School of Physician Assistant Studies   Theses, Dissertations and Capstone Projects

8-14-2010

The Efficacy of Baclofen in Reducing Alcohol Consumption and Decreasing Alcohol Craving in Alcohol Dependent Adults

Kelsey Bock
Pacific University

Follow this and additional works at: http://commons.pacificu.edu/pa

Part of the Medicine and Health Sciences Commons

Recommended Citation

The Efficacy of Baclofen in Reducing Alcohol Consumption and Decreasing Alcohol Craving in Alcohol Dependent Adults

Abstract

Background: Many people suffer from alcoholism which can be a debilitating disease. With only three medications on the market to treat alcoholism, research to find new pharmaceuticals is important. The recent publication of a book promoting baclofen, a GABA agonist normally used to treat spasticity, as a treatment for alcoholism, has brought public attention to the topic. For potential patients who have read the book and clinicians who treat alcoholism, this systematic review examines claims that baclofen decreases alcohol cravings and has a possible clinical use in the treatment of alcoholism.

Methods: An exhaustive search of available medical literature, published in English, was conducted using MEDLINE, Evidence-Based Medicine Reviews Multifile, and CINAHL with the keywords "baclofen" and "alcoholism." A bibliographical search of the literature was done to find further articles and information. Each study needed to evaluate both abstinence and craving for alcohol. Due to the fact that there is limited research available on the topic, all available articles were included.

Results: The search yielded 2 random controlled trials, 2 open label studies, and 3 case reports. Both random controlled trials (RCT) showed statistically significant results in increased abstinence and decreased craving in baclofen versus placebo group. Both open label studies showed decreased craving with baclofen use, and one showed increased abstinence, while the other showed a decrease in alcohol consumption. All three case reports described accounts of severe alcoholics whose alcoholism was successfully treated with higher doses of baclofen. Minimal to no side effects were seen in all trials and no patients described craving or euphoric effects from taking baclofen.

Conclusion: Even with the need for more research on the topic, baclofen should be considered as another medication to try in the treatment of alcoholism. Patients with intense cravings for alcohol may have greater benefit in cessation of alcohol use as baclofen significantly and quickly decreases cravings. Both the high safety and low side effect profile make baclofen a reasonable option to try. Since the amount of research on the topic is minimal, clinicians need to use their judgment and may want to try baclofen only after first attempting other treatment options. The duration and dosage of baclofen is uncertain and will need to be adjusted on a patient by patient basis.

Degree Type
Capstone Project

Degree Name
Master of Science in Physician Assistant Studies

First Advisor
Annjanette Sommers MS, PA-C

Second Advisor
Rob Rosenow PharmD, OD

Keywords
baclofen, alcoholism

Subject Categories
Medicine and Health Sciences

Rights

NOTICE TO READERS

The Efficacy of Baclofen in Reducing Alcohol Consumption and Decreasing Alcohol Craving in Alcohol Dependent Adults

Kelsey Bock

A Clinical Graduate Project Submitted to the Faculty of the

School of Physician Assistant Studies

Pacific University

Hillsboro, OR

For the Masters of Science Degree, August 14, 2010

Faculty Advisor: Annjanette Sommers MS, PAC
Clinical Graduate Project Coordinators: Annjanette Sommers MS, PAC & Rob Rosenow PharmD, OD

Biography

Kelsey Bock grew up in Great Falls, Montana, and graduated from Great Falls High School. She then went on to receive her bachelor's degree in biochemistry from Montana State University, Bozeman. After all the years of hard work through high school and college, she took a few years off to really experience all that Montana has to offer. She took a job as a waitress at the country's only private ski resort, the Yellowstone Club. This allowed her to pursue her interest in skiing and investigate the world of the wealthy. After three years without an ACL injury and with no sugar daddy on the horizon, she determined she must support herself and applied to PA school. Luckily, throughout the years, Kelsey had also worked as a medical assistant and certified nursing assistant in an urgent care clinic, for an OB GYN, and on the hospital OB and surgical floors. In 2008, she left the mountains of Montana and went to Hillsboro, Oregon to start PA school at Pacific University. After graduation, she hopes to return to the mountains and join a family practice clinic and continue all her activities in the great outdoors.

Abstract

Background: Many people suffer from alcoholism which can be a debilitating disease. With only three medications on the market to treat alcoholism, research to find new pharmaceuticals is important. The recent publication of a book promoting baclofen, a GABA agonist normally used to treat spasticity, as a treatment for alcoholism, has brought public attention to the topic. For potential patients who have read the book and clinicians who treat alcoholism, this systematic review examines claims that baclofen decreases alcohol cravings and has a possible clinical use in the treatment of alcoholism.

Methods: An exhaustive search of available medical literature, published in English, was conducted using MEDLINE, Evidence-Based Medicine Reviews Multifile, and CINAHL with the keywords "baclofen" and "alcoholism." A bibliographical search of the literature was done to find further articles and information. Each study needed to evaluate both abstinence and craving for alcohol. Due to the fact that there is limited research available on the topic, all available articles were included.

Results: The search yielded 2 random controlled trials, 2 open label studies, and 3 case reports. Both random controlled trials (RCT) showed statistically significant results in increased abstinence and decreased craving in baclofen versus placebo group. Both open label studies showed decreased craving with baclofen use, and one showed increased abstinence, while the other showed a decrease in alcohol consumption. All three case reports described accounts of severe alcoholics whose alcoholism was successfully treated with higher doses of baclofen. Minimal to no side effects were seen in all trials and no patients described craving or euphoric effects from taking baclofen.

Conclusion: Even with the need for more research on the topic, baclofen should be considered as another medication to try in the treatment of alcoholism. Patients with intense cravings for alcohol may have greater benefit in cessation of alcohol use as baclofen significantly and quickly decreases cravings. Both the high safety and low side effect profile make baclofen a reasonable option to try. Since the amount of research on the topic is minimal, clinicians need to use their judgment and may want to try baclofen only after first attempting other treatment options. The duration and dosage of baclofen is uncertain and will need to be adjusted on a patient by patient basis.

Keywords: baclofen, alcoholism

Acknowledgements

To my friends and family who still called, even when all I could think to talk about was school.

To my mom, who listens to all my venting and then, no matter what, always tells me I am great.

To Chad who continually supports my dreams and goals, and still likes me while I am achieving them.

To my classmates, who made life throughout PA school survivable. After all the threatening, I never did poke my eyes out. Alison, you made PA school fun. (If I end up doing that interpretive dance you signed us up for, I am taking this acknowledgement back)

Table of Contents

List of Tables

List of Abbreviations

GABA………………………………………………………..gamma aminobutyric acid

FDA...Food and Drug Administration

NNT………………………………………………………..Number Needed to Treat

OCDS…………………………………………………..Obsessive Compulsive Drinking Scale

ACS………………………………………………………….Alcohol Craving Scale

PACS…………………………………………………………Penn Alcohol Craving Scale

RCT………………………………………………………...Randomized Controlled Trials

The Efficacy of Baclofen in Reducing Alcohol Consumption and Decreasing Alcohol Craving in Alcohol Dependent Adults

BACKGROUND

Worldwide, alcohol causes 1.8 million deaths (3.2% of total) and is the fifth leading cause of premature death and disability in the world according to the WHO.[1,2] People who suffer from alcoholism are at increased risk for liver cirrhosis, pancreatic diseases, and accidents.[2] With such detrimental effects and such a large number of individuals suffering from alcoholism, there is a great deal of discussion around the topic. The recent American release (2008) of a book called, _The End of My Addiction_, by Olivier Ameisen,[3] a French cardiologist, has brought increased attention on a drug called baclofen as a "cure" for alcoholism. In his book, Ameisen claims to have successfully suppressed his alcoholic cravings by taking high dose baclofen and thus "curing" his alcoholism. This medication is typically used to treat spasticity, and he believes its physiological actions could indicate it in the treatment of alcoholism.[3]

Alcoholism is a multifaceted disease originating from genetic disposition and environmental factors [4] and can manifest itself in various subtypes of alcohol dependent patients.[5] Most pharmacological treatments for alcoholism focus on the craving for alcohol which is thought, in part, to involve gamma aminobutyric acid (GABA) dysregulation. Baclofen is a GABA B-receptor agonist, and may help this dysregulation in certain alcoholics.[5] Alcohol craving can be from the desire to gain the positive effects from drinking alcohol which are transmitted through multiple neurochemical systems.[6] Based on the Three Dimensional Psychobiological Model by Verheul,[7] one type of craving, relief craving, is described as a desire to decrease tension or minimize negative emotional states. Relief craving is thought to be caused by a "GABAergic/glutamatergic dysregulation."[5] GABA is an inhibitory neurotransmitter that can promote a sense of calm. A decrease in GABA, either from genetics or from a personality trait is thought to be a factor in some individuals with high anxiety.[5]

Alcohol, via the corticomesolimbic pathway causes the release of GABA along with other neurotransmitters such as: opioids, serotonin, glutamate, and acetylcholine.[6] After chronic use of alcohol the balance of this pathway is affected and adaptations are made by the system to maintain balance when alcohol is withdrawn. This leads to alcohol withdrawal symptoms and a craving to drink in order to avoid the discomfort of withdrawal.[6]

Although baclofen's exact mechanism of action is unknown, as a GABA agonist, it is believed to play a part in the regulation of GABA.[8] In its current treatment for spasticity, it is approved by the Food and Drug Administration (FDA) in titrated amounts up to 80 mg/day, given on a three times daily schedule.[8] In patients with multiple sclerosis, baclofen has been found to be safe in doses up to 270 mg/day.[9] The common side effects of baclofen (>10%) are muscle weakness and central nervous system (CNS) depression to include drowsiness, vertigo, dizziness, and insomnia.[10]

The treatment for alcoholism is a multidisciplinary treatment combining pharmacological agents and psychosocial therapy to alter an alcoholic's lifestyle and to encourage abstinence from all alcohol use. Currently, there are three agents approved by the FDA for the treatment of alcohol dependence. Disulfiram changes alcohol metabolism thereby causing unpleasant effects after alcohol consumption.[6] Naltrexone works by interacting with the opioid and dopamine systems and may help decrease craving.[6] Acamprosate helps maintain abstinence, and its exact mechanism is not yet understood.[6] Although each of these drugs has shown some efficacy,[11-13] each drug has its limitations and there are studies that show modest to no efficacy in long term treatment of alcohol dependence.[13-15] Thus, there is a need to pursue additional pharmaceutical agents with which to treat alcoholism. This systematic review examined original research that looks at the efficacy of baclofen for alcohol dependence and to reduce alcohol craving.

METHODS

An exhaustive literature search was performed in MEDLINE, CINAHL, and Evidence-Based Medicine Reviews Multifile, using the search terms "alcoholism" and "baclofen." A bibliographical search of the literature was done to find further articles and information. Web of Science was used to search forward to see if the found literature, was cited in any recent relevant studies. To find current trials being conducted, clinicaltrials.gov was searched using the key words baclofen and alcoholism.

Inclusion criteria were all trials, including case reports, that were published in English. All participants had to be diagnosed with alcohol dependence based on DSM-IV criteria. Each study needed to evaluate both abstinence and craving for alcohol. Due to the fact that there is limited research available on the topic, all available articles were included.

All trials were evaluated using an originally designed scoring system to assess validity (see table II and table III). Scoring was based on the type of trial, the randomization of the trial, the description of randomization, the blinding within the trial, the blinding method, and the description of drop-outs. The scoring system also took into account that the craving results were based on a specified validated scaling system, and alcoholic drinks as recorded by participants and family members. The validity scale was used to assess the studies but was not used as exclusion criterion.

RESULTS

After the exhaustive search, 2 randomized controlled trials (RCT), 2 open label studies, and 3 case reports were found from the electronic search. All 7 studies were included in the review.

Each trial was evaluated on abstinence from alcohol, craving for alcohol, and side effects. Doses of baclofen are given on a three times daily schedule in all trials. All the randomized controlled trials and open label studies have, as part of their experimental design, some type of psychological counseling. Counseling type and amount of counseling differed between studies. Each of the

participants in the case studies had previously failed to complete numerous treatments, be it psychological counseling and/or pharmacotherapies. Characteristics of each study can be found in the characteristics of reviewed articles table (see table I). A summary of results for each article can be found in the summary table (see table IV).

Randomized Controlled Trials

In 2002, Addolorato et al[16] published the first RCT on the efficacy of baclofen. The study received a validity score of 7/8 and missed one point because there was no description of randomization. Thirty-nine alcohol dependent adults were randomized (randomization type not specified); 20 in the baclofen group and 19 in the placebo group. The baclofen group was given 15 mg/day of baclofen for 3 days and then 30 mg/day of baclofen for the remainder of the 4 weeks. Participants had referred family members to aid in the administration of the drug, baclofen or placebo. In the baclofen group, 14/20 remained abstinent, 4/19 remained abstinent in the placebo group. Drop-outs were considered to have relapsed. The p value was calculated to <0.005 and the number needed to treat (NNT) was 2. These are statistically significant results, but imprecise due to small sample size. The Obsessive Compulsive Drinking Scale (OCDS) was used to measure craving and showed a mean value at baseline for the baclofen group of 26 and placebo group of 22. The score after 4 weeks was about 6 for the baclofen group and 12 for the placebo group with a p value < 0.05. No patient dropped out of study due to side effects. Baclofen/placebo side effects were: sleepiness 2/0, tiredness 1/0 vertigo 1/0, abdominal pain 0/1. All side effects resolved within 1-2 weeks.

In 2007, Addolorato et al[17] looked at efficacy and safety of baclofen for treatment of alcoholism in alcoholic adults with liver cirrhosis. With an improved experimental design, this trial received a validity score of 8/8. Eighty-four participants were randomized (balanced with blocks), 42 into baclofen group, 42 into placebo group. Each group was assessed for similarities such as age, sex,

employment, marital status, and education. The baclofen group was given 15 mg/day of baclofen for 3 days and then 30 mg/day of baclofen for the remainder of the 12 weeks. Participants had referred family members to aid in the administration of the drug, baclofen or placebo. In the baclofen group, 30/42 remained abstinent and 12/42 remained abstinent in the placebo group. Drop-outs were considered to be relapsed. An odds ratio of 6.3 [95% CI 2.4-16.1] with a p value of 0.0001 and a NNT of 2.3 was calculated for abstinence results. The OCDS score showed a mean value at baseline for the baclofen group at about 27 and for the placebo group at about 25. The scores after 12 weeks was about 3 for the baclofen group and 7 for the placebo group, with a p value of 0.0004. All results were considered statistically significant. No participants dropped out due to side effects. The side effects recorded for baclofen/placebo: headache 4/4, tiredness 1/1, vertigo 2/1, sleepiness 1/0. Hepatic safety was evaluated by testing liver enzymes. Participants in the baclofen group had statistically significant decreases in alanine aminotransferase (p=0.0195), gamma glutamyltransferase (p=0.0155), bilirubin (p=0.0318), and international normalized ratio (p=0.0140) in comparison to the placebo group. Albumin levels were elevated in the group allocated baclofen with a p value<0.0001, which is also statistically significant. There were no significant changes in mean cellular volume, aspartate aminotransferase, or creatinine.

Open Label Studies

A preliminary open label study was done in 2000 by Addolorato et al.[18] Its validity score was 3/10 for using a validated scaling system to measure craving, having family members distribute the medication, and accounting for all drop-outs. Ten alcohol dependent male adults enrolled in the study. One participant dropped out of the study and was excluded from statistical analysis. Each participant was given 15 mg/day of baclofen for 3 days and then 30 mg/day of baclofen for the remainder of the 4 weeks. Participants had referred family members to aid in the administration of the baclofen. 7/9

patients remained abstinent throughout experimental period of 4 weeks. The Alcohol Craving Scale (ACS) was used to measure craving. At baseline patients had median score of 9 with actual results ranging from 3-14 and at end of week 4, a median score of 0 with actual results of 0-4. No additional participants dropped out of the study due to side effects. All side effects (headache, vertigo, sleepiness, tiredness, abdominal pain, and constipation) resolved after 1-2 weeks of first taking baclofen.

At the University of North Carolina in Chapel Hill, in 2004, Flannery et al[19] conducted a preliminary open label study. Its validity score was 2/8 because it did account for all drop outs and used a validated scaling system for craving. Twelve alcohol dependent adults (9 men, 3 women) qualified for the study. Of the twelve, 4 were diagnosed with depression and 2 of these were being treated with medication for depression. Each participant was given 15 mg/day of baclofen for 3 days and then 30 mg/day of baclofen for the remainder of the 12 weeks. The Penn Alcohol Craving Scale (PACS) was used to measure craving. Participants administered their own medication. No patient remained abstinent throughout the 12 week study. Only 4/12 participants finished all 12 weeks of the study. Number of drinks/day at baseline were 7.6 ±2.2 and during treatment on average 4.7 ± 3.5 a decrease of 61.8% (p<0.01). Patients were abstinent 9.4±10.6% of the time at baseline and 31.0±34.2% of treatment days (p<0.01). Two participants in the study increased their rates of heavy drinking and 3 participants had fewer abstinence days during treatment. Craving scores reduced significantly at p<0.01. Baseline PACS scores 18.4±5.1 decreased to 12.4±5.4 by end of treatment. All statistics were calculated based on the number of days each patient was treated prior to dropping out. Two patients dropped out due to side effects.

Case Studies

Dr. Olivier Ameisen, the author of the book, *The End of my Addiction*,[3] wrote a case report based on his experiences taking baclofen and this was published in 2005.[20] The validity score for this

article is 0/8. He was a 50 year old male, diagnosed with alcohol dependence and comorbid anxiety. He began taking baclofen at 30 mg/day and remained abstinent from that time forward (9 months at time of publication of the study). He increased his baclofen dosing 20 mg every third day until a max of 270 mg/day. At 120 mg/day his anxiety was controlled, and he had a complete absence of craving at 270 mg/day. He experienced somnolence at 270 mg/day and decreased his dose to a maintenance dose of 120 mg/day with 40 mg as needed for stressful occasions. At 120 mg/day, Ameisen experienced no side effects. No scales were used, all results were based on personal perspective.

One year later, in 2007, a case report by William Bucknam,[21] an addiction psychiatrist, was published. This article has a validity score of 0/8. A 59 year old, alcohol dependent male with anxiety and major depressive disorder was treated with baclofen. Scales were not used to assess craving, all results were based on the patient's personal perspective. Over a month, the patient took increased doses of baclofen up to 100 mg/day. According to Bucknam, the patient reported a "complete satisfactory response. Drinking was now an alien world to him." During stressful occasions, participant took 140 mg/day. The patient occasionally chose to drink, but never had more than 3 drinks on one occasion or 12 per week. In addition to baclofen, the patient was taking paroxetine for his anxiety. He experienced no side effects from baclofen.

In 2007, a report by Agabio et al[22] was published about a schizophrenic, 55 year old, alcohol dependent male who was treated with 30 mg/day of baclofen for his alcoholism. He remained abstinent for 18 weeks at which point, he consumed one drink. His baclofen dose was increased to 75 mg/day. After one year on baclofen, the patient had only consumed the one drink. His craving was assessed using the OCDS scale and his scores went from 34 at baseline to an average of less than 10. He experienced mild sedation at the beginning of treatment as his only side effect and this resolved. Because OCDS was used as a scaling system for craving, the validity score for this report was 1/8.

DISCUSSION

Limitation of Study

As a result of the lack of research on the topic of baclofen as treatment for alcoholism, all located articles were included in this study. The variety of study types makes it difficult to make solid conclusions. The participants in each study varied significantly, but in all, encompassed the common population seen to have alcoholism. The most evident and important limitation to all of these studies is the lack of participants.

Both RCTs had experimental design flaws. Addolorato et al[16] 2002 never describes the type of randomization used and does not discuss if the groups are equal in terms of support systems, family, job stability, age, or sex. Addolorato et al[17] 2007 improved on these design flaws. Both articles need a standardized method of recording alcohol intake versus relying on patients and their families to record intake. Also, Addolorato et al[16] 2002 was only 4 weeks in duration as compared to Addolorato et al[17] 2007 was only 12 weeks.

The open label studies are limited in validity due to their design. Both studies were also of short duration. In Flannery et al[19] 2004, no participants remained abstinent which made it unique from all the other reports. The study had low intensity psychosocial counseling; it recruited participants who were interested in reducing their alcohol intake, not in abstaining from alcohol, nor did it have family members aiding in the dispensing of baclofen. These design flaws could be responsible for the questionable results.

The case studies are the least valid as they are single case reports. Ameisen[20] 2005 has increased bias because it was a self report and no one else was involved in his treatment or monitoring his results. Each participant varied significantly with their comorbid diagnosis: Ameisen was depressed[20], Bucknam's[21] patient had anxiety and major depressive disorder, and Agabio's[22] patient had schizophrenia. Bucknam's[21] patient was taking paroxetine in addition to the baclofen, suggesting

that the combination of both medications could have contributed to his results. These studies also used significantly higher doses of baclofen for treatment than those in the RCTs[16, 17] and the open label studies[18, 19]. The advantage of these studies was the duration of time each patient was followed, which amounted to about a year for each patient.

Baclofen and Craving

All trials demonstrated a decrease in alcohol craving with the use of baclofen. In all the trials, the largest decrease in craving occurred the first week of treatment. It could be assumed that the quick relief of craving, attributable to baclofen, aided in the increased ability for a patient to remain abstinent. In both RCTs,[16, 17] there was also a drop in craving scores in the placebo group, although not as significant as in the baclofen group. This could be attributed to psychological counseling, personal focus on abstaining, and to medical management. In the case of Ameisen,[20] he felt complete suppression of craving and "indifferent" to alcohol at 270 mg/day, suggesting that it may require high doses of baclofen to increase the ability for patients to decrease cravings. At 100 mg/day, Bucknam's[21] patient had enough control over his cravings, that if he chose to drink, he was able to drink three drinks per occasion and stop drinking. Based on these clinical trials, baclofen decreases the craving for alcohol.

Baclofen and Abstinence

Abstinence from alcohol is the only true treatment for alcoholism. Until complete absence from alcohol consumption is achieved, damage to the body still occurs. In Addolorato et al[17] 2007, the abstinence rates in baclofen versus placebo had p values <0.0001 and an odds ratio of 6.3 with a confidence interval of 2.4-16.1 concluding that the results were statistically significant. There is some lack of precision due to the small sample size. The number needed to treat was calculated at 2.3 which

is a remarkable result. Addolorato etal[16] 2002, has similar results with a p value <0.005, and a number needed to treat at 2 (confidence interval was not calculated). These RCTs conclude that the efficacy of baclofen in treating alcoholism is substantial.

The open label studies, as one would expect, were not as conclusive as the RCTs. Flannery et al[19] 2004 had no participants who remained abstinent throughout the entire trial period. A decrease in alcohol usage and an increase in abstinent days was shown to be statistically significant when participants were taking baclofen. Interestingly, 2 participants in the study increased their rates of heavy drinking and 3 participants had fewer abstinence days during treatment. The results from this article are difficult to assess considering only one-third of the patients finished the trial, and all statistics were calculated based on the number of days treated before the patients dropped out. This and a poor study design decreases validity in the results. Addolorato et al[16] 2002, an open label study, showed that 7/9 participants remained abstinent.

All of the case reports showed life altering benefits to baclofen use.[20-22] All three patients were abstinent and remained abstinent for about 1 year until each study was published and all were still taking baclofen. The most significant aspect of the studies was the increased dosage of baclofen. Although these are not valid reports, it does raise the question of whether higher doses of baclofen are needed in some patients to get the desired results, or if conversely, if higher doses of baclofen yield better results.

Baclofen Side Effects and Safety

The most common side effect seen in all the studies was CNS depression. Most of these side effects resolved within 1-2 weeks of continuous use of baclofen. In only one study, did participants drop out due to side effects.[19] The small side effect profile makes baclofen a medication that patients are likely to be compliant with.

The safety of baclofen has been shown in each of these studies, as no participant suffered any single organ or systemic event that would lead to the need to discontinue the drug. In accordance, it was found that patients with liver cirrhosis who took baclofen showed no hepatic side effects. Liver enzymes improved with the use of baclofen and the absence of alcohol intake.[17] Baclofen has minimal metabolization in the liver.[10] Creatinine clearance did not differ between the baclofen and placebo groups showing baclofen does not cause renal damage.[17] A high dose of baclofen for long term use in the treatment of multiple sclerosis has been shown to be safe.[9] It can be assumed that using high doses for the treatment of alcoholism would also be safe. Another important consideration for the safety of baclofen is the abuse potential. No participant in any of the studies had cravings for baclofen and no one had any euphoric events when taking baclofen, suggesting abuse potential is very low.

Baclofen and Alcoholism Treatment

The treatment of alcohol dependence is as complicated as the disease itself and requires psychological counseling combined with pharmaceutical agents. It is important to consider, in each of these trials, the role of psychological counseling in recovery. Since each study used different counseling methods, it is difficult to compare the effects of counseling. Another key factor is the desire each patient had to stop drinking. Each patient must have had enough motivation to take the medication and attend the counseling sessions. Baclofen is typically given on a three times daily schedule which requires more dedication from the patient. As a result, in general, compliance of patients taking baclofen may be low. Another key issue to alcohol treatment is maintaining abstinence. None of these studies looked at relapse rate after stopping baclofen. Throughout the systematic review, no articles were found that addressed how long a patient must stay on baclofen to treat alcoholism. The efficacy of baclofen may be altered if a patient develops dependency symptoms with the cessation of baclofen. Another consideration is the long term use of baclofen and if it continues to be effective over

time. Since baclofen is a generic drug, the cost is substantially lower than the other medications used to treat alcoholism. This is a very important factor, as many patients suffering from alcoholism have limited financial resources.[10] Baclofen as an agent to combat alcoholism appears promising. More research needs to be conducted with larger RCTs and longer duration of treatment with follow up after cessation of baclofen use. It would also be useful to see if a combination of baclofen with other alcohol treatment drugs increased treatment efficacy.

CONCLUSION

Baclofen should be considered as another medication to try in the treatment of alcoholism. Patients with intense cravings for alcohol may have greater benefit in cessation of alcohol use as baclofen significantly and quickly decreases cravings. Both the high safety and low side effect profile make baclofen a reasonable option to try. Since the amount of research on the topic is minimal, clinicians need to use their judgment and may want to try baclofen only after first attempting other treatment options. The duration and dosage of baclofen is uncertain and will need to be adjusted on a patient by patient basis.

REFERENCES

1. Is Harmful Use of Alcohol a Public Health Problem? Available at:

http://www.who.int/features/qa/66/en/index.html. Accessed January/19, 2010.

2. Gold MS, MD, Aronson, Mark D, MD Gold. Screening for and diagnosis of alcohol problems. In: Schwenk TL, MD, Hermann R, MD, eds. *UpToDate.* Waltham, MA: UpToDate; 2010.

3. Ameisen O. *The End of My Addiction.* New York, New, York: Farrar, Strauss and Giroux; 2008.

4. Baustian GH, MD, Sudak D, MD, Gross D, MD. Alcohol abuse and dependence. In: *First Consult.* MD Consult; 2010.

5. Addolorato G, Abenavoli L, Leggio L, Gasbarrini G. How many cravings? pharmacological aspects of craving treatment in alcohol addiction: A review. *Neuropsychobiology*. 2005;51:59-61.

6. Krishnan-Sarin S, Ph.D., O'Malley S, Ph.D., Krystal JH, M.D. Treatment implications using neuroscience to guide the development of new pharmacotherapies for alcoholism. *Alcohol Research and Health*. 2008;31:400-407.

7. Verheul R, Van Den Brink W, Geerlings P. A three-pathway psychological model of craving for alcohol. *Alcohol Alcohol*. 1999;34:197-222.

8. Medication Packet Insert Information for Baclofen Tablet 10 mg. Available at: http://drugs.medsort.com/drugs/DrugPackageInsert.aspx?MedID=4577. Accessed January/20, 2010.

9. Smith CR, LaRocca NG, Giesser BS, Scheinberg LC. High-dose oral baclofen: Experience in patients with multiple sclerosis. *Neurology*. 1991;41:1829-1831.

10. Baclofen: Drug information. In: Basow DS, ed. *UpToDate*. Waltham, MA: UpToDate; 2010.

11. Fuller R, Branchey L, Brightwell D, et al. Disulfiram treatment of alcoholism. A veterans administration cooperative study. *JAMA*. 1986;256:1449.

12. Carmen B, Angeles M, Ana M, María AJ. Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: A systematic review. *Addiction*. 2004;99:811-828.

13. Mann K, Lehert P, Morgan MY. The efficacy of acamprosate in the maintenance of abstinence in alcohol-dependent individuals: Results of a meta-analysis. *Alcoholism-Clinical and Experimental Research*. 2004;28:51-63.

14. Srisurapanont M, Jarusuraisin N. Opioid antagonists for alcohol dependence. *Cochrane Database Syst Rev*. 2002;(2):CD001867.

15. Wright C, Moore RD. Disulfiram treatment of alcoholism. *Am J Med*. 1990;88:647-655.

16. Addolorato G, Caputo F, Capristo E, et al. Baclofen efficacy in reducing alcohol craving and intake: A preliminary double-blind randomized controlled study. *Alcohol Alcohol*. 2002;37:504-508.

17. Addolorato G, Leggio L, Ferrulli A, et al. Effectiveness and safety of baclofen for maintenance of alcohol abstinence in alcohol-dependent patients with liver cirrhosis: Randomised, double-blind controlled study. *Lancet*. 2007;370:1915-1922.

18. Addolorato G, Caputo F, Capristo E, Colombo G, Gessa GL, Gasbarrini G. Ability of baclofen in reducing alcohol craving and intake: II--preliminary clinical evidence. *Alcohol Clin Exp Res*. 2000;24:67-71.

19. Flannery BA, Garbutt JC, Cody MW, et al. Baclofen for alcohol dependence: A preliminary open-label study. *Alcohol Clin Exp Res*. 2004;28:1517-1523.

20. 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 and Alcoholism*. 2005;40:147-150.

21. Bucknam W. Suppression of symptoms of alcohol dependence and craving using high-dose baclofen. *Alcohol Alcohol*. 2007;42:158-160.

22. Agabio R, Marras P, Addolorato G, Carpiniello B, Gessa GL. Baclofen suppresses alcohol intake and craving for alcohol in a schizophrenic alcohol-dependent patient: A case report. *J Clin Psychopharmacol*. 2007;27:319-320.

TABLES

Table I: Characteristics of Reviewed Articles

Author and Journal	Addolorato et al[16] *Alcohol and Alcoholism*	Addolorato et al[17] *The Lancet*	Addolorato et al[18] *Alcoholism: Clinical and Experimental Research*	Flannery et al[19] *Alcoholism: Clinical and Experimental Research*	Ameisen, O.[20] *Alcohol and Alcoholism*	Bucknam W.[21] *Alcohol and Alcoholism*	Agabio et al[22] *Journal of psycho-pharmacology*
Date published	2002	2007	2000	2004	2005	2007	2007
Type of study	Randomized controlled study	Randomized controlled study	Open label study	Open label study	Self Case Report	Case Report	Case Report
Participants/ population	20 baclofen group 19 placebo group	42 baclofen group 42 placebo group *Note: all participants have liver cirrhosis*	10 males *Note: 34-54 y/o*	9 men, 3 women *Note: 4/12 diagnosed with depression*	50 y/o male *Note: Diagnosis of anxiety disorder**	59 y/o male *Note: diagnosis of major depressive disorder and anxiety*	55 y/o male *Note: diagnosis of schizophrenia*
Intervention	Baclofen 15 mg/day for 3 days, then 30 mg/day for 27 days	Baclofen 15 mg/day for 3 days, then 30 mg/day for 87 days	Baclofen 15 mg/day for 3 days, then 30 mg/day for 27 days	Baclofen 15 mg/day for 3 days, then 30 mg/day for 27 days	Baclofen 30 mg/day, adding 20 mg/day every 3 days until max of 270 mg/day Additional 20-40 mg dose as needed Maintenance dose 120 mg/day	Increased dose to max of 100mg/day -Used additional 40 mg/day as needed for stress	Baclofen 30 mg/day for 18 weeks -Increased dose to 75 mg/day for rest of the year
Validity score (0-8)	7/8	8/8	3/8	2/8	0/8	0/8	1/8

Table II: Validity Scoring System

Criterion	Score +1	Score 0
Trial type	Randomized controlled trials	Open label study, Case studies
Randomization	Study was described as randomized	Study was not described as randomized
Randomization description	Method to randomize was described and appropriate	Method of randomization was not described
Blinded	Study was double blinded	Study was not double blinded
Blinding method	Method of blinding was described	Method of blinding was not described
Drop-outs	Drop-outs were described	Drop-outs were not described
Craving Results based on validated scaling system	Validated scaling system used	No validated scaling system used
Referred family member to aid in distribution of medication and help record number of drinks	Referred family member used	Referred family member not used

Table III: Validity Scores for Reviewed Articles

Criterion (Scores 1 point for each)	Addolorato et al 2002[16]	Addolorato et al 2007[17]	Addolorato et al 2000[18]	Flannery et al 2004[19]	Ameisen 2005[20]	Bucknam 2007[21]	Agabio et al 2007[22]
Trial type	1	1	0	0	0	0	0
Randomization	0	1	0	0	0	0	0
Randomization description	1	1	0	0	0	0	0
Blinded	1	1	0	0	0	0	0
Blinding method	1	1	0	0	0	0	0
Drop-outs	1	1	1	1	0	0	0
Craving Results based on validated scaling system	1	1	1	1	0	0	1
Referred family member to aid in distribution of medication and help record number of drinks	1	1	1	0	0	0	0
Total Score	7	8	3	2	0	0	1

Table IV: Summary of Results

Study	Addolorato et al 2002[16]	Addolorato et al 2007[17]	Addolorato et al 2000[18]	Flannery et al 2004[19]	Ameisen 2005[20]	Bucknam 2007[21]	Agabio et al 2007[22]
Abstinence	Baclofen: 14/20 Placebo: 4/19	Baclofen: 30/42 Placebo: 12/42	Baclofen: 7/9	Baclofen: 0/12	Baclofen: 1/1	Baclofen: 1/1	Baclofen: 1/1
p value NNT* 95 % CI**	<0.005 2 N/A	<0.0001 2.3 2.4-16.1	N/A	N/A	N/A	N/A	N/A
Craving scale	OCDS	OCDS	ACS	PACS	None used	None used	OCDS
Mean craving baseline value	Baclofen≈26 Placebo≈22	Baclofen≈28 Placebo≈25	Baclofen≈9	Baclofen: 18.4	N/A	N/A	Baclofen:34
Mean craving final baseline	Baclofen≈6 Placebo≈ 12	Baclofen≈3 Placebo≈7	Baclofen≈0	Baclofen: 12.4	N/A	N/A	Baclofen <10
Number of dropouts due to side effects	0	0	0	2	0	0	0

*Number needed to treat
**Confidence Interval