Drug therapy for delirium in terminally ill adults: A Cochrane systematic review

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Care and support through terminal illness

Background

Delirium is common in palliative care, occurring in up to 88% of patients in the weeks or hours preceding death. Our Cochrane review on drug therapy for delirium was published in 2012[1]. It identified one trial. New trials have been conducted and an updated review is now recognised as a Cochrane priority.

Aims

To evaluate the evidence from randomised controlled trials (RCTs) examining the effectiveness and safety of drug therapies to treat delirium in adults with a terminal illness.

Methods

We searched for RCTs comparing any drug treatment with any other treatment for delirium in terminally ill adults. Primary outcomes included delirium symptoms at 24 hours and between 24 and 48 hours; and adverse events (AEs). Risk of bias assessment was conducted; we assessed overall quality of evidence using GRADE.

Results

Search results: We retrieved 9,431 citations. Four studies were included in the final review.

Description of included studies: The network map, illustrates the different combinations of drugs compared across studies. Midalozam was not compared in any study *(Figure 1).*

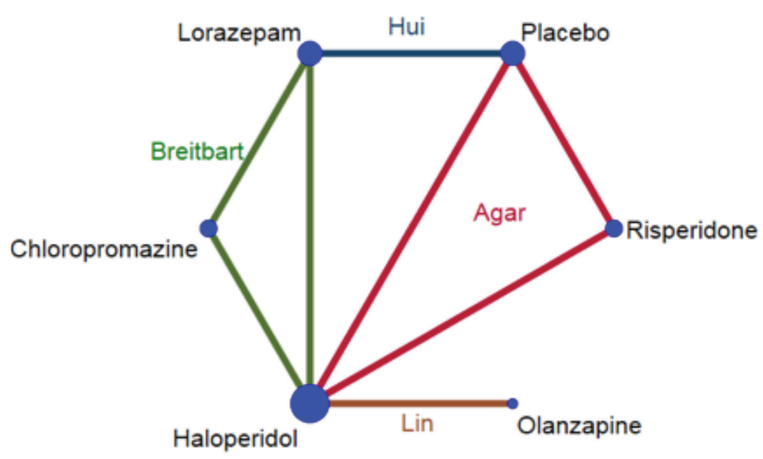

Figure 1: Network map of included studies and comparisons.

Risk of bias: All trials were vulnerable to bias, commonly due to small sample size or incomplete outcome data *(Figure 2)*.

Figure 2: Risk of bias assessment presented as percentages.

Effect of drug therapies on delirium symptoms:

Figures 3 and 4 illustrate the mean difference between trial arms at two time-points. In Agar 2017 participants in the Risperidone arm experienced more delirium symptoms than those receiving Placebo at 24 hours (MD 0.76, 95% CI 0.3 to 1.22) and 48 hours (MD 0.85, 95% CI 0.32 to 1.38). Participants in the Haloperidol arm experienced more delirium symptoms than those receiving Placebo at 48 hours (MD 0.49, 95% CI 0.10 to 0.88).

In Breitbart 1996, Lorazepam resulted in more delirium symptoms at 48 hours compared with Haloperidol (MD -4.88, 95% CI -9.70 to -0.06) and Chloropromazine (MD -5.25, 95% CI = -10.12 to -0.38).

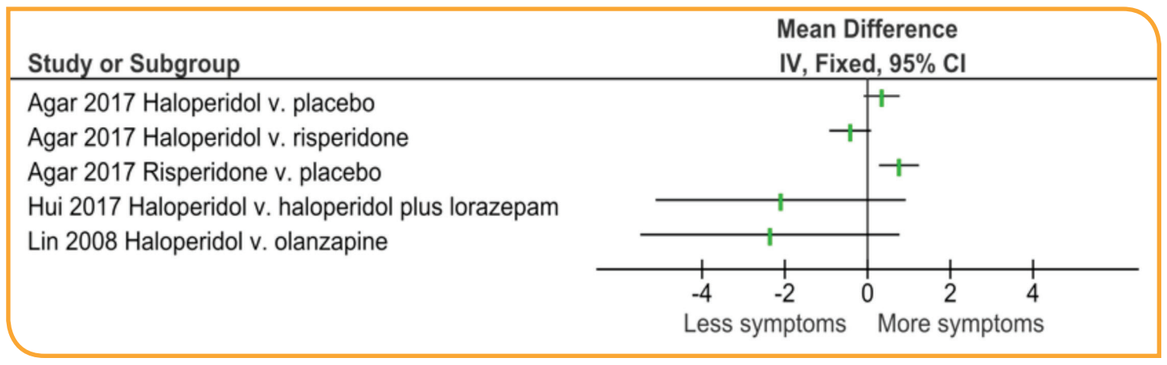

Figure 3: Within 24 hours of initial treatment.

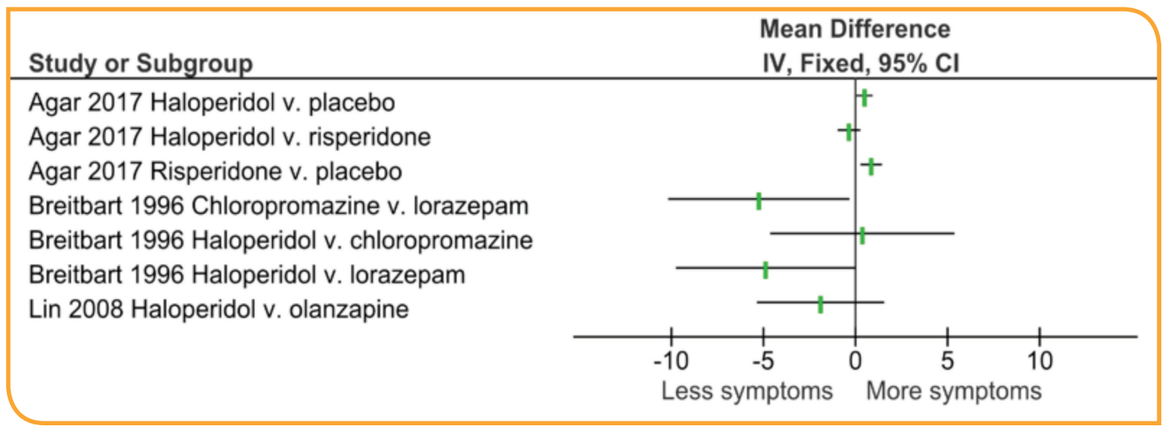

Figure 4: Between 24 and 48 hours of initial treatment.

Effect of drug therapies on adverse events (AEs):

Mixed results reported. In Breitbart 1996, patients receiving Lorazepam experienced over-sedation, disinhibition, ataxia, and increased confusion; no clinically significant AEs were observed in the Chlorpromazine or Haloperidol arms. In Hui 2017, Lorazepam was used as an adjunct to Haloperidol, no increase in AEs was identified compared to Placebo plus Haloperidol.

In Agar 2017, in comparison to Placebo, patients receiving Haloperidol (MD 0.79, 95% CI 0.17 to 1.41) and Risperidone (MD 0.73, 95% CI 0.09 to 1.37) experienced more non-severe extrapyramidal effects.

Conclusion

This review identified four trials. It found low quality evidence examining the impact of antipsychotics and benzodiazepines on delirium symptoms and AEs in terminally ill adults. Results for each comparison were based on single studies. Undertaking trials in this patient group is methodologically complex. Only one study compared drug therapy with placebo. This limited our ability to answer our review questions.

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REFERENCES: [1] Candy, B., Jackson, K., Jones, L., Leurent, B., Tookman, A., & King, M. (2012). Drug therapy for delirium in terminally ill adult patients. Cochrane Database Syst Rev., 11, CD004770.