Reducing Benzodiazepine Use for Alcohol Withdrawal: Symptom-Triggered Compared with Fixed-Schedule Therapy

Daeppen JB, Gache P, Landry U, et al. Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: a randomized treatment trial. Arch Intern Med 2002;162:1117–21.

Study Overview

Objective. To compare the dosing requirements and complications associated with an individualized (PRN) benzodiazepine treatment protocol compared with a fixed-schedule dosing protocol for alcoholic withdrawal.

Design. Prospective, randomized double-blinded controlled trial.

Setting and participants. Consecutive patients admitted to 1 of 2 inpatient alcohol treatment programs in Lausanne and Geneva university hospitals in Switzerland over a 14-month period. Exclusion criteria included last alcoholic beverage intake greater than 72 hours prior to admission; daily use of medications to treat alcohol withdrawal for the 30 days prior to admission; major medical, psychiatric, or cognitive comorbidity; and opiate or stimulant dependence.

Intervention. Eligible patients were randomly assigned to either symptom-triggered therapy or fixed-schedule therapy. Physicians, nurses, research assistants, and patients were blinded to the treatment allocation. Patients in the fixed-schedule dosing received oxazepam every 6 hours: 4 doses of 30 mg each and then 8 doses of 15 mg each. 30 minutes after each capsule, the patients were assessed using the Clinical Institute Withdrawal for Alcohol scale (CIWA-Ar) and, based on these scores, were given additional medications. The symptom-triggered group received a placebo every 6 hours. 30 minutes after each placebo tablet they were assessed using the CIWA-Ar and given additional medication as necessary. All patients were observed for signs of withdrawal for 48 hours after the completion of the study.

Main outcome measures. The main outcome measured was total dosage of oxazepam required over the course of the hospitalization. Other data collected included CIWA-Ar scores (a validated index of alcohol withdrawal severity) and retrospective self-reported ratings of well being and health-related quality of life.

Main results. 251 consecutive patients were asked to participate in the trial, and 126 ultimately were randomized. 9 patients were excluded after randomization due to initially unrecognized exclusion criteria. 117 eligible patients were left for comparison; 61 patients were randomized to the fixed-schedule group, and 56 were assigned to the symptom-triggered group. The groups were similar in most characteristics except that the fixed-schedule group had a longer time since their last use of alcohol compared with the symptom-triggered group (19 hours versus 14 hours; $P = 0.04$). All patients randomized to the fixed-schedule group were treated with oxazepam, while only 39% (22/56) of the symptom-triggered patients received oxazepam ($P < 0.001$). The total dosage of oxazepam required for the fixed-schedule treatment group was 231.4 mg compared with 37.5 mg for the symptom-triggered group ($P < 0.001$). The treatment duration was longer for the fixed-schedule group compared with the symptom-triggered group (63 hours versus 20 hours; $P < 0.001$). The severity of withdrawal symptoms, as assessed by the CIWA-Ar, was generally higher for the symptom-triggered group than the fixed-schedule group. There were no significant differences between the groups on the ratings for well being, vitality, or energy. There was one episode of a withdrawal seizure in the symptom-triggered group.

Conclusion. Treatment of alcoholic withdrawal with an individualized, symptom-triggered benzodiazepine treatment regimen is safe and is associated with less medication usage and shorter treatment duration compared with fixed-schedule dosing.

Commentary

While the use of benzodiazepines for alcohol withdrawal have been shown to be effective and safe when compared with other non-benzodiazepine agents [1], the ideal dosing strategy has not been identified. Some trials have suggested that individualized dosing schedules would use less medication and have no more side effects than a predefined fixed protocol [2]. However, the use of an individualized or PRN

strategy requires trained health care professionals to assess the appropriateness of pharmacologic therapy. To justify this added workload, it is important to determine the clinical benefits of an individualized treatment protocol.

Daeppen et al have performed a well designed, double-blinded, randomized controlled trial that lends support to the suggestion that symptom-based protocols might be better. There were striking differences between the 2 groups with respect to total dose required and duration of dose. Patients in the symptom-triggered group had higher withdrawal severity scores. While higher scores may indicate more discomfort, this was not supported by patients' self-reported well-being schedule.

One limitation to this study is that the nurses responsible for making the assessments were trained in recognizing alcohol withdrawal symptoms and were specifically employed by a detoxification unit. Thus, these findings might not be generalizable to other acute care facilities. Second, because of the stringent exclusion criteria, only a small proportion of patients (6%) admitted to the detoxification units were ultimately randomized. By eliminating patients with comorbid medical or psychiatric illnesses and polysubstance abuse, the authors selected a very homogenous population that might not be representative of most patients presenting with alcohol withdrawal symptoms.

Applications for Clinical Practice

Using a symptom-triggered benzodiazepine dosing regimen for alcohol withdrawal is safe, effective, and results in less medication usage and a shorter duration of usage in a select group of patients.

–Review by Harvey J. Murff, MD, MPH

References

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2. Saitz R, Mayo-Smith MF, Roberts MS, et al. Individualized treatment for alcohol withdrawal. A randomized double-blind controlled trial. JAMA 1994;272:519–23.

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