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


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

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.
- **Patients:** 158 participants between 21 and 65 years of age who met DSM-IV criteria for alcohol dependence; scored ≥8 on the alcohol use disorders identification test; reported drinking a mean of ≥35 standard drinks/week for men and ≥21 standard drinks/week for women during the 90 days before enrolment; and had a negative urine toxicological screen for narcotics, amphetamines, or sedative hypnotics. Exclusion criteria included a current axis 1 psychiatric diagnosis (other than alcohol or nicotine dependence), a Clinical Institute Withdrawal Assessment for Alcohol-Revised score >15, and clinically significant physical problems.
- **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.

MAIN RESULTS

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,1 turned out not to be effective in a sample seeking treatment who had more severe problems.2 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 that 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 psychotherapy may also be important; naltrexone appears to be more effective when combined with cognitive behavioural psychotherapy than with 12 step facilitation.2 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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