British Journal of Medicine & Medical Research
4(5): 1164-1174, 2014

SCIENCEDOMAIN *international*
www.sciencedomain.org

Prescribing Guide for Baclofen in the Treatment of Alcoholism – for Use by Physicians

Pascal Gache[1], Renaud de Beaurepaire[2*], Philippe Jaury[3], Bernard Joussaume[4], Annie Rapp[5] and Patrick de La Selle[6]

[1]20 rue des Deux-Ponts, 1205 Genève, Switzerland.
[2]Groupe Hospitalier Paul-Guiraud, 54 avenue de La République, 94806 Villejuif, France.
[3]Département de Médecine Générale, Université Paris Descartes, Sorbonne Paris Cité, Faculté de médecine, Paris, France.
[4]3 place Estienne d'Orves, 83150 Bandol, France.
[5]243 boulevard Raspail, 75014 Paris, France.
[6]6 rue Paul Brousse,34000 Montpellier, France.

Authors' contributions

This work was carried out in collaboration between all authors. Author PG wrote the first draft, other authors RB, PJ, BJ, AR and PLS participated equally in the manuscript. All authors read and approved the final manuscript

Study Protocols

Received 23rd September 2013
Accepted 24th October 2013
Published 8th November 2013

ABSTRACT

The purpose of this guide is to help doctors prescribe baclofen in the treatment of alcohol problems as there is, to date, no standardized way to prescribe this molecule in the treatment of alcohol dependence. The Recommended Medical Practices in respect of baclofen prescription generally proposes, for neurological treatment, increasing dosage by 15mg every 3 days, while suggesting flexibility, that is to say, adapting dosages individually. The proposals below reflect the experience of the authors to this paper, experience which itself has been based on the original method described by Olivier Ameisen [1,2]. The authors have, between them, treated more than 1500 patients with this medication, and they have learned gradually and empirically how to use baclofen to help patients in the best possible way with alcohol problems. The experience of the authors is that there is no absolute consensus and that prescribers may have different approaches and practices in the conduct of treatment. At the present time, it is impossible to give a definitive answer to the question.

**Corresponding author: Email: debeaurepaire@wanadoo.fr;*

The bibliography (see References) includes four papers describing clinical experiences in which the authors have compiled their results [3,4,5,6].Other reports from the literature have also been taken in to account [7,8,9]. These recommendations are intended to help the prescription ofbaclofen.

Keywords: Off-label; high dose; side-effects; prescription schedule.

1. AMEISEN'S POSTULATE FOR THE HIGH DOSE PRESCRIPTION OF BACLOFEN

Alcoholism is a neurobiological disease which is symptom-driven; the elimination of these symptoms (loss of control of consumption, for example) suppresses the disease. Baclofen is, to date, the single molecule that has shown an ability to suppress the motivation to drink in experiments with rats; the use in humans should give similar results (translational model [1]. The reading ofAmeisen's book is recommendedto familiarize with the use ofbaclofenin the treatment of alcohol dependence.

2. FOR WHOM TO PRESCRIBE AND WHEN TO PRESCRIBE BACLOFEN? AS THE FIRST TREATMENT? WHEN ALL ELSE HAS FAILED?

The latest release of the French Society for Studies in Alcoholism (SFA) states that baclofen could be a therapeutic option when all other treatments properly conducted have failed. This is what happened to Olivier Ameisen when, almost in desperation, he self-administered 270mg of baclofen. Since 2006, when prescription of baclofen for alcoholism started, it has been mainly for patients who had tried repeatedly but failed to achieve sobriety. But with the media interest, more and more therapeutically "new" patients are asking for treatment with baclofen. Must we comply with their requests? Certainly an increase in prescribing is to be foreseen as a consequence of the results of ongoing controlled studies and of the clinical experience of prescribers. Some of us prescribe baclofen as a primary treatment for alcoholism, others only after other therapeutic approaches have failed, but in the absence of formal comparisons of baclofen with other treatments for alcohol dependence, it is difficult to give a categorical answer to this question. Here are some points which may help making adecision to prescribe:

- What is the history of the patient's alcohol use?
- What is the impact of alcohol consumption in the patient's life: severe? minimal?
- Has the patient ever followed non-drug treatments, in alcohol rehab centers, for example, for his alcohol problems? Which? How long? With what results?
- Has the patient ever taken medication to treat his alcohol problems? Which? With what results?
- What does the patient expect from baclofen? Does he know that the treatment is experimental and has not received formal approval from the authorities for use in alcohol problems?
- Has the patient been diagnosed with any psychopathological disorders: depression, anxiety, bipolar disorder? personality disorders?
- Is the patent taking any psychotropic medication? Which? Since when? With what effects?
- Does the patient have any current medical problems or a history, particularly, of epilepsy, liver, kidney, heart disorders, and incipient or active stomach ulcers?

- What is his daily environment? Social network? Family support? Employment status?

Taking into account these parameters, you can decide if you want to proceed with prescribing high doses of baclofen in the knowledge that the contra-indications are only of relative importance, with the exception of severe kidney disease and epilepsy. The considerations which are important in making the decision are primarily the history of the patient's attempts and failures at alcohol treatment, and the patient's motivation to take baclofen.

3. WHAT INFORMATION IS IT ESSENTIAL TO GIVE YOUR PATIENT BEFORE PRESCRIBING BACLOFEN?

1. Treatment with baclofen is intended to make one indifferent to alcohol, that is to say, to make the preoccupation with alcohol disappear from one's mind. Alcohol will gradually become a thought like any other, one which is no longer perpetually fixed in one's brain. The ultimate goal is to feel free from the urge to drink. Strict and permanent effortful abstinence from alcohol is no longer sought after.
2. Baclofen is an "old" drug which has been on the market for over 40 years. It is used to decrease muscular spasticity, that is to say, the muscle stiffness related to inactivity observed, for example, in individuals with paralyzed lower limbs. As a result, we have a good understanding of the adverse side effects and experience with its use over a sufficient length of time. There are also some studies of the use of baclofen at high doses [10,11] and its potential interactions with alcohol [12]. We therefore know pretty much what is to be expected with this medication.
3. The dose needed for one to reach the stage of indifference is not standard and will be determined based on the patient's reactions and feelings during the administration of the medication and the slow, careful and progressive increase of dosage. The patient himself will know when he feels he is at the right dose. The effective dose and the adverse side effects cannot be predicted before initiating treatment.
4. The maximal dose the patient will take will be highly variable, sometimes much higher than the doses usually prescribed for this medication and will vary between 0.5mg/kg/day to 5mg/kg/day or more. That is, for a person weighing 70kg, from 30mg to 350mg per day.
5. A slow and gradual increase in the dosage of the medication is essential to avoid the adverse side effects that occur when increasing the dose too quickly. On average, it takes 6 to 12 weeks to reach the effective dose.
6. The adverse side effects are well known but do not follow the same pattern in everyone. One may not have any adverse reaction, or, on the other hand, several that may be more or less unpleasant. Their development is variable but overall they tend to fade over time. They are reversible, in any event, as soon as you reduce the dose or, as the case may be, stop the medication. All of them are benign, except seizures, respiratory depression, severe mental confusion and severe mood disturbances (mania or depression).
7. The duration of treatment will depend on the patient's feelings. Some patients stop after a few months and have no further problem with alcohol without taking baclofen, but in most cases they must continue the treatment because they relapse if they stop taking baclofen.

8. Generally the patient will stay for several weeks or even months at the maximum effective dose, and, after a certain period of time, will gradually reduce the dose until he finds his maintenance dose. We lack experience to be more precise.
9. No consistent interactions are known between baclofen and any type of medication. The clinical observation shows the sedative effects of benzodiazepines and antipsychotics may be potentiated by baclofen, but, as far as we know, there is no published literature reporting these potentiating effects. Both baclofen and alcohol impair cognitive performance, the impairment being potentiated by the combination of the two [12]. No interactions have been reported between baclofen and drugs of abuse, such as cocaine, opiates, stimulants or cannabis. Baclofen is almost exclusively excreted unchanged through the kidney (excluding potential metabolic interactions or competition with degradation enzymes).

4. HOW TO PRESCRIBE BACLOFEN?

4.1 Initiating Treatment

There is a consensus that it is necessary **to increase the dosage gradually and at a sufficiently slow rate**. Generally one starts with small daily doses of about 10 or 15mg, then one increases to 30mg 3-4 days later and then increases by 10mg every 3 to 5 days until one reaches the therapeutic dose, which varies from one person to another and is unpredictable. There does not seem to exist any correlation between weight and dose.

Most prescribers recommend **not increasing too quickly, even if the drug is well tolerated**. Some, however, use a faster increase of 20mg every 3-4 days during the first two weeks, and often the second fortnight, and then slow the progression after the first month to a the slower rate of increase of 10mg every 3 to 4 days or 20mg per week.

When side effects become too severe, it is advisable to remain at the same dosage or to reduce slightly the dose. The two options are available to the prescriber: if the adverse reaction improves rapidly one can increase dose; if it does not improve rapidly, it will be wise to return to the lower dose that did not cause the side effect. We can then try again to increase after one to two weeks if the dose is not sufficient (possibly using half-tablets).

Some prescribers remain longer at certain dosages: 30mg, 60mg, 100mg, 150mg... But most see no real advantage in doing that.

Studies have shown that the average therapeutic dose is around 150mg/day and ranged from 30mg/day to 400mg/day. It is the clinical view and the feeling of the patient that must guide dose adjustment. The treatment is totally customized to the individual patient after the first two weeks of treatment in accordance with the patient's response to therapy. There is no established ceiling dose as long as the patient tolerates the treatment.

Experience has shown that it is not necessary to be sober to start treatment with baclofen. This decision will be discussed with the patient based on his clinical situation and the advantages or disadvantages of withdrawal. It is useful to remember that baclofen lowers the epileptic seizure threshold. Baclofen can also increase the alcohol-induced incoordination. Patients may be asked to deliberately moderate alcohol consumption during the first weeks of treatment, till "indifference" sets in. This will make the patient feel that he is actively involved in his treatment: he avoids social occasions for drinking, becomes aware of his

rituals and habits related to alcohol and frees himself of them, seeking other ways than taking alcohol to cope with life's stresses. But such an advice is not obligatory.

4.2.1 Continuing treatment

When the desired dose is reached and is well tolerated, it is recommended to stay at that dose for 2 to 3 months (sometimes less and sometimes more) and then try to reduce the dose to find the lowest effective dose. There is no established pattern as to how to reduce the dose. One way to determine the effective dose is to reduce the dose until the urge to drink returns, and then increase the dosage one level above this dose. The decrease can be done either very slowly (10 to 30mg per week) or in larger increments (back rapidly to two-thirds of the dose), the lower level being maintained for 1 or 2 months. The maintenance dose is often between one third and half the maximum dose reached.

4.2.2 Maintain lifelong treatment?

Baclofen has not been prescribed for long enough in alcohol addiction that we have the necessary clinical experience to be able to say how long the treatment will last. Experience has shown that it has been possible for some people to stop baclofen after a few months or years of treatment, but this is a minority of patients, while others must wait and see. Baclofen is very unlikely a lifelong treatment.

5. WHAT ARE THE ADVERSE SIDE EFFECTS OF BACLOFEN AND HOW TO MITIGATE THEM?

Side effects (SEs) are potentially numerous and clearly unpredictable in their occurrence during treatment, apart from the drowsiness that is the most common SE during this treatment. The list below is not exhaustive but represents both the main effects encountered during the administration of baclofen and the ways to mitigate them. It is important to emphasize the fact that irregular or disorganized taking of baclofen is a frequent cause of SEs. SEs have a fortunate tendency to disappear or lessen with a reduction in dose. They are also always reversible upon discontinuation of treatment. Discontinuation must be slow and progressive. Abrupt baclofen withdrawal may induce confusion, hallucinations and seizures. Baclofen is primarily excreted unchanged in the urine and should be used with caution in patients with renal disease.

It is curious but nonetheless remarkable that many patients continue their treatment in spite of suffering from some potentially very unpleasant side effects.

5.1 The Most Common Side Effects

Sleepiness: the best known and most anticipated of SEs. Patients frequently describe a sudden and almost irresistible desire to sleep rather than true sleepiness. It often occurs during the first days of treatment. It tends to lessen as time passes. It is sometimes very troublesome especially among working people. It is often reported as having a maximum effect after lunch, so much so that some patients start taking their tablets after lunch to avoid the postprandial sleepiness. Car drivers and people using potentially dangerous tools (such as saws or other dangerous devices) must be carefully warned not to use their vehicles or tools, especially early in treatment.

Fatigue: This is another commonly reported effect whose development is similar to that of somnolence. Patients may report the feeling of fatigue or of somnolence or both simultaneously. Like somnolence, fatigue resolves favorably over time.

Dizziness: Of variable intensity, patients describe this as an uncomfortable sensation during which they are afraid of falling. In terms of symptomatology this is a false vertigo. These sensations of dizziness often occur in the morning and resolve during the day. When they are too troublesome, it may be necessary to reduce the dose temporarily or permanently.

Headaches: These are reported as mainly occurring in the morning, in the skull and sometimes throbbing; they fade during the day. They often respond well to conventional analgesics. They usually diminish with continued treatment. They are sometimes accompanied by bizarre feelings, such as having the head tightened or crushed.

N**ausea, vomiting, gastrointestinal disorders:** The frequent complaints are difficult to relate to baclofen, especially in early treatment because they are often symptoms described by patients at that time and especially if they stop drinking. It seems nonetheless that nausea in particular is the subject of numerous but temporary complaints.

Sleep disorders: A paradoxical effect. Patients may complain of daytime sleepiness and sleep disorders. The addition of a hypnotic is desirable when the sleep deficit is too high. However, this can be dangerous in alcoholics with respiratory problems: The additive effects of alcohol, baclofen and a hypnotic could cause respiratory depression. These sleep disorders may be accompanied by psychomotor agitation of variable intensity and sometimes painfully felt by those around them. They are sometimes accompanied by very realistic or even frightening dreams or nightmares which can be very destabilizing.

5.2 The Least Frequent SEs

Tremors: in the upper extremities, they are typically mild. They do not reduce much with continued treatment.

Double vision: highly related to the muscle-relaxant properties of baclofen, it resolves well with continued treatment.

Painful paraesthesia in arms and legs: Occurring generally at night, it can be quite debilitating and seriously jeopardize the continuation of treatment. Patients report a sensation of tightness or even crushing in the upper and lower limbs accompanied by paraesthesia of varying intensity. This often persists and usually requires a temporary reduction or sometimes permanent reduction in dose.

Nocturnal apnoea: A temporary cessation of breathing during sleep. These brief apnoeas should lead the physician to examine the possibility of a true sleep apnoea syndrome which may have been revealed or even triggered by taking baclofen. A specific treatment of sleep apnoea is needed before continuing baclofen treatment.

Mania or hypomania mood shift: This is probably infrequent but nevertheless rather “disturbing” clinically. It takes the form of a reduction in the duration of sleep, diurnal excitement, nocturnal agitation, tachypsychia (acceleration of the succession of thoughts), behavioural disinhibition, verbal diarrhoea (logomania) and sometimes confused ideas. These symptoms may occur for the first time in patients with no history of bipolar disorder.

They necessitate the reduction or cessation of the treatment, depending on their severity. It is sometimes necessary to prescribe a sedative, or better still a mood regulator (such as valproic acid) until symptoms disappear. However, valproic acid can be hepatotoxic, potentially dangerous in a patient with alcoholic cirrhosis.

Confusional syndrome/delirium: Onset may be sudden or gradual. It is potentiated by the concomitant use of alcohol and benzodiazepines. The patient may present in a disturbing manner to those around him yet be unaware of his condition. This syndrome may necessitate a reduction in dosage or cessation of the treatment or admission to hospital. More frequently, the confusion has a minor form, consisting in transient memory impairment, or moments of distractibility or perplexity. The syndrome always disappears when the treatment is discontinued.

Morbid thoughts: They may reveal an underlying depression hitherto offset by the consumption of alcohol or be the result of a sudden and painful awareness (painful lucidity) of a particularly deteriorated somatic, mental, emotional or social condition.

Other adverse effects: Some patients have complained of pain in the gums, of slurred speech, unilateral or bilateral tinnitus, chest tightness, oedema of the lower limbs or urinary problems. Baclofen also induces ovarian cysts in 4% or more of female patients.

Anorgasmia/loss of libido: This side effect, not described in published studies, seems in fact to be frequent but is not always reported in the lists of SEs. Future studies should seek to assess its frequency.

6. BACLOFEN: IS IT SUFFICIENT ON ITS OWN?IS THERE A PLACE FOR OTHER APPROACHES ALONG WITH THIS PRESCRIPTION?

Baclofen is intended to make patients indifferent to alcohol and free them from their addiction. Olivier Ameisen, having followed a large number of treatments and attended thousands of AA meetings before taking baclofen, has written very clearly in his book [2], that baclofen had allowed him to put into practice what he had learned during his cognitive behavioural psychotherapy and his AA meetings. Baclofen gave him the space to reflect and to redirect his life. He was able to do this by applying all the strategies he had learned so far but could not use because his cravings were too intrusive.

Many of us have been struck by the nature of consultations with patients on baclofen. Very often, and certainly in the early stages, they are simply pharmacotherapy consultations during which there is no mention of adverse side effects, doses of baclofen or variations of craving. When the effective dosage is reached at the cost of adverse effects, many difficulties remain, particularly psycho-social difficulties. Baclofen, even when it is very effective, does not cure solitude, the sheer pain of living, difficulties with interpersonal relations, or unemployment, but it allows one to take one's distance and face reality, and thus sometimes to suffer acutely as one becomes aware of the mess one has made of one's life. In this context, it is essential that patients continue to get support on their journey towards their psycho-social recovery. And it is appropriate at this stage to encourage and help patients to improve their psychological state, to overcome their isolation and to find pleasure in life. To do this, a multidisciplinary approach is important.

In the presence of anxiety, depression, bipolar disorder, or borderline states where alcoholism is a symptom, psychiatric treatment adapted to these conditions will be

maintained. Baclofen does not present contra-indications with the usual psychotropic drugs (benzodiazepines, hypnotics, SSRIs, neuroleptics...). Benzodiazepines and hypnotics can induce additive respiratory depression with baclofen.

Psychotherapy, cognitive-behavioural or not, and participation in support groups is of great help, although this will be difficult for the group when patients have not chosen completeabstinence. All this remains to be developed. The paradigm shift brought about by baclofen treatment requires rethinking the therapeutic methods for the whole field of alcoholism.

The value of baclofen consists in this new space that it gives patients, to rethink and reorganize their lives. As with any withdrawal, a period of moderate or severe depression may occur. The patient finds himself facing his own reality, which was hiding behind alcohol. To accompany him on this personal journey is part of the treatment plan.

The patient's entourage, those close to the patient, must also move from insistence on abstinence, with its attendant pressures, to encouragement to reduce consumption and to maintain compliance with baclofen treatment. Some prescribers will find it useful to establish systematic contact with the patient's immediate family and friends, even having them attend at their offices, so as to assist them with this change of attitude.

7. WHAT ARE THE RISKS OF PRESCRIBING BACLOFEN: OFF-LABEL PRESCRIBING?

Prescribing a drug outside of its usual and accepted uses is widely practiced in medicine regardless of the specialty (general medicine, paediatrics, psychiatry...). It has often happened that it is discovered that a molecule can have unsuspected properties in an unexpected therapeutic area (aspirin/cardio, carbamazepine as a mood stabilizer, antidepressants in chronic pain, etc.).

Legislators have foreseen this situation and provided for it (for France [13]). Off-label prescribing is permitted under the following conditions:

- Scientific data justify this therapeutic use.
- It is required as a treatment due to the failure of properly conducted conventional therapies.
- The patient has been given comprehensive information concerning the potential benefits and risks of the treatment.
- Informed consent of the patient and his written acceptance to take this treatment with full knowledge of the risks involved.
- Appropriate medical monitoring.
- The patient is informed of the possibility of non-reimbursement of the prescription.

Under these conditions, the off-label prescription is legitimate and ethically defensible, but it will remain an off-label prescription and in this sense always entails some risk if something goes wrong and there are serious adverse reactions (e.g., a drowsy patient who falls asleep at the wheel of his car and causes an accident).

7.1 Consent for Treatment with Baclofen (To be filled and signed by the patient before treatment initiation)

- I hereby certify that I have received from Dr. X detailed information regarding the treatment with baclofen in high doses (HD) to treat my problems with alcohol.
- I know that this treatment has not received formal authorization from the competent authorities. I want to take this treatment despite the potential side effects because so far I have not found any effective solution to my problems with alcohol.
- I understand that the main side effects are: drowsiness, fatigue, headaches, dizziness and sleep disturbance. In rare cases, delirium may occur. Dr. X has informed me that this state of mental confusion requires stopping the increase of doses and perhaps stopping treatment.
- I have clearly informed Dr. X of all my medical history, so that he could determine whether particular rules of caution should be applied to my baclofen prescription.
- Due to possible withdrawal symptoms upon discontinuation of baclofen, I know that one should not abruptly stop taking baclofen, but gradually decrease as instructed by Dr. X.
- I undertake not to drive my car or use dangerous machinery for at least the time of the increase in dosage and to resume such activities only in consultation with Dr. X.
- I undertake to follow scrupulously the directions and prescriptions made by Dr. X and to keep him/her informed of the difficulties and problems that may occur during this treatment.
- Should I encounter serious problems related to this treatment, I strongly urge my relatives not to initiate legal proceedings against Dr. X (this point is not unanimous among prescribers).

- I have had sufficient time to make my decision to undergo this treatment.

_____"read and approved"

Name:

Date:

7.2 Baclofen Treatment Schedule

There is no prescription schedule (titration) for baclofen which has absolute validity and each doctor can prescribe it differently. The principle of prescription is that, to avoid reactions of intolerance, patients must slowly and progressively become habituated to the effects of baclofen.The simplest way to prescribe baclofen, and probably the most widely used, consists in giving one more tablet (10mg) every three days, tid (morning, noon and evening) (reaching approximately 100mg per month). We propose below another schedule, a cautious qid schedule. This prescription schedule is a pattern we have adopted by consensus, without claiming that this is necessarily the best regimen. In particular, the bedtime prescription, which may not be necessary given that patients rarely drink during nighttime, is not used by all the authors.

7.2.1 Schedule with four doses per day

Baclofen 10mg (up to 200mg/day)

Day	8 a.m.	1 p.m.	6 p.m.	At bedtime	Total
D1 D2 D3 D4 D5	½	/	/	½	1
D6 D7 D8 D9D10	½	½	½	½	2
D11 D12D13 D 14 D15	1	½	½	1	3
D16D17 D18 D19 D20	1	1	1	1	4
D21 D22 D23 D24 D25	1½	1	1	1½	5
D26 D27 D28 D29 D30	1½	1½	1½	1½	6
D 31 D32 D33 D34 D35	2	1½	1½	2	7
D36 D37 D38 D39 D40	2	2	2	2	8
D41 D42 D43 D44 D45	2½	2	2	2½	9
D46 D47 D48 D49 D50	2½	2½	2½	2½	10
D51 D52 D53 D54 D55	3	3	3	3	12
D56 D57 D58 D59 D60	4	3	3	4	14
D61 D62 D63 D64 D65	4	4	4	4	16
D66 D67 D68 D69 D70	5	4	4	5	18
D71 and following	5	5	5	5	20

- Do not shorten the stages to less than 3 days even if treatment is well tolerated.
- Extend the duration of the stages beyond 5 days if levels of drowsiness or some other bothersome side effect has not disappeared.
- If unbearable side effects occur, reduce the dosage to the level below, wait a week or 2, and increase slowly the dosage using half-tablets. In case of recurrence of these events, you must not increase the dose, you stick to the dose that does not cause these effects, and see your physician.
- Do not stop taking baclofen abruptly, but gradually decrease over 10-15 days.
- If there is a strong urge to drink, take 10mg (1 tab.) of baclofen, or more.
- Do not drive your car during the increase of dosage.

ACKNOWLEDGEMENTS

The authors are grateful to David Harris for translating this guide from French.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. 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 Alcohol. 2005;40:147-5.
2. Ameisen O. The End of My Addiction. New York: S Crichton Books; 2008.
3. Ameisen O, de Beaurepaire R. Suppression de la dépendance à l'alcool et de la consommation d'alcool par le baclofène à haute dose: un essai en ouvert. Ann Med-Psychol. 2010;168:159-62. French.

4. Dore GM, Lo K, Juckes L, Bezyan S, Latt N. Clinical experience with baclofen in the management of alcohol-dependent patients with psychiatric comorbidity: a selected case series. Alcohol Alcohol. 2011;46:714-2.
5. Rigal L, Alexandre-Dubroeucq C, de Beaurepaire R, Le Jeunne C, Jaury P. Abstinence and 'low risk' consumption one year after the initiation of high-dose baclofen: a retrospective study among 'high risk' drinkers. Alcohol Alcohol. 2012;47:439-42.
6. de Beaurepaire R. Suppression of alcohol dependence using baclofen: a 2-year observational study of 100 patients. Front Psychiatry. 2012;3:103.
7. Bucknam W. Suppression of symptoms of alcohol dependence and craving using high-dose baclofen. Alcohol Alcohol. 2007;42:158-60.
8. 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;27:319-20.
9. Pastor A, Jones DM, Currie J. High-Dose Baclofen for Treatment-Resistant Alcohol Dependence. J Clin Psychopharmacol. 2012;32:266-8.
10. Smith CR, LaRocca NG, Giesser BS, Scheinberg LC. High-dose oral baclofen: experience in patients with multiple sclerosis. Neurology. 1991;41:1829-31.
11. Leung NY, Whyte IM, Isbister GK. Baclofen overdose: defining the spectrum of toxicity. Emerg Med Australas. 2006;18:77-82.
12. Evans SM, Bisaga A. Acute interaction of baclofen in combination with alcohol in heavy social drinkers. Alcohol Clin Exp Res. 2009;33:19-30.
13. Paoletti O. La prescription hors AMM. Neurologie. 2003;6:46-48. French.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history.php?iid=315&id=12&aid=2459