12-month follow-up of baclofen treatment in patients with alcohol use disorder and other psychiatric comorbidities

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Abstract

Aims: In France, Baclofen has been authorized for alcohol use disorder treatment for about 18 months. The efficacy of this medication is still controversial in the literature and little is known on the impact of long-term baclofen treatment in naturalistic settings. The aim of this study was to evaluate the 12-month follow-up efficacy of baclofen treatment in alcohol use disorders patients in naturalistic settings.

Methods: In an open-label study, consecutive alcohol use disorder patients who have initiated a baclofen treatment in an outpatient addiction clinic in Bordeaux (France) were assessed at treatment initiation and at least once a month. Here, we analyzed the alcohol use, craving, side effects, treatment retention, over the first 12 months of treatment.

Results: The sample consisted in 82 patients, 71% males, 42.5 y.o. (SD= 9.7), 40% exhibited another addictive comorbidity, 79% tobacco use disorder, 62% a mood disorder, and 60% an anxiety disorder. They reported 18.3 days (SD=11.1) of alcohol use past 30 days in average, 16.7 AU (SD=12.3) per drinking day, and 23.9 days (SD= 9.9) of craving past 30 days in average. The mean baclofen dose was 132mg/day (SD= 76, range: 20-300). At 12 months, 26% have stopped treatment because of side effects (33%), inefficacy (24%), or lack of treatment compliance (19%), or death (24%). At 12 months, 91% reported a significant decrease of craving, 12% stopped alcohol use, and 37% reported a decrease of alcohol use. Although 63% did not report any change in alcohol use, the number of drinks per drinking day decreased and the severity of alcohol use significantly decreased (p<.0001). Side effects were mild but reported by 63% of the patients, mainly sedation (39%), dizziness (9%), headache (6%), GI (6%), sexual disorder (6%).

Conclusions: Although these findings showed some benefits of baclofen treatment in alcohol use disorder patients with other comorbidities, the impact on alcohol use seemed to be moderate. Further studies are needed to identify the factors associated with the efficacy of baclofen treatment.

Introduction (1)

- Baclofen
  - GABA B receptor agonist
  - Long-lasting treatment for spasticity (Sachais 1977)
  - Over last decade = promising medication for treatment of addiction (Abagio 2013)
- Baclofen in Alcohol Use Disorder (AUD)
  - Efficacy inconclusive with dose of 30mg/day
    - 2 studies = Significant benefit vs. placebo (Addolorato 2002, 2007)
    - 1 study = No difference vs. placebo (Garbutt 2010)
  - Potential effect with higher dose ranged from 80mg to 400mg/day (Rigal 2012)

Introduction (2)

- France
  - March 2014: "Temporary Recommendations for Use" of baclofen for AUD
    - For individuals who experienced approved pharmacological treatment (i.e. acamprosate, naltrexone, disulfiram) for AUD previously without efficacy
  - Rapid increase of baclofen prescription for AUD (Dupouy 2014)
  - Dose higher than 30mg/day allowed
  - Length of baclofen treatment ranged 74 – 377 days, median = 144 days (Dupouy 2014)

Objective

- To evaluate the 12-month follow-up efficacy of baclofen treatment in AUD
  - In naturalistic settings
  - In outpatient addiction clinic, Bordeaux, France

Methods

- Open-label study
- Inclusion
  - Consecutive AUD individuals who have initiated a baclofen treatment
  - In an outpatient addiction clinic in Bordeaux (France)
- Assessment
  - At treatment initiation
    - mASI (Denis 2015), MINI
  - At least once a month thereafter
    - Alcohol use: alcohol use past 30 days, drinking per days
    - Craving: days past 30 days and intensity
    - Side effects

Results – Sample description

- Sample n=82
  - Males: 71% (n=58)
  - Age: mean 42.5 (SD= 9.7), range 24-70
- History of alcohol use
  - Past 30 days before baclofen Tx
    - Mean: 18.3 days (SD= 11.1)
    - Mean: 16.7 alcohol unit (SD= 12.3) per day
  - Lifetime
    - Mean: 15.6 years (SD= 9.5), range 2-41
  - Previous Tx
    - Mean: 3.0 (SD=2.8), range 3-13
      - Authorized prescription of baclofen only for AUD individuals who received previous pharmacological Tx without efficacy
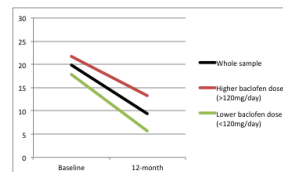
Results – Comorbidities

- Addiction comorbidities
  - 40% with another drug use disorder
    - Cannabis 27%, opiates 14%, bzd. 8%, cocaine 7%
  - Other non-substance addictive disorder
    - Gambling 3%, gaming 3%, eating disorder 1.5%
  - 79% with tobacco use disorder
- Psychiatric comorbidities
  - At least one psychiatric comorbidity: 77%
    - Mood disorder: 62%
    - Anxiety disorder: 60%

Results – Baclofen treatment

- Treatment retention at 12-month: 74% (n=61)
  - Length in Tx: mean 258 days (SD=121), range 41-365
- Reasons for dropped out (n=21)
- Side effects   33%
- Non perceived efficacy   24%
- Non observance   19%
- Death   24%
  - 2 suicide, 1 heart attack, none attributable to baclofen
- Baclofen dose
- Maximum dose:
  - Mean 146.1 mg/day (SD=85.6), range 20-300, median= 135mg/day
- Maximum well tolerated dose
  - Mean 131.9 mg/day (SD=76.0), range 20-300, median= 120mg/day

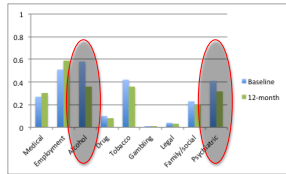## Results – Efficacy of baclofen (1)

- Change in alcohol use
  - 37% (n=30) stopped or reduced their alcohol use
    - 12% (n=10) stopped alcohol use
    - 24% (n=20) decreased their alcohol use

- Significant decrease of alcohol over 12-month
  - Change in alcohol use is not linked to:
    - Baclofen dose ($F_{(1,16)}=0.38$, p=0.54)
    - Psychiatric comorbidities ($F_{(1,51)}=0.88$, p=0.35)
    - SUD comorbidities ($F_{(1,51)}=1.62$, p=0.21)
  - Linked to length in Tx
    - Higher decrease in alcohol use if at least 6 months in Tx ($F_{(1,26)}=9.58$, p=0.004)

- Effect on alcohol craving
  - 32/35 (91%) reported a decrease of alcohol craving

Results – Efficacy of baclofen (2)

- Severity of addiction – mASI Composite Scores

- Significant decrease of
  - Alcohol score $(F_{(1,24)}=22.4, p<0.001)$
  - Psychiatric score $(F_{(1,24)}=5.8, p=0.02)$

- None of these changes are linked to:
  - Baclofen dose
  - Length in baclofen Tx
  - Psychiatric comorbidities
  - SUD comorbidities

Results – Side effects

- 63% (n=52) reported side effects
- Intensity: Mild to moderate (clinician's rating)
- Main side effects reported
- Sedation   39%
- Dizziness   9%
- Headache   6%
- GI   6%
- Sexual dysfunction 6%
- Sleep apnea   6%

Results – Conclusion

- Some benefits of baclofen treatment in alcohol use disorder patients
  - Even associated with other comorbidities
    - Psychiatric and/or SUD
- Potential better efficacy if
  - Dose higher than 120mg/day
  - For more than 6 months
- Further studies are needed to identify the factors associated with the efficacy of baclofen treatment
  - RCTs
  - Comparison with other pharmacological treatment
    - e.g. topiramate, naltrexone, nalmefene

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