Oral topiramate was effective as an adjunct to standardised medication compliance management in alcohol dependence


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆

**MAIN RESULTS**

In adults with alcohol dependence, is oral topiramate effective for reducing drinking, promoting abstinence, and decreasing craving as an adjunct to standardised medication compliance management?

**METHODS**

- **Design:** randomised placebo controlled trial.
- **Allocation:** (concealed)*†.
- **Blinding:** blinded (participants, healthcare providers, data collectors, outcome assessors, data analysts, data safety and monitoring committee, and manuscript writers)*†.
- **Follow up period:** 12 weeks.
- **Setting:** San Antonio, Texas, USA.
- **Interventions:** oral topiramate (at escalating doses from 25 mg/d to 300 mg/d for the first 8 wk, and then at 300 mg/d for wk 8 to 12) (n = 75) or matching placebo (n = 75) for 12 weeks as an adjunct to brief behavioural treatment to enhance compliance given by trained nurse practitioners.
- **Outcomes:** self reported drinking behaviour, plasma γ glutamyl transferase levels, self reported craving, and adverse events.
- **Patient follow up:** 95% (150 participants; mean age 42 y, 71% men).

*See glossary. †Information provided by author.

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Analysis was by intention to treat. At 12 weeks, participants who received topiramate had 2.88 fewer drinks/day (95% CI 1.27 to 4.50 drinks/d, p = 0.0006), 3.10 fewer drinks per drinking day (CI 1.31 to 4.88 drinks/drinking d, p = 0.0009), 27.6% (CI 13.0% to 42.2%, p = 0.0003) fewer heavy drinking days (heavy drinking days defined as those with ≥5 drinks/d for men and ≥4 drinks/d for women), 26.2% (CI 12.4% to 40.0%, p = 0.0003) more days of drinking abstinence, and a log plasma γ glutamyl transferase ratio of 0.07 (0.02 to 0.11, p = 0.0046) less than those who received placebo. Self reported craving, measured on the 14 item obsessive compulsive drinking scale, showed that participants who received topiramate reduced drinking obsessions, automaticity of drinking, and interference due to drinking compared with those who received placebo. No serious adverse events were reported in either group.

**CONCLUSION**

In adults with alcohol dependence, oral topiramate was effective for reducing drinking, promoting abstinence, and decreasing craving as an adjunct to standardised medication compliance management.

**Commentary**

The study by Johnson et al showed striking reductions in drinking among adults treated with topiramate, with the effect increasing over the 12 week study. Nevertheless, caution is warranted before applying this finding to clinical practice because the study patients are different in important ways from typical patients presenting in medical settings. Firstly, we know that naltrexone, which was shown to be efficacious in early studies, turned out not to be effective in a sample of patients who were more severe problems. Secondly, only 103 of 367 (28%) of participants who were screened completed the protocol. Although such selection bias is typical of randomised controlled trials, this means that the results are not necessarily generalisable outside the subset of patients. Therefore, in order to have more confidence in the results, they need to be replicated in other centres, and in more typical clinical populations. Finally, subjects received a "minimal psychosocial adherence enhancement procedure" in addition to medication or placebo. Such procedures were developed because it is considered unethical to deprive subjects of all psychosocial treatment, and brief counselling helps to enhance medication compliance. Although brief counselling is undoubtedly beneficial, providing more intensive psychosocial services may attenuate the effect of medication. In addition, the type of psychosocial therapy may also be important; naltrexone appears to be more effective when combined with cognitive behavioural psychotherapy than with 12 step facilitation. A lesson learned from previous medication trials for this devastating condition is that understanding the role of these factors requires multiple studies. These caveats notwithstanding, this exciting study marks an important advance in the treatment of alcohol dependence.

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