Pentoxifylline improved short-term survival in severe acute alcoholic hepatitis

Akriviadis E, Botla R, Briggs W, et al. **Pentoxifylline improves short-term survival in severe acute alcoholic hepatitis: a double-blind, placebo-controlled trial.** Gastroenterology. 2000 Dec;119:1637-48.

QUESTION

In patients with severe acute alcoholic hepatitis, what are the effectiveness and safety of pentoxifylline (PTX)?

DESIGN

Randomized {allocation concealed*}†, blinded (patients and outcome assessors),* controlled trial with 4-week follow-up.

SETTING

The Liver Unit of the University of Southern California at Rancho Los Amigos Medical Center, Downey, California, United States.

PATIENTS

102 patients (mean age 42 y, 74% men) with severe alcoholic hepatitis (Maddrey discriminant factor ≥ 32), jaundice, and ≥ 1 of the following findings: palpable tender hepatomegaly, fever, leukocytosis, hepatic encephalopathy, or hepatic systolic bruit. Exclusion criteria were concomitant bacterial infection, active gastrointestinal hemorrhage, severe cardiovascular or pulmonary disease, decreasing serum bilirubin values or rapid improvement of other liver test results, or advanced alcoholic cirrhosis. 1 patient dropped out.

INTERVENTION

49 patients were allocated to PTX, 400 mg orally 3 times daily, and 52 were allocated to identical capsules containing vitamin B_{12} (control treatment).

MAIN OUTCOME MEASURES

Primary outcome measures were short-term survival, progression to the hepatorenal syndrome, and adverse effects.

MAIN RESULTS

Fewer deaths occurred among patients who received PTX than among those who received the control treatment (P = 0.037) (Table). The hepatorenal syndrome also occurred less frequently in patients who received PTX (P = 0.002) (Table). Patients in the PTX group tended to have more side effects, especially gastrointestinal-related effects, but this difference was not statistically significant (P = 0.12).

CONCLUSION

In patients with severe acute alcoholic hepatitis, pentoxifylline decreased progression to the hepatorenal syndrome and improved short-term survival.

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*See Glossary.

†Information provided by author.

Pentoxifylline (PTX) vs control treatment at 4 weeks in patients with severe acute alcoholic hepatitis‡

Outcomes	PTX	Control	RRR (95% CI)	NNT (CI)
Death	25%	46%	47% (8 to 70)	5 (3 to 35)
Hepatorenal syndrome	8%	35%	76% (40 to 91)	4 (3 to 10)

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

In 1991, McHutchison and colleagues (1) claimed that 10 days of PTX therapy in patients with alcoholic hepatitis resulted in less renal impairment and, perhaps, fewer deaths. Akriviadis and colleagues, from the same center, confirm this observation.

Some data have suggested that glucocorticoids improve short-term survival, particularly in patients with encephalopathy and without gastrointestinal bleeding (2). This treatment has been recommended for patients with a discriminant function > 32 (3). Akriviadis and colleagues did not compare PTX with steroid therapy. Previously, they failed to show that glucocorticoids had any efficacy in 3 trials. Another meta-analysis showed that confounding factors were responsible for the apparent benefit of treatment (4). A recent multicenter trial from Spain found that patients randomized to steroids had increased post-discharge mortality (5). Hence, although many physicians are routinely using glucocorticoids to treat severely ill patients with alcoholic hepatitis, the evidence is not solid.

Because PTX is available for treatment of intermittent claudication, it will be tempting to use it. The only available data, however, come from a single center that has been unable, on several occasions, to show efficacy of another treatment that has been found to work elsewhere. We may not be able to extrapolate their data. External validation from at least 1 or 2 other centers is needed before we can recommend PTX as standard therapy for severe acute alcoholic hepatitis.

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References

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