A panacea for alcohol cravings

DR MICHAEL TAM
BSC(MED), MBBS, MMH(GP), FRACGP
Senior Lecturer, Discipline of GP, USyd;
Staff Specialist, SWSLHD & Ingham Inst.

Are there reliable studies that back the use of baclofen in my 35-year-old patient?

CLINICAL SCENARIO

Jorge, an unemployed 35-year-old factory worker with alcohol dependence, saw me recently at the local health district GP unit.

As we talked about his drinking, I recalled a conference presentation on the use of baclofen as a treatment for alcohol use disorders. What is the evidence for this therapy?

CLINICAL QUESTION

What is the effect of baclofen as a treatment in people with alcohol use disorders on the rate of abstinence?

THE RESEARCH EVIDENCE

Step 1: The Cochrane Library
A protocol for a systematic review on this topic exists in the Cochrane Library, but it has yet to be completed and published.

Step 2: TripDatabase
I conducted a search using the TripDatabase PICO search tool (Participant: "alcohol use disorder", Intervention: "baclofen", Comparator: "placebo", Outcomes: "abstinence").

This identified another yet-to-be-published systematic review under way, published in the PROSPERO register from the University of York Centre of Reviews and Dissemination.

I limited the search results to primary research only, which identified eight randomised trials. None of the published trials can be considered definitive.

The paper by Garbutt et al (2010) published in the journal, Alcoholism: Clinical and Experimental Research,[1] was designated as being estimated at low risk of bias by TripDatabase, and in a population without significant comorbidity (relevant to Jorge).

I'll look at this paper in detail, and will briefly cover some of the other studies in the discussion.

CRITICAL APPRAISAL

I will use the randomised controlled trial appraisal sheet from the Centre for Evidence Based Medicine .[2]

PICO

Participants: who was studied?
Eighty adults from the US, aged between 18 and 60, recruited through newspaper and radio advertisements, meeting DSM-IV criteria for current alcohol dependence, with at least two heavy-drinking days per week on average during the four weeks before screening.

Important exclusions: clinically significant medical disease (eg cirrhosis) and psychiatric illness (eg psychosis), positive urine toxicology and pregnant women.

Out of 121 participants screened, 80 were randomised, and 61 completed the study.

The mean age of the participants was about 50, with about 25 years of alcohol use.

The mean number of (US) standard drinks per day was seven (about 10 Australian standard drinks).

Intervention: what was the exposure?
Baclofen 10 mg, three-times-a-day,

What were the results?

Primary outcomes (baclofen vs placebo):

- No meaningful difference in the average percentage of heavy drinking days:
  - 25.9% vs 25.5%, p = 0.5
- No meaningful difference in the average percentage of abstinent days:
  - 49.9% vs 50.6%, p = 0.50

Other outcomes:

- No statistically significant differences were found between groups for craving or depression.
- The baclofen group did have lower levels of anxiety severity.

DISCUSSION AND CONCLUSION

Almost a quarter of participants dropped out of this study, which is usually considered significant.

This might not affect the overall conclusion, however, as the direction of bias would be towards exaggerating the beneficial effect of baclofen.

In this study, baclofen was not statistically or clinically superior to placebo on either the proportion of heavy drinking days, or abstinent days, over three months.

Earlier case reports and open-label studies have suggested that baclofen might be an effective treatment for alcohol use disorders.

Data from randomised trials have varied. Most of the studies have been small, of short duration, in cohorts with significant comorbidity (eg cirrhosis), and with some potentially problematic outcome measures.

In my assessment of all the randomised trials that I could identify, those that reported benefit from baclofen[3-7] have tended to be very small (all fewer than 100 participants), less recent, and possibly at higher risk of bias.

The trials that did not find a benefit of baclofen over placebo,[1,8,9] were more recent, and possibly at lower risk of bias.

Notably, the largest study (180 participants) in a US Veteran Affairs population with comorbid chronic HCV, published this year, did not find a beneficial effect with baclofen.

The empirical evidence does not support the use of baclofen as a routine treatment for alcohol use disorders.

This was not a treatment I recommended to Jorge. ■

References available on request

Stat Facts

INTENTION TO TREAT ANALYSIS
In randomised trials, noncompliance (to the study protocol) and missing outcomes (e.g., participant drop-outs) can lead to exaggerated estimates of treatment effects. One way to address this is for the data to be analysed according to the "intention-to-treat" principle – to include all participants who were randomised in the study.[10]

over 12 weeks, with eight sessions of a low-intensity psychosocial intervention.

Comparator: what was the control/alternative?
Placebo tablets, but otherwise the same as the intervention group.

Outcomes: what was measured?
Primary outcome: the percentage of heavy drinking days, and percentage of abstinence.

Internal validity: are the trial results valid?
Randomised patient assignment?
Yes. The randomisation process was computer-generated and stratified by gender.

Groups similar at the start?
Mostly. The groups were largely similar (see Table 1 from the paper).[1]

Groups treated equally apart from assigned treatment?
Yes.
All patients accounted for?
No. Almost a quarter (24%) of the participants did not complete the study. The analysis was conducted on an intention-to-treat basis (see Stat Facts).

Measures objective/Or patients and clinicians kept blinded?
Yes/Probably. There was some validation of patient reported drinking behaviours with the use of breathalysers. The study appeared to have been double-blinded, though the effectiveness of blinding was not reported.