasized careful patient selection and increased monitoring to prevent corrected QT (QTc) interval elongation which can lead to sudden cardiac death. The extra burden placed on management of patients with droperidol has greatly decreased its use and availability in the US. This report provided an update from previously published data regarding the use of droperidol in acute care settings."

Methodology (*Study design)*:
Systematic review that included 1 RCT, 3 retrospective observational studies, one published guideline and two systematic reviews that included 23 and 58 RCTs respectively.
A literature search was conducted, with selection criteria including adult patients in acute care settings comparing the intervention of droperidol to standard care (other antipsychotic drugs). Outcomes included the effectiveness and safety of medications as well as recommendations regarding patient monitoring. Study designs included were health technology assessments, systematic reviews, randomized controlled studies, observational comparative studies and evidence-based guidelines.

RESULTS:

- Droperidol is as effective as haloperidol and olanzapine for the sedation of adult patients with uncontrolled aggression, anxiety, or violent behavior in acute care settings. (Class B)
- There are no statistically significant differences in adverse event frequency or severity inadult patients treated with droperidol compared with haloperidol or olanzapine. (Class A)
- Guidelines published in 2015 support the safety and efficacy of droperidol treatment for agitation based on high-quality relevant evidence.
- There is insufficient evidence to support electrocardiogram or telemetry monitoring of patients who were administered less than 2.5 mg of droperidol. (Class A)

Strengths:
All primary studies were based in US which supports generalizability. Authors used validated PRISMA quality checklist for systematic reviews. Each RCT has its own set of strengths and weaknesses so it would be impractical to go over each study though the authors provided levels of evidence. Several of these studies were appraised as high-quality (AMSTAR 2 for SRs, Downs and Black checklist for randomized/non-randomized, and AGREE II for guidelines). As a whole, the evidence was *consistent* that no other antipsychotic drug was superior to droperidol, however, some studies did support superiority of droperidol over other medications

Weaknesses:
This systematic review included a large quantity of overlap since the same publications are cited in both systematic reviews. In addition, the authors state that full details of all patient characteristics (beyond baseline QT intervals) that might pose a risk for potential adverse events were not reported which limiting external generalizability. No studies presented baseline QTc or examined QTc as a potential risk factor before droperidol administration.

My Clinical Bottom Line: No other tested antipsychotic drug (haloperidol, olanzapine, lorazepam, or zipradisone) appears to demonstrate superiority to droperidol, in fact, some evidence shows it may even be superior. There are no statistically significant differences in adverse events frequency of severity in adult patients with droperidol versus haloperidol or olanzapine.