BACLOFEN FOR TREATMENT OF ALCOHOL USE DISORDER: SECONDARY ANALYSES AND IMPLICATIONS OF THE AUSTRALIAN BACALD TRIAL.

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Introduction and aims: Baclofen remains a controversial pharmacotherapy for alcohol use disorder. The BacALD trial recently reported a medium effect size for baclofen (30-75 mg/day) for delaying lapse and relapse. Here we aim to i) report secondary analyses from the BacALD study and to ii) relate BacALD findings to recent meta-analyses and consensus statements.

Design and methods: We evaluated three moderators of response to baclofen (a) a single nucleotide polymorphism (rs29220) in the GABA B receptor gene (GABBR1), (b) neurometabolites including GABA, glutamate (Glu) and glutathione (GSH) obtained by proton magnetic resonance spectroscopy (MRS) and (c) clinical moderators including liver disease (ALD) and intercurrent use of antidepressants (AD). To address aim 2, the findings were related to three recent meta-analyses, consensus statement and practice recommendations.

Results: GABBR1 rs29220 polymorphism moderated response to baclofen for time to relapse (OR: 3.40, 95% CI:1.01-11.46) and percentage days abstinent (p<0.05). On MRS, baclofen increased parietal concentrations of GSH (p<0.01) compared to placebo. GSH predicted heavy drinking days at 12 weeks follow-up suggesting a role for neuro-oxidative stress. Clinical predictors of baclofen effect included baseline drinking level, presence of ALD but not concurrent AD. The clinical findings were consistent with recent meta-analyses and an international consensus statement (Lancet Psychiatry 2018).

Discussion and conclusions: These results indicate that baclofen may play a role in treatment of AUD particularly in those with ALD and high drinking levels. Pharmacogenomic findings require validation before clinical application.

Implications for Practice or Policy: The present findings have implications for clinical use of baclofen but in view of significant adverse events, use of this medication may best be limited to specialist services.

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