

The Use of Topiramate for Weight Loss in Obese Patients

Clinical Question: There is retrospective evidence to suggest that the anti-epileptic medication topiramate may cause weight loss. This study attempted to evaluate prospectively the use of topiramate as potential agent to aid in weight loss.

Article: Bray, et. al., "A 6-Month Randomized, Placebo-Controlled, Dose-Ranging Trial of Topiramate for Weight Loss in Obesity." *Obesity Research*. 2003 Vol. 11:6 pp. 722-33.

Study Design: Randomized, double-blinded, placebo-controlled, dose-ranging trial
- Conducted w/ healthy obese adults ages 18 to 75 recruited from 17 US centers

-Inclusion criteria were pts w/

- BMI ≥ 30 to < 50 kg/m² or
- BMI ≥ 27 to < 50 kg/m² (if subject had controlled HTN and/or dyslipidemia)

-Exclusion criteria were pts w/

- recent wt change
- diabetes
- uncontrolled HTN
- liver disease
- renal dysfunction
- cardiovascular, endocrine, neurological or psychiatric disease

- Initial H&P, baseline measurements, labs, ECGs performed then pts randomized to receive either placebo, 64, 96, 192, 384 mg of topiramate daily (five arms). (Table 1), (Figure 2)
- Adhered to an up to 12 week drug titration schedule. (Figure 1)
- Length was 24 weeks total
- If adverse effects were experienced in any group, the site was allowed to reduce the dose by one level and continue treatment in a blinded fashion. Only one dose reduction allowed. (Table 1)
- Subjects, investigators, and those administering the treatments were blinded
- All pts participated in the same behavioral modification program including diet and exercise. All pts were given a Food and Activity Tracker and encouraged to use this (no data from these are reported)
- At the end of the maintenance period, pts were tapered off of medication
- Assessments at visits included wt, BP, fasting blood samples
- Sample size determined based on aim of achieving 90% power to detect 4% difference b/t mean wt loss in the placebo group and active doses
- Primary outcome was percent change from baseline body weight at week 24 (row A)
- Secondary outcomes were wt loss in kg (row B), BMI (row C), percentage of subjects who had at least 5% (rowD) or 10% (row E) wt loss, lipid profile, fasting plasma glucose, HbA1c, SBP (row F), DBP (row G)

Results:

- How large was the treatment effect? (Data presented is only ITT-LOCF data)

		Placebo	64mg	96mg	192mg	384mg
A	wt chg (%)	-2.6	-5	-4.8	-6.3	-6.3
B	abs wt chg (kg)	-2.8	-5.2	-5	-6.4	-6.6
C	BMI (kg/m ²)	-0.5	-1.5	-1.4	-1.9	-1.8
D	% subjects w/ $\geq 5\%$ wt loss	19	41	43	53	47
E	% subjects w/ $\geq 10\%$ wt loss	7	16	18	29	22
F	SBP (mmHg)	-1.2	-5.8	-7.5	-7.1	-4.5
G	DBP (mmHg)	-1.6	-3.2	-4.6	-4.3	-2

	Placebo	64mg	96mg	192mg	384mg
Absolute Benefit Increase	*	22	24	34	28
NNT (5% data or row D)	*	4.5	4.2	2.9	3.6
Absolute Benefit Increase	*	9	11	22	15
NNT (10% data or row E)	*	*	9.1	4.5	6.7

Absolute Benefit Increase (ABI) = EER-CER

NNT = 100*(1/ABI)

- Figure 4A % of subjects w/ at least 5% or 10% wt decrease in all groups
- No significant difference in fasting glucose, insulin, HbA1c, or fasting lipids
- Table 2 shows adverse events
- Of note, adverse events were cause of discontinuation in 11% in placebo and 21% of topiramate group (p<0.05)

Are the results valid?:

- Was the assignment of patients to treatment randomized? Yes
- Were all patients who entered the trial properly accounted for and attributed at its conclusion? Figure 2 shows patient tracking. Investigators analyzed data using both ITT-LOCF and "completers" values
- Were patients, their clinicians, and study personnel 'blind' to treatment? Yes
- Were the groups similar at the start of the trial? Table 1 shows baseline characteristics however no data is given as to whether there is statistically significant difference. Greater than 80% of pts were premenopausal women. 17% in placebo treated for HTN and 13% in TPM-treated group were treated for HTN (no p-value given).
- Aside from the experimental intervention, were the groups treated equally? Yes

Will the results help me care for my patient?:

- Can the results be applied to my patient care? Given the inclusion/exclusion criteria set forth at the outset of the trial, I believe that only a select few patients from our general medicine clinic would qualify for this study. It would be interesting to see what the outcomes would have been in a patient population with multiple co-morbidities as we tend to see in our clinics.
- Were all clinically important outcomes considered? As the authors point out, a longer trial would be interesting to see where the nadir of topiramate treatment might be. Additionally, other outcomes such as progression to diabetes, cardiovascular morbidity/mortality, ability to maintain weight loss would have been interesting had they been measured.
- Are the likely treatment benefits worth the potential harms and costs? Given the short range of this study and the relatively high number of adverse events (resulting in a significant number of dropouts), it is premature to advocate topiramate in the treatment of weight loss. Perhaps, if studies demonstrate that the lower doses can effectively and more permanently keep weight down, there may be a role for topiramate.