Review: Sedative–hypnotic agents reduce mortality and duration of delirium in the alcohol withdrawal syndrome

Mayo-Smith MF, Beecher LH, Fischer TL, et al. **Management of alcohol withdrawal delirium: an evidence-based practice guideline.** Arch Intern Med. 2004;164:1405-12.

QUESTION

What is the optimal drug treatment for alcohol withdrawal delirium?

METHODS

Data sources: MEDLINE (1966 to September 2001) and bibliographies of relevant studies, reviews, and textbooks.

Study selection and assessment: Prospective controlled trials on the management of patients meeting the *Diagnostic and Statistical Manual of Mental Disorders, 4th edition*, criteria for alcohol withdrawal delirium.

Outcomes: Mortality, duration of delirium, time required for control of agitation, proportion with adequate control of delirium, and treatment complications.

MAIN RESULTS

9 controlled trials were included. Publication dates ranged from 1959 to 1978. 5 trials (n = 386) compared sedative–hypnotic agents with neuroleptic drugs and evaluated mortality. The sedative–hypnotic drugs were paraldehyde, diazepam, chlordiazepoxide, and pentobarbital (1 trial combined chloral hydrate with paraldehyde). The neuroleptic drugs were chlorpromazine, promazine, and perphenazine (1 trial combined chloral hydrate with promazine). Of the 2 trials in which deaths occurred, neuroleptic drugs had a relative risk for death of 6.6 (95% CI 1.2 to 34.7). 5 trials (n = 289) compared different sedative–hypnotic agents (diazepam, chlordiazepoxide, pentobarbital, paraldehyde, and barbital). Only 2 deaths were reported in a paraldehyde group showing no statistical difference for mortality among the agents. Of 4 trials comparing sedative–hypnotic agents with neuroleptic drugs for duration of delirium, 3 trials showed a benefit with sedative–hypnotic agents with decreases in duration ranging from 22 to 48 hours. No differences in duration of delirium were seen among trials comparing different sedative–hypnotic agents. Of 2 trials that evaluated the time to control agitation, 1 showed a greater decrease in time with diazepam than with paraldehyde (1.1 vs 3.0 h, P = 0.02) and 1 trial comparing diazepam with barbital showed no difference (11 vs 8 h, $P > 0.05$). Of 2 trials that evaluated adequate control of delirium, 1 showed better control with diazepam than paraldehyde and the other showed no difference between perphenazine and pentobarbital, with high rates of response for both drugs. Of 2 trials that evaluated treatment complications, 2 patients developed respiratory arrest with paraldehyde, and 1 patient treated with pentobarbital developed lethargy progressing to coma.

CONCLUSION

In patients with alcohol withdrawal delirium, sedative–hypnotic drugs reduce mortality and duration of delirium more than neuroleptic drugs, with no differences among different sedative–hypnotic drugs.

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COMMENTARY

Alcohol withdrawal delirium is a serious illness with several therapeutic options. Clinical practice suggests that the importance of alcohol withdrawal delirium may be underrecognized, thus delaying effective treatment, which should be rapid and closely monitored. While oral medication is adequate for patients with minor symptoms of alcohol withdrawal, an intravenous route must be seriously considered for delirium, because these patients are often unable to swallow, and indeed are in extremis.

Although benzodiazepines are first-line treatment, questions remain about specific drug selection, dosage, and administration route. For instance, do high initial doses shorten delirium more than lower doses? The review by Mayo-Smith and colleagues shows that doses should be repeated and reassessed every few minutes. A set endpoint is necessary, as defined by "light somnolence." Clinicians should consider a well-monitored care setting for these patients and entertain a broad differential diagnosis, as well as examine for concurrent medical illness (1).

Further research questions on alcohol withdrawal delirium include the use of such ancillary medications as magnesium, thiamine, and multivitamin supplements. As this review shows, the evidence for magnesium administration has not been adequately assessed. Similarly, the evidence for thiamine replacement is weak. Considering that thiamine is cheap, it is not unreasonable to provide it, although the required doses and frequencies to prevent the Wernicke–Korsakoff syndrome are unknown (2). Finally, the use of intravenous multivitamin supplements in the face of probable nutritional deficiency in alcoholic persons remains controversial. Little evidence exists to support the use of this medication via the intravenous route, which is considerably more expensive than the equivalent tablet.

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References

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