Pharmacotherapy of Alcohol Withdrawal Delirium in Patients Admitted to a General Hospital

Mayo-Smith et al[1] have provided an important guideline for the management of alcohol withdrawal delirium in hospitalized patients with alcohol dependence. Based on thorough examination of the literature, they recommend benzodiazepines as the first line of treatment because "these drugs reduce mortality, reduce the duration of symptoms, and are associated with fewer complications compared with neuroleptic agents."[1]

As a working group appointed by the Dutch Association of Psychiatry, we developed an evidence-based practice guideline for delirium including alcohol withdrawal delirium.[2] Contrary to Mayo-Smith et al,[1] we concluded that, in medically ill patients admitted to a general hospital, haloperidol is the first line of treatment for suspected alcohol withdrawal delirium. After all, it is impossible to decide whether delirium was actually caused by alcohol withdrawal and/or by medical illness. Moreover, as Mayo-Smith et al[1] rightly mention, only 5% of patients withdrawing from alcohol develop delirium, raising the risk of overstating the causal role of alcohol. Treatment with benzodiazepines is advised as an adjunctive therapy in case of concomitant alcohol withdrawal syndrome and severe agitation.[2]

Also, the conclusion of Mayo-Smith et al[1] that neuroleptics are not recommended in alcohol withdrawal delirium is based on research done more than 25 years ago, between 1959 and 1978. At that time, diagnostic criteria were less clear, and old-fashioned neuroleptic agents such as the phenothiazines chlorpromazine, promazine, and perphenazine were used. Because of their serious anticholinergic and anti–α_1-adrenergic adverse effects, phenothiazines are no longer recommended for any delirium, let alone alcohol withdrawal delirium.

Surprisingly, Mayo-Smith et al[1] advise the butyrophenon haloperidol as adjunctive neuroleptic therapy for alcohol withdrawal delirium in the same dosing regimen proposed for delirium due to medical illness although research evidence for the effectiveness in alcohol withdrawal delirium is lacking. But more importantly, the authors do not comment on the difficulties in diagnosing delirium due to alcohol withdrawal as opposed to medical illness. This may create the danger that the medical staff will not look further for treatable causes of delirium once a diagnosis of alcohol withdrawal delirium has been made. We must, however, be aware that alcohol withdrawal is most likely not the (only) cause of delirium in patients who have been admitted to a general hospital. Otherwise, the medical care of delirious patients who are suspected of alcohol dependence is in danger.

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1. Mayo-Smith MF, Beecher LH, Fischer TL, et al. Management of alcohol withdrawal delirium: an evidence-based practice guideline. *Arch Intern Med*. 2004; 164:1405-1412.
2. Dutch Association for Psychiatry. *Practice Guideline for Delirium* [in Dutch]. Assen, the Netherlands: Boom. In press.

Alendronate and Risedronate: Reports of Severe Bone, Joint, and Muscle Pain

The oral bisphosphonate alendronate sodium (Fosamax; Merck & Co Inc, Whitehouse Station, NJ) was first approved for osteoporosis by the Food and Drug Administration (FDA) in September 1995. From its initial marketing date and up to November 2002, the FDA received Serious Adverse Event (SAE) (defined as death, life-threatening, hospitalization [initial or prolonged], disability, congenital anomaly, required intervention to prevent permanent impairment or damage, or important medical event) reports of severe bone, joint, and/or muscle pain, that developed in 112 women, 4 men, 1 adult of unknown sex, and 1 child after starting therapy with the drug. The age range was 7 to 84 years (n=109; median=67 years). The child was a 7-year-old boy who mistakenly received alendronate instead of methylphenidate and developed extreme bone pain in his hips, knees, and ankles after 1 dose.

Bones, joints, and muscles throughout the body were affected. In some individuals, pain began at 1 site and then migrated and became diffuse. It was often described as "severe," "extreme," "disabling," or "incapacitating." Many patients were unable to walk, climb stairs, or perform usual activities. Some became bedridden, and others required walkers, crutches, or wheelchairs. Many underwent numerous diagnostic tests with mostly normal findings.

For the 96 patients with information, the alendronate doses were 5 mg/d (n=4; 4%); 10 mg/d (n=71; 74%); 20 to 35 mg/d (n=4; 4%); and 70 mg/wk (n=17; 18%). The median time to onset of pain after starting alendronate therapy was 14 days (n=107; range, same day to 52 months [mean=91 days]). Pain was treated with a variety of analgesics including opioids and ketorolac. Of 83 patients with information, 55 (66%) experienced relief after alendronate therapy was discontinued. Nine (11%) of the 83