

Letter to the Editor: No Baclofen for Alcohol Use Disorders Even More When Liver Disease Is Serious!

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Accepted Article

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No baclofen for alcohol use disorders even more when liver disease is serious!

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AB and FN serve as unpaid experts for several taskforces for the French national agency of medicine and health product safety (Agence Nationale de Sécurité du Médicament et des Produits de Santé), none of which were related to the topic. No other competing interests.

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Caputo and colleagues wrongly promoted baclofen for patients with end-stage alcoholic liver disease.(1)
First, there is no reason to use it. A recent Cochrane review found a negative benefit harm:ratio of baclofen. This precludes any off-label use. Preliminary hypotheses from two short series from the same team have been ruled out by a recent robust trial in 320 patients which failed to demonstrate an effect of baclofen in the maintenance of abstinence.(2) Concerning use of the baclofen for only decreasing the amount drunk (so-called “harm reduction”), there is no evidence on relevant clinical outcomes yet.(3) The largest trial, NCT01604330, in this indication is problematic: data collection ended in 2015 but no publication yet, only a meeting presentation with no benefit but a two fold increase in mortality.(4) We attempted to obtain clinical study reports, statistical analysis plan, and individual patient data as part of the Restoring Invisible and Abandoned Trials initiative (2) The sponsor, the drug company, the French drug agency declined our requests.

Second, there are major reasons to avoid it. A French pharmaco-epidemiological study in 165,334 patients treated for alcohol use disorders between 2009 and 2015 showed a dose related increase mortality with off-label baclofen (HR = 1.4 for 30-75 mg/day, 1.5 for 75-180 mg/day; 2.3 over 180mg/day) vs acamprosate and naltrexone.(5) Australia's largest Poisons Information Centre confirmed this increase in serious adverse effects with off-label use for alcohol use disorders.
E in EBM means evidence not expectations. Moreover, could it be wise to only aim for harm reduction in a patient with end-stage alcoholic liver disease? Abstinence is the only rational goal. Who would advise a patient recovering from stroke to try to decrease it smoking addiction by one or two cigarettes a day? Last, off-label drug use is too frequently not supported by sound scientific evidence, hinders the development therapeutic innovation, is costly to the healthcare system, and exposes patients to the unnecessary risk of serious adverse events for an all too often uncertain benefit.

1 Caputo F, Domenicali M, Bernardi M. Diagnosis and treatment of alcohol use disorder in patients with end-stage alcoholic liver disease. Hepatology 2018. Online Nov 24. doi: 10.1002/hep.30358.
2 Reynaud M, Aubin HJ, Trinquet F et al. A randomized, Placebo-controlled study of high-dose baclofen in Alcohol-Dependent Patients-The ALPADIR Study. Alcohol Alcohol 2017;52:439-446.
3 Palpacuer C, Duprez R, Huneau A et al. Pharmacologically controlled drinking in the treatment of alcohol dependence or alcohol use disorders: a systematic review with direct and network meta-analyses on nalmefene, naltrexone, acamprosate, baclofen and topiramate. Addiction 2018;113:220-237.
4 Naudet F, Braillon A. Lancet Psychiatry. Baclofen and alcohol in France. 2018;5:961-962.
5 Chaignot C, Zureik M, Rey G, Dray-Spira R, Coste J, Weill A. Risk of hospitalisation and death related to baclofen for alcohol use disorders: Comparison with nalmefene, acamprosate, and naltrexone in a cohort study of 165 334 patients between 2009 and 2015 in France. Pharmacoepidemiol Drug Saf 2018;27:1239-1248.

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