

# Baclofen at a Tailored Dose Reduces Alcohol Use, Craving and Adverse Consequences of Drinking in Alcoholics with Medical Disease due to Alcohol Dependence

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## Introduction

Baclofen is a GABA<sub>B</sub> receptor agonist which has traditionally been used to treat spasticity although there is a growing interest in its role in treating alcohol craving and withdrawal. Two randomised controlled trials of fixed-dose baclofen have found significant improvements in alcohol intake, craving and duration of abstinence when compared to placebo controls.<sup>1,2</sup> Clinical experience of using off-licence baclofen suggests that the effective dose needs to be 'tailored' to the individual, including the use of as required doses. This is probably because of individual variation in the pharmacodynamics of baclofen, particularly in the presence of physical co-morbidities such as chronic liver disease.<sup>3</sup> The aim of this study was to determine whether treatment with tailored dose baclofen has an effect on self reported alcohol consumption, alcohol craving, perceived consequences of drinking, treatment satisfaction, quality of life, depression and anxiety.

## Methods

Over a one year period 53 patients who were hospitalised for severe medical consequences of their alcohol dependence were treated with baclofen outwith the product licence. The treatment dose ranged from 15 mg/day to 360 mg/day. The 41 patients alive at time of the survey were sent a questionnaire to assess treatment satisfaction (Treatment Satisfaction Questionnaire for Medication - TSQM) as well as current and pre-baclofen treatment measures (retrospectively reported for the time 6 months prior to treatment initiation) on the following: alcohol consumption, alcohol craving (*Alcohol Urge Questionnaire - AUQ*), harmful consequences of drinking (*Drinker Inventory of Consequences Short Inventory of Problems - DrInC-SIP2R*), depression and anxiety (*Hospital Anxiety and Depression Scale - HADS*) and quality of life (*ALQoL9*). The data was analysed using SPSS. As some of the data was not normally distributed the Wilcoxon matched pairs sign test was used to measure the significance of any change.

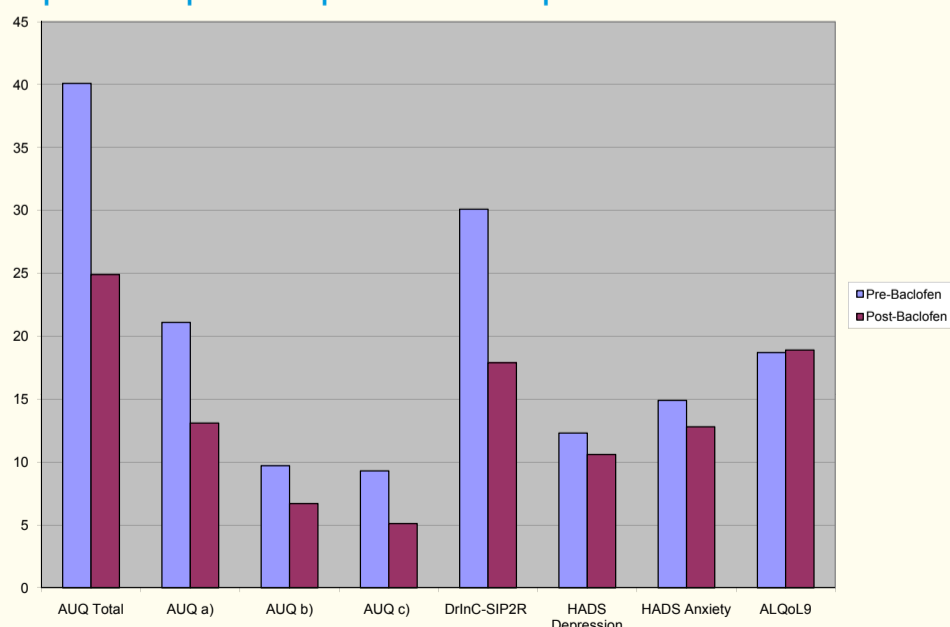
## Results

A total of 18 patients (44%) completed the follow-up questionnaire. The average age was 50.2 and 61% were male. There was no difference between responders and non-responders in terms of age or gender. The average duration from starting baclofen treatment to follow-up was 23 months. Subjects reported the dose of baclofen needed to block alcohol cravings were on average 25mg per dose and 95mg per day. Of respondents, 60% had not needed to use baclofen in the preceding week. The comparison of pre-baclofen and post-baclofen psychometric measures showed a significant decrease in reported craving and consequences of drinking (table 1 and graph 1).

Table 1 – Analysis of pre-baclofen and post-baclofen measures.

	Pre-Baclofen mean ± SD	Post-Baclofen mean ± SD	Wilcoxon Z	P value
Craving (AUQ)	40.1 ± 1.4	24.9 ± 1.5	2.89	0.004
- a) desire for a drink	21.1 ± 7.7	13.1 ± 8.6	2.71	0.007
- b) ability to avoid alcohol	9.7 ± 3.7	6.7 ± 4.4	2.00	0.045
- c) expectations of positive effects	9.3 ± 4.6	5.1 ± 3.7	2.59	0.009
Consequences (DrInC-SIP2R)	30.1 ± 12.6	17.9 ± 14.6	2.27	0.02
Depression (HADS)	12.3 ± 6.2	10.6 ± 7.3	0.67	0.50
Anxiety (HADS)	14.9 ± 5.9	12.8 ± 6.4	1.42	0.16
QOL (ALQoL9)	18.7 ± 8.0	18.9 ± 9.9	0.07	0.94

Graph 1 – Comparison of pre-baclofen and post-baclofen measures.



## Craving

Alcohol craving as reported at the time of survey compared with 6 months prior to treatment initiation improved significantly (mean AUQ score 40.1 vs 24.9). The sub-scales for desire for a drink (p=0.007), ability to avoid alcohol (p=0.045) and expectations of positive effects (p=0.009) were all significantly improved.

## Harmful Consequences of Drinking

The adverse consequences of drinking showed wide variation between individuals across the domains of physical, social, intrapersonal and interpersonal harm. This reflected the different ways in which alcohol abuse can result in impairment. The current consequences, compared with retrospectively reported consequences 6 months before baclofen was started, showed a clinically relevant improvement from a mean DrInC-SIP2R score of 30.1 to a mean score of 17.9. This improvement was statistically significant.

## Depression, Anxiety and Quality of Life

Although scores for depression and anxiety showed improvement this did not reach statistical significance. There was no apparent change in self-reported quality of life following baclofen treatment over the follow-up period.

## Treatment Satisfaction

The mean reduction in alcohol consumption was 6.9% ± 1.3%. The overall satisfaction with treatment was high with the TSMQ global score being 68%. The sub-scores were 59% for effectiveness, 90% for side effects and 71% for convenience. The most commonly reported side effects were tiredness and urinary incontinence.

## Discussion

In this study tailored-dose baclofen appears to be effective at reducing reported alcohol consumption, craving and harmful consequences of drinking. One proposal for the variation in outcomes of clinical trials involving baclofen has been the differences in study populations.<sup>4</sup> This study shows some benefit with baclofen in a population with serious physical complications of alcohol dependency where more traditional options such as disulfiram and acamprosate would be contraindicated. As baclofen is mostly renally excreted (about 85%) then it may be a more realistic therapeutic option for patients with hepatic disease.

Randomised controlled trials into the effectiveness of baclofen have used fixed doses of 30mg per day but the use of tailored dosing may allow higher doses to be used. Researchers have called for more research into the role of high-dose baclofen in treating alcohol dependence with case reports describing effectiveness at 140mg and 270mg per day.<sup>5,6</sup> Indeed when our respondents were asked what dose of baclofen was needed to block alcohol cravings the average responses were 25mg per dose and 95mg per day. Doses over 100mg per day, the maximum BNF limit, may therefore be needed in some patients.

Studies have found that baclofen can significantly reduce measures of anxiety but not depression. As alcohol is a depressant this is perhaps surprising. Our study has found that both anxiety and depression reduce although not to a significant level. The lack of change in quality of life may have been due to the pre-existing medical problems in this study population. Clearly, with retrospective reporting, a main weakness in this study, further prospective investigation is needed.

A potential disadvantage of baclofen is the need for multiple dosing due to its short half life and proponents of baclofen have called for a sustained release form to be developed. However, the TSMQ score for 'convenience' was good as was the overall treatment satisfaction. The most commonly described side effect was tiredness which is also the finding of other studies.

## Conclusions

Tailored baclofen treatment in alcohol dependent patients with medical disease reduces self reported alcohol consumption and results in significant improvement in craving and negative consequences of drinking. There may also be improvements in depression and anxiety but quality of life appears unaffected. The overall satisfaction with tailored baclofen treatment is high. Baclofen is a promising treatment option for alcohol dependency which needs further study.

## References

1. Addolorato G et al. Baclofen efficacy in reducing alcohol craving and intake: a preliminary double-blind randomized controlled study. *Alcohol* 2002; 37; 504-508.
2. Addolorato G et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol dependent patients with liver cirrhosis: randomised, doubleblind controlled study. *Lancet* 2007; 370; 1915-22.
3. Heydtmann M. Baclofen effect related to liver damage. *Alcohol: Clinical and Experimental Research* 2011; 35 (5)
4. Leggio L, Garbutt JC & Addolorato G. Effectiveness and Safety of Baclofen in the Treatment of Alcohol Dependent Patients. *CNS & Neurological Disorders - Drug Targets* 2010; 9, 33-44.
5. Bucknam W. Suppression of symptoms of alcohol dependence and craving using high-dose baclofen. *Alcohol* 2007; 42; 158-160.
6. Ameisen O. Complete and prolonged suppression of symptoms and consequences of alcohol-dependence using high-dose baclofen: a self-case report of a physician. *Alcohol* 2005; 40; 147-150.

