One year of baclofen in 100 patients with or without cirrhosis: a French real-life experience

Camille Barrault[a], Hortensia Lison[d], Françoise Roudot-Thoraval[b], Armand Garioud[d], Charlotte Costentin[c], Véronique Béhar[a], Mourad Medmoun[d], Georges Pulwermacher[d], Hervé Hagège[a] and Jean-François Cadranel[d]

Background Several studies have suggested the efficacy of baclofen in reducing alcohol consumption, leading to a temporary recommendation for use in France.

Aim Our aim was to report our experience in using baclofen in alcohol-dependant patients with or without liver cirrhosis.

Patients and methods Consecutive patients from two liver and alcohol units were recruited over a 3-year period and received increasing doses of baclofen associated with social, psychological, and medical care.

Results One hundred patients were treated, of whom 65 were cirrhotic. After 1 year, 86 patients were still being followed up. At a mean dosage of 40 mg/day (extremes: 30–210), the median daily alcohol consumption reduced from 80 to 0 g/day ($P < 0.001$). Twenty patients drank a small amount of alcohol of up to 30 g/day and 44 patients were completely abstinent. These declarative results were associated with a significant improvement in alcohol-related biological markers in this 'low-consumption' group of 64 patients: the median γ-glutamyl transferase decreased from 3.9 to 2.0 UNL ($P < 0.001$), the mean aspartate transaminase decreased from 2.6 to 1.2 UNL ($P < 0.001$), and the mean corpuscular volume decreased from 101 to 93 μm^3 ($P < 0.001$). In cirrhotic patients, bilirubinemia decreased significantly from 22 to 11 $\mu mol/l$ ($P = 0.026$), prothrombin time increased from 68 to 77% ($P < 0.001$), and albuminemia increased from 34.1 to 37.4 g/l ($P < 0.001$). Twenty patients reported grades 1–2 adverse events. No liver or renal function deterioration occurred in cirrhotic patients.

Conclusion In our cohort, baclofen associated with a global care was very well tolerated even in cirrhotic patients. The marked reduction in alcohol consumption in 64 patients translated into a significant improvement in biological markers and in liver function tests. Baclofen could be very useful, especially in cases of severe alcoholic liver disease. *Eur J Gastroenterol Hepatol* 00:000–000 Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.

Introduction

Alcoholic liver disease (ALD) is the most prevalent cause of advanced liver disease in Europe. In Europe, 6.5% of all deaths and 11.6% of disability-adjusted life-years (DALYs) are attributable to alcohol. The burden of alcohol is the highest of total illness and premature deaths of all WHO regions. Alcohol consumption is responsible for 3.8% of global mortality and 4.6% of DALYs lost because of premature death [1–4]. In France, alcohol is the first cause of hospitalization, with 580 000 in patients [5] a year, leading to 49 000 deaths attributable to alcohol in 2009 [6].

Baclofen is a γ-amino-butyrate acid-B (GABA-B) receptor agonist with renal elimination. It has been used since 1975 to treat neurological spasticity with a good tolerance. Although its mechanism of action in addictions is not well established, some preclinical and clinical studies have suggested its efficacy in reducing alcohol consumption [7,8]. GABA agonists inhibit dopaminergic pathways and could block the 'reward effect' of alcohol. It could reduce or suppress ≪craving≫, 'reward' leading to a reduction of alcohol consumption or abstinence at a low dose [8] or a high dose [9–12]. It has been tested at a low dose in a randomized study in cirrhotic patients in 2007 [13] and at a high dose in an open-label series [12].

In France, the use of baclofen in difficult-to-treat alcohol-dependent patients is authorized since June 2012, but some addiction specialists started to use it off-label for some patients in a 'compassionate' way on the basis of these studies. On 14 March 2014, a temporary recommendation for use of baclofen to reduce alcohol consumption or to maintain abstinence after alcohol withdrawal was made by the French drug agency [14]. Two French randomized studies versus placebo (bacloville and alpadir) have been completed, whose preliminary results (*http://isbra-esbra-2016.org/essential_grid/high-dose-baclofen-for-the-treatment-of-alcohol-drinkers-bacloville-clinicaltrials-gov-identifier-nct01604330/*, *http://isbra-esbra-2016.org/essential_grid/a-randomized-double-blind-placebo-controlled-efficacy-study-of-high-dose-baclofen-in-alcohol-dependent-patients-the-alpadir-study/*) suggest a slight superiority of baclofen in terms of abstinence and reduction in alcohol consumption, but almost 1/3 of patients were lost to follow-up. Nevertheless, the final results are not yet available.

Moreover, in the special population of cirrhotic patients, there is a relative emergency in stopping or at least reducing alcohol consumption, but few treatments are available [15]:

(i) disulfirame has dangerous neurological and hepatic side effects and is no longer recommended in France; (ii) naloxone (which is not recommended in cirrhotic patients) and acamprosate are used in abstinent patients after alcohol withdrawal; (iii) nalmefene could be used in patients with Child-Pugh (CP) A or B cirrhosis, but not in case of opioid substitution and was not available in France before September 2014; and (iv) γ-hydroxybutyrate is not available in France.

We aimed to report our experience of baclofen use in a series of consecutive alcohol-dependant patients with or without ALD.

Patients and methods

Between June 2010 and October 2013, 100 consecutive patients followed up in two French liver units of nonacademic hospitals, located close to Paris (Creil and Créteil) and including addiction specialists, were offered treatment by baclofen for alcohol dependence (*Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. criteria). The goal of baclofen treatment was to reduce alcohol consumption or to obtain or maintain abstinence. It was prescribed in three situations: (i) outpatients who asked for it; (ii) patients who wanted to reduce alcohol consumption (sometimes as a first step in the path to abstinence); and (iii) to maintain abstinence after voluntary or involuntary withdrawal (e.g. hospital stay for ALD) when acamprosate and/or naltrexone (or disulfiram) had previously failed or were contra-indicated.

Inclusion criteria

Patients could be hospitalized for a physical complication of alcohol (alcoholic liver disease, alcohol-related pancreatitis, alcohol withdrawal, etc.) or seen as outpatients with or without ALD. Patients were of any sex over 18 years of age. Normal renal function (creatinine level) was requested to initiate treatment.

Exclusion criteria

Contra-indications for baclofen treatment were uncontrolled epilepsy, patent hepatic encephalopathy, and renal failure. Patients did not receive baclofen in case of unstable psychiatric condition such as melancholic depression or unstable psychosis. By contrast, follow-up by a psychiatrist for other reasons was not an exclusion criterion.

Initiation of treatment

Before treatment initiation, patients received oral and written information by the prescribing physician on baclofen use. Patients were aware of off-label use of this treatment, prescribed at a potentially higher dose than for neurological indications, and of potential adverse events. We used a 'à la carte' treatment without a pre-established dose with a close medical supervision by the referent physician. A hepatologist or a medical addiction specialist initiated baclofen treatment at an initial dose of 15 mg/day (5 mg three times a day). The dose was slowly increased (10 mg every 3 days) until achievement of alcohol indifference, meaning absence of craving or low craving (using a visual analogical scale). In case of any side effect, dose escalation was stopped or reduced until improvement. The dose could sometimes be temporarily reduced in case of adverse events. Medication was always associated with standard medical, psychological, and social care in the context of a multidisciplinary team including a hepatologist, a medical addiction specialist, social workers, and psychologists, providing at least supportive psychotherapy. One month medication was dispensed by the patient's usual pharmacy.

Data collection

Patients

We prospectively collected demographic data, addiction data (daily alcohol consumption, history of alcohol consumption), and medical data (presence of cirrhosis and CP score, baclofen dosage).

Biological data collected were: (i) data on alcohol consumption: mean corpuscular volume (MCV), γ-glutamyl transferase (GGT), aspartate transaminase (AST), platelets and (ii) liver function tests (cirrhotic patients): prothrombin time, international normalized ratio, bilirubinemia, albuminemia. These biological data were recorded at baseline and at regular intervals during a 1-year follow-up (first month, third month, sixth month, ninth month, and 12th month). Side effects were regularly determined. We present the 12 month results for the first 100 patients treated before the extension to a national survey.

Statistical study

Results are presented as number (%) for categorical data and mean ± 1SD or median (interquartile range) for continuous data depending on the distribution.

Baseline and 12 month data were compared using the Wilcoxon test for paired variables and the Mann–Whitney test for unpaired continuous variables. *P* values up to 0.05 were considered significant. Analyses were carried out using SPSS (SPSS Corp, Chicago, Illinois, USA) and Stata (Stata Corp, College Station, Texas, USA) statistical packages.

Results

Patients population

One hundred patients were included and initiated baclofen. The main demographic data at baseline are shown in Table 1.

Clinical background

Seventy-five (75%) patients were men, 10 patients (eight cirrhotic patients) had associated chronic hepatitis C, three patients were hepatitis B surface antigen carriers, and none was HIV seropositive. One patient was treated by peginterferon and boceprevir during follow-up. Sixty-five (65%) patients had cirrhosis; CP grade was A in 43 (66%) cases, B in 12 (18.5%) cases, and C in 10 (15.5%) cases. Sixteen (16%) patients had chronic pancreatitis.

Biological background

Baseline values of biomarkers are presented in Table 2. We observed higher values of alcohol consumption markers (MCV, GGT, platelets count) along with markers of ALD

(AST) and hepatic insufficiency (albuminemia, bilirubinemia, and PT) in cirrhotic patients.

Addiction background

The initial median daily alcohol consumption (DAC) was 80 (50–120) g/day (ranging from 0 to 440). In the cirrhotic patients, the median DAC was 93 (60–128) g/day. The majority of patients had consulted an addiction specialist in their medical history: 75% had had one or many medical examinations, whereas 36% had experienced an outpatient withdrawal, 43% had a hospital withdrawal, and 42% had been hospitalized for a long duration in an addiction unit. Patients had been 'heavy drinkers' for a mean period of 14.9 ± 7.1 years.

Follow-up

A hepatologist and an addiction specialist followed up all cirrhotic patients. An addiction specialist trained in hepatology followed up noncirrhotic patients.

At 12 months, 86 of 100 patients were still being followed up (Fig. 1). Twelve patients were lost to follow-up and were considered 'treatment failure'. Two patients died (one death related to an esophagus carcinoma and one death related to a severe alcoholic hepatitis after 3 months of treatment). Among the 86 followed-up patients, 83 were still being treated at the end of follow-up. Three patients spontaneously decided to stop baclofen before the end of follow-up: one patient reported an excessive number of pills (24 pills a day) with an insufficient effect on consumption and two other patients stopped treatment because they no longer drank.

Baclofen posology

The mean dose of study medication was 40 (30–60) mg/day. The maximum dose reached was 240 mg/day during the study in one cirrhotic patient. Eight patients received at least 120 mg/day during the study (two of them stopped treatment before M12). Four of these eight patients had cirrhosis, but no one experienced a neurological adverse event (no patent hepatic encephalopathy). Most of the patients continued on baclofen after the end of the study.

Baclofen and alcohol consumption

At a median baclofen dosage of 40 (30–60) mg/day, we observed a significant decrease in the median daily alcohol consumption from 80 (50–120) to 0 (0–30.5) g/day (extremes: 0–140) ($P = 0.004$). In cirrhotic patients, the median DAC decreased from 93 (60–128) to 0 (0–37.5) g/day.

A reduction of more than 50% of initial alcohol intake was observed in 77 (77%) patients; this group was named the 'response group' as defined by Ameisen *et al.* [16]. Among these patients, a 'low-consumption group' was defined by a DAC of up to 30 g/day (French alcohol consumption low-risk threshold [15]). Among these 64-pooled patients, 44 were completely abstinent and 20 had a residual median consumption of 10 g/day (extremes: 5–30) at the end of the study. These declarative data were associated with an improvement in alcohol-related markers: a significant decrease in the mean MCV from 101 ± 10 to $93 \pm 4 \, \mu m^3$ ($P < 0.001$), mean AST from 2.6 ± 1.8 to 1.2 ± 0.4 UNL ($P < 0.001$), and median GGT from 3.9 (2.4–6.1) to 2.0 (1.4–2.2) UNL ($P < 0.001$). In the 'non response group' (23%), patients maintained a high level of drinking (stable alcohol intake or small reduction) ($n = 7$), had stopped treatment ($n = 2$), were lost to follow-up ($n = 12$), or died ($n = 2$). In contrast, we observed no improvement in alcohol-related markers in the high-consumption group (Table 3).

Then, two separate groups could be distinguished: a 'low-consumption group' defined by a DAC of up to 30 g/day and a 'high-consumption group' of 22 patients who

Table 1. Initial medical and social data in the entire population and in the cirrhosis subgroup

	n (%)			
Population data	Total ($n = 100$)	No cirrhosis ($n = 35$)	Cirrhosis ($n = 65$)	*P*
Age (mean ± SD) (years)	53.0 ± 9.5	50.1 ± 11.3	54.5 ± 8.1	0.026
Male [*n* (%)]	74 (74)	24 (69)	50 (77)	0.364
Living alone	32 (32)	11 (31)	21 (32)	0.928
Working	39 (39)	11 (31)	28 (43)	0.022
Pancreatitis	16 (16)	7 (20)	9 (14)	0.423
DAC [median (interquartile range)] (g/day)	80 (50–120)	80 (50–120)	93 (60–128)	0.237
Inpatient or outpatient detoxification	58 (58)	19 (54.3)	38 (58.5)	0.833
Medical history of addictologist follow-up	75 (75)	30 (85.7)	45 (69.2)	0.091
Medical history of long-duration hospitalization	42 (42)	19 (54)	23 (35)	0.090
Child Pugh A	–	–	43 (66)	–
Child Pugh B	–	–	12 (18)	–
Child Pugh C	–	–	10 (15)	–

DAC, daily alcohol consumption.

Table 2. Initial biological data in the entire population and in the cirrhosis subgroup

	Mean ± SD			
Biological data	Total ($n = 100$)	No cirrhosis ($n = 35$)	Cirrhosis ($n = 65$)	*P*
Prothrombin time (%)	79 ± 20	97 ± 14	69 ± 15	< 0.001
Bilirubinemia [median (interquartile range)] (µmol/l)	16 (9–35)	8 (6–10)	24 (15–48)	< 0.001
Albuminemia (g/l)	35.3 ± 5.6	38.0 ± 4.1	34.3 ± 5.7	0.004
AST (× UNL)	2.6 ± 1.7	2.2 ± 1.3	2.8 ± 1.8	0.073
ALT (× UNL)	2.4 ± 1.8	1.9 ± 1.1	2.6 ± 2.1	0.108
GGT [median (interquartile range)] (× UNL)	3.9 (2.5–6.4)	3.0 (1.7–5.4)	5 (2.7–8.2)	0.013
MCV (µm³)	101 ± 9	100 ± 10	102 ± 8	0.278
Platelets (10^9/l)	170 ± 71	218 ± 74	145 ± 55	< 0.001

ALT, alanine transferase; AST, aspartate transferase; GGT, γ-glutamyl transferase; MCV, mean corpuscular volume.

drank more than 30 g/day, with a median DAC of 60 g/day (extremes: 35–80). No predictive factor of response was identified as shown in Table 4.

In the subgroup of cirrhotic patients, improvement in the biological alcohol-related markers (Table 4) was parallel to an improvement in hepatic liver function tests despite no difference in biological data between low-consumption and high-consumption groups at day 0. In contrast, at the end of the study, we observed in cirrhotic patients with low alcohol consumption ($n = 41$) a significant decrease in the median total bilirubinemia from 22 to 11 µmol/l ($P = 0.026$) and a significant increase in the mean albuminemia from 34.1 to 37.4 g/l ($P = 0.007$) and the mean prothrombin time from 68 to 77% ($P < 0.001$).
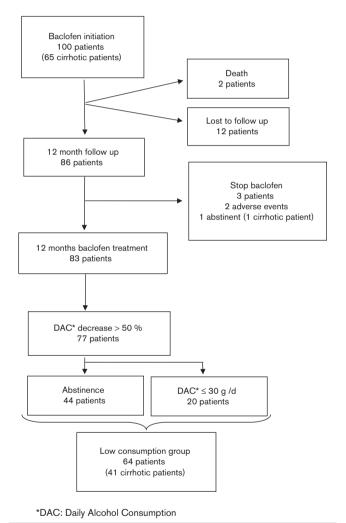
Table 4. Comparison of medical and social data between low-consumption and high-consumption groups

| | n (%) | | |
	DAC ≤ 30 g/day at 12 months	DAC > 30 g/day at 12 months	P
Age (mean ± SD) (years)	51.8 ± 10.2	54.8 ± 8.7	0.209
Male	45 (70.3)	17 (77.3)	0.530
Living alone	19 (29.7)	6 (27.3)	0.830
Not working	44 (68.7)	15 (68.2)	1.000
Cirrhosis	41 (64.1)	15 (68.2)	0.727
Outpatient detoxification	23 (35.9)	8 (36.4)	0.971
Inpatient detoxification	30 (40.6)	8 (36.4)	0.392
Addictologist examination	45 (70.3)	19 (86.4)	0.137
Long duration hospitalization	25 (39.1)	10 (45.5)	0.599

DAC, daily alcohol consumption.

It is noteworthy that no improvement was observed in the high-consumption group (Table 3). An improvement in the CP score was observed in 11 patients: two patients moved from CP-C to CP-B, three from CP-C to CP-A, and five moved from CP-B to CP-A. Moreover, in one case, the reduction of alcohol consumption and improvement in hepatic function enabled the initiation of hepatitis C virus, leading to hepatitis C virus cure.

Factors associated with treatment success

Baseline demographic and medical data were comparable in the high-consumption and the low-consumption groups (Table 5). Baseline biological data were comparable, except albuminemia (higher in the high-consumption group). Surprisingly, patients with low consumption had a significantly lower end dose of baclofen: 40 (30–50) mg than patients with a high consumption: 55 (40–75) mg/day ($P = 0.005$). This could suggest a relative resistance to treatment in this population. We also may have increased the dose in some patients because of lack of efficacy.

Safety

Tolerability of the study medication was fair in all patients. No evidence of baclofen abuse or overdose was identified. No drug-related serious adverse events occurred, in particular, no patent hepatic encephalopathy or liver function deterioration or renal impairment. The two deaths were not related to baclofen: one patient died of severe alcohol hepatitis before 3 months and one patient died of esophagus carcinoma. However, we observed minor side effects in 12 (28%) cases: five cases of vertigo and seven cases of drowsiness, improving with decreased dosing.

Fig. 1 . Patients' follow-up and results.

Table 3. Biological data evolution (between day 0 and month 12) in the low-consumption and high-consumption groups of all patients

| | DAC ≤ 30 g/day at 12 months (n = 62) | | | DAC > 30 g/day at 12 months (n = 22) | | |
Biological data	Day 0	Month 12	P	Day 0	Month 12	P
AST (mean ± SD) (× UNL)	2.6 ± 1.8	1.2 ± 0.4	< 0.001	2.6 ± 1.5	1.7 ± 0.7	0.006
GGT [median (interquartile range)] (× UNL)	3.9 (2.4–6.1)	2.0 (1.4–2.2)	< 0.001	5.0 (2.8–7.8)	3.0 (2.3–5.5)	0.26
MCV (mean ± SD) (µm³)	101 ± 10	93 ± 4	< 0.001	103 ± 5	97 ± 8	0.002
Platelets (10⁹/l) [median (interquartile range)]	158 (123–219)	204 (121–254)	0.039	176 (133–216)	161 (116–200)	0.145

At M12, between-group differences were significant at $P < 0.001$ for AST, GGT, and MCV; there was a trend for platelets with $P = 0.076$.
AST, aspartate transferase; DAC, daily alcohol consumption; GGT, γ-glutamyl transferase; MCV, mean corpuscular volume.

Table 5. Biological data evolution (between day 0 and month 12) in the low-consumption and high-consumption groups of cirrhotic patients

Biological data	DAC ≤ 30 g/day at 12 months (n = 41)			DAC > 30 g/day at 12 months (n = 15)		
	Day 0	Month 12	P	Day 0	Month 12	P
Prothrombin time (%)	68 ± 14	77 ± 15	< 0.001	75 ± 9	75 ± 13	0.826
Bilirubinemia (µmol/l)	22 (13–49)	11 (8–26)	0.026	22 (17–33)	23 (14–32)	0.755
Albuminemia (g/l)	34.1 ± 5.2	37.4 ± 6.1	0.007	36.8 ± 6.0	36.1 ± 6.1	0.732
AST (× UNL)	2.8 ± 2.1	1.2 ± 0.3	< 0.001	2.8 ± 1.4	1.8 ± 0.8	0.004
GGT (× UNL)	4.5 (3–7)	2.0 (1.5–2.5)	< 0.001	5.0 (3–10)	4.0 (3–8)	0.451
MCV (µm^3)	102 ± 8	93 ± 4	< 0.001	102 ± 5	97 ± 9	0.025
Platelets (10^9/l)	146 ± 6.2	162 ± 81	0.310	156 ± 4.4	140 ± 5.4	0.311

AST, aspartate transferase; DAC, daily alcohol consumption; GGT, γ-glutamyl transferase; MCV, mean corpuscular volume.

One patient experienced a temporary withdrawal of 10 days. One patient terminated treatment because of uncomfortable hyperhidrosis and another because of the number of pills (24 pills a day) without major effects on alcohol consumption (but alcohol consumption increased thereafter). Surprisingly, no baclofen withdrawal syndrome was observed in patients who stopped baclofen suddenly. In the other cases of treatment termination, baclofen was decreased slowly (one pill a day).

Discussion

In this open prospective study carried out in two liver units, a series of 100 patients received baclofen for alcohol disorder for at least 12 months. The median dose of baclofen was 40 mg/day, but 15 patients received more than 90 mg/day, of whom eight received more than 120 mg/day. Baclofen treatment was initiated in some patients since 2010. It is noteworthy that 65 out of these 100 patients were cirrhotic and one-third had decompensated cirrhosis. This recruitment bias in patient selection is related to the fact that the main investigators that is C.B., H.L., A.G., and J.F.C. were hepatologists working in nonacademic hospital liver units.

The first important result of our study is the high level of medical adherence in this usually considered 'difficult-to-treat' population: actually, 86 of 100 patients were still being followed up at 12 months and 83 were still being treated with baclofen. However, we had no way to monitor medication adherence and no blood levels were available at this time. In these two structures, the care of alcohol-dependent patients closely involved both hepatologists and addiction specialists who were working 'hand to hand'. A social care and a psychological counseling were systematically offered to our patients. This can explain the very high level of adhesion to treatment at 12 months. This adherence may also been explained by the severity of the hepatic disease because very sick patients might be more willing to improve their health condition.

In 77 (77%) patients, baclofen was associated with a strong reduction in alcohol consumption (DAC decrease > 50%) [16] over 12 months. Moreover, 64 (44%) patients were either fully abstinent or had very low alcohol consumption: less than 30 (20%) g/day. These declarative data are strongly supported by a significant improvement in nonspecific but usual biological parameters of alcohol consumption (mean corpuscular volume, GGT, AST) only in patients achieving alcohol reduction. Moreover, in cirrhotic patients achieving alcohol reduction, parameters of hepatic insufficiency clearly improved.

No evidence of baclofen abuse or overdose was identified, nor withdrawal syndrome in the cases of sudden medication discontinuation. Baclofen was well tolerated, with minor side effects, even in the 65 cirrhotic patients.

To our knowledge, use of baclofen in a cirrhotic population has not been described in studies, except in the study by Addoloratto's *et al.* [13]. Some cirrhotic patients might have received baclofen in the study by Yamini *et al.* [17], but data are not precise. In our study, in many cirrhotic patients, the CP score improved. Indeed, reducing or stopping alcohol consumption may have a major impact on survival in alcoholic cirrhotic patients by reducing biological liver abnormalities. Our results are clinically highly relevant, especially in CP-C patients. Only two publications have reported similar data [13,17]. Although uncontrolled, our results are highly comparable to those of Addolorato *et al.* [13]. In the above controlled study, a low dose of baclofen (30 mg daily) led to abstinence more often in patients receiving baclofen that in the placebo group. However, the duration of this study was limited to 3 months, whereas our patients were treated for 12 months. It was often necessary to increase the initial 30 mg dose. In line with abstinence or alcohol reduction, biological markers of alcohol consumption improved and in cirrhotic patients, the CP score improved even in non abstinent patients. This could have a major impact on survival. The abstinence rate in our study is lower than that observed by Yamini *et al.* [17], who achieved a 100% abstinence rate; however, their patients had alcoholic hepatitis and received treatment during the hospitalization for alcoholic hepatitis. Confounding factors with treatment for alcoholic hepatitis made the interpretation of improvement in liver function tests very difficult. Moreover, the tolerance was very good in cirrhotic patients, and the frequency and intensity of side effects were similar to those noted in noncirrhotic patients. Neither patent hepatic encephalopathy nor renal impairment was observed. In fact, there is an urgent need to stop or at least to reduce alcohol consumption in patients with cirrhosis. The objective is abstinence, but some studies have suggested that reduction of alcohol consumption could be a first step before abstinence. In case of ALD, the first goal is risk reduction. Few treatments of alcohol dependence have been evaluated in cirrhotic patients. Naloxone is not recommended because of its potential hepatotoxicity. Acamprosate has been fully tested. It has no impact on the risk of hepatic encephalopathy. However, its efficiency is low in patients with cirrhosis [18]. Nalmefene aims at reducing alcohol consumption. This drug has a partial hepatic metabolism, has not been tested in cirrhotic patients, and is not recommended by the marketer in Child C cirrhosis. It cannot be

used in case of opioid substitution. Besides, this drug was not available in France before September 2014. Disulfiram has dangerous side effects and is no longer recommended, and GHB is not available in France. Finally, EASL guidelines on the management of alcohol-dependent patients recommended that in patients with advanced ALD, recent studies suggested that baclofen was safe and effective to prevent alcohol relapse on the basis of the literature at that time [4]. Thus, a close follow-up of these patients is mandatory to individually adapt the correct dosage. Interestingly, our results at 12 months are very close to what we reported at 3 and 9 months in the cirrhotic patients [19], suggesting that close follow-up along with the adaptation of the dose allows to maintain abstinence under treatment. Our observational study is open labeled and some bias may exist (no control group, severity of the liver disease, efficacy of physician and psychological support, baclofen placebo effect, etc.), but it was not in favor of baclofen because patients receiving this drug were usually those who could have not stopped and had a high craving (difficult-to-treat patients). The majority of patients had an addiction follow-up, acamprosate or naltrexone treatment, or long-duration hospitalization in their medical history.

Initial demographic and medical data were comparable in the high-consumption and the low-consumption groups. In our population, social or medical factors were not shown to predict baclofen response. This suggests that baclofen treatment could be initiated regardless of addiction background.

Conclusion

Twelve month results of this prospective case series suggest that baclofen – in association with psychological and medical care – is well tolerated even in cirrhotic patients and could help to reduce alcohol consumption in alcohol-dependent individuals. This decrease was strongly supported by an improvement in alcohol-related biological markers. In cirrhotic patients, we observed an improvement in liver function tests even in those who only reduced their alcohol consumption to less than 30 g/day with minor and tolerable side effects. It could be very useful in these 'vital emergency' patients. These encouraging results should be validated by a large multicenter study: an ANGH French national survey on baclofen use named 'OBADE' was started in March 2015 and has enrolled more than 200 patients to date.

Acknowledgements

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