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TOPIC HIGHLIGHT

Francesca Cainelli, MD, *Series Editor*

Alcoholic liver disease

Radan Bruha, Karel Dvorak, Jaromir Petrtyl

Radan Bruha, 4th Department of Internal Medicine, General Teaching Hospital, First Faculty of Medicine, Charles University, 12808 Prague, Czech Republic
Karel Dvorak, Jaromir Petrtyl, 4th Department of Internal Medicine, General Teaching Hospital, First Faculty of Medicine, Charles University, 12808 Prague, Czech Republic
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Correspondence to: Radan Bruha, MD, PhD, 4th Department of Internal Medicine, General Teaching Hospital, First Faculty of Medicine, Charles University, U Nemocnice 2 st, 12808 Prague, Czech Republic. bruha@cesnet.cz
Telephone: +420-224-962506 Fax: +420-224-923524
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Abstract

Alcohol use disorders affect millions of individuals worldwide. Alcohol consumption is directly associated with liver disease mortality and accounts for elevated social and economic costs. Alcoholic liver disease (ALD) may take the form of acute involvement (alcoholic hepatitis) or chronic liver disease (steatosis, steatohepatitis, fibrosis and cirrhosis). The severity and prognosis of alcohol-induced liver disease depends on the amount, pattern and duration of alcohol consumption, as well as on the presence of liver inflammation, diet, nutritional status and genetic predisposition of an individual. While steatosis is an almost completely benign disease, liver cirrhosis is associated with marked morbidity, mortality and life expectancy shortening. The median survival of patients with advanced cirrhosis is 1-2 years. Severe acute alcoholic hepatitis (AH) is associated with mortality as high as 50%. It has been managed with corticoids, pentoxifylline and enteral nutrition, although evidence based data are still conflicting. Some author suggest that pentoxifylline could be a better first-line treatment in patients with severe AH. Absolute abstinence is a basic condition for any treatment of acute or chronic ALD, the other therapeutical procedure being of a supportive nature and questionable significance. Acamprosate appears to be an effective treatment strategy for supporting continuous abstinence in alcohol dependent patients. Patients with advanced liver cirrhosis who demonstrably abstain can be considered for liver transplantation, which leads to a markedly prolonged life expectancy. The crucial step in ALD prevention is in the prevention of alcohol abuse, whereas the prevention of liver injury in active alcohol abusers is not clinically applicable.

Key words: Alcohol; Alcoholic liver disease; Liver cirrhosis; Liver fibrosis; Steatohepatitis; Steatosis

Peer reviewers: Dr. Henning Gronbaek, cal Department V, Aarhus University Hospital, Norrebrogade 44, Aarhus 8000, Denmark; Dr. Hongzhi Xu, Massachusetts General Hospital, 51 Blossom Street, Room 435, Boston, MA 02148, United States

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INTRODUCTION

Alcohol is a most frequent cause of liver disease in western countries[1]. Mortality due to liver cirrhosis in those countries is in direct proportion to absolute alcohol consumption per capita-the highest in France and Spain (over

30 deaths per a population of 100 000 per year), the lowest in the northern European countries (up to 5 deaths per 100 000 inhabitants per year). In Central Europe, the figure is 15 deaths due to cirrhosis per 100 000. The highest mortality is in men aged 35-64 years, lower in women (Figure 1)[2]. The past two to three decades have seen a stabilization if not a drop in the intake of alcohol in western countries, while a very adverse trend is reported from Eastern Europe and developing countries[3].

In what is an alarming development, alcohol abuse also afflicts societies and nations without any "drinking tradition", such as in Asia. For example, in a cross-sectional study of two rural communities in China (in which almost 10 000 inhabitants were interviewed for current and lifetime alcohol use)[4], the age-standardized prevalence of lifetime alcohol dependence ranged from 4.8% to 11.8% in different regions. Unlike most western reports, alcohol dependence shows a higher prevalence than the abuse itself.

Coincidence with HIV infection is another attribute of alcohol abuse. This was described in India for example, where the recent increase in alcohol consumption in many sectors of the general population is coupled with strong evidence of the role of alcohol in the spread of HIV infection and other health risks[5]. An even more critical situation appears to have developed in Africa. Pithey *et al*[6] performed a systematic review of sub-Saharan African studies concerning the association between alcohol abuse and HIV infection. Their findings strongly support an association between the two factors. A Fisher *et al*[7] study of high-risk African women showed, even after adjustment for demographic and employment variables, that drinkers were more likely to be HIV positive than non-drinkers (relative risk 2.1). Problem drinkers were also more likely to have engaged in several types of high-risk sexual behavior and to have other sexually transmitted infections, including HSV-2.

Many studies have shown that the amount of undiluted ("pure") alcohol consumed and the duration of that consumption are closely related to cirrhosis. According to some reports, cirrhosis does not develop below a lifetime alcohol consumption of 100 kg of undiluted alcohol[8]. This amount corresponds to an average daily intake of 30 grams of undiluted alcohol for 10 years. Heavy alcoholics consuming at least 80 g of alcohol per day for more than 10 years will develop liver disease at a rate of nearly 100%. A detailed study of 256 heavy drinkers admitted to hospital not because of liver complaints, found steatosis at a rate of 45%, steatohepatitis at 34%, steatohepatitis with cirrhosis at 10% and cirrhosis alone at 10% in their liver biopsies[9]. Formerly, 40-60 g of undiluted alcohol (i.e., 2-3 beers) per day used to be reported as a safe limit for men, less (20 g/d) for women. Data from the "Dionysos" study show, however, that consumption of more than 30 g of pure alcohol daily, regardless of sex, already increases the risk of liver disease[10].

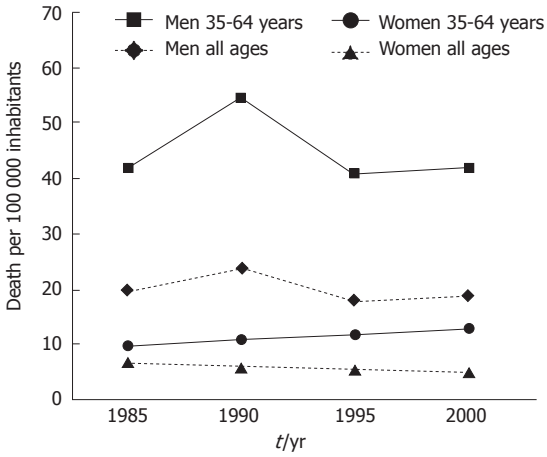

Figure 1 Mortality from cirrhosis in Czech Republic[2].

For practical purposes, alcohol intake is rated by the count of "drinks". The National Institute on Alcohol Abuse and Alcoholism defines a standard drink as 11-14 g of alcohol, which corresponds to approximately one drink of 40% spirit, one glass of wine or one 0.33 l (12-oz) beer. Hence, a "safe" daily intake of alcohol should not be more than two "drinks". On the contrary, moderate ethanol consumption (mainly wine) may mean a reduced cardiovascular risk[11], especially in women[12].

Much the same applies to Asians. For example, in the Chinese population, the ethanol risk threshold for developing alcoholic liver disease (ALD) is 20 g per day with the risk increasing in proportion to the daily intake[13]. Those drinking 20 g of ethanol per day and for less than 5 years are safe from ALD. In this study of 1270 alcohol drinkers, obesity also increases the risk. Abstinence and weight reduction will directly improve the prognosis of ALD.

As for liver injury, it has been postulated for many years that the type of alcoholic beverage makes little, if any difference. Nevertheless, some authors have proposed that mortality from cirrhosis is associated with the consumption of spirits more strongly than with other alcoholic beverages[14]. It is not clear whether this effect can be put down to the drinkers' socio-behavioral characteristics or to increased toxicity of alcoholic beverages[15].

ALD may take the form of acute involvement (alcoholic hepatitis) or chronic liver disease (steatosis, steatohepatitis, fibrosis and cirrhosis). Their progression also depends on the pattern of alcohol intake-drinking alcohol at mealtimes results in a lower risk of liver disease than consumption at other times; fitful, intermittent drinking is more sparing for the liver than a continuous supply of alcohol[16].

Although ALD is a disease that displays an absolute requirement for a voluntary environmental exposure (the consumption of alcohol), many other factors, including genetic host system attributes, are involved in the ALD evolution and progression.

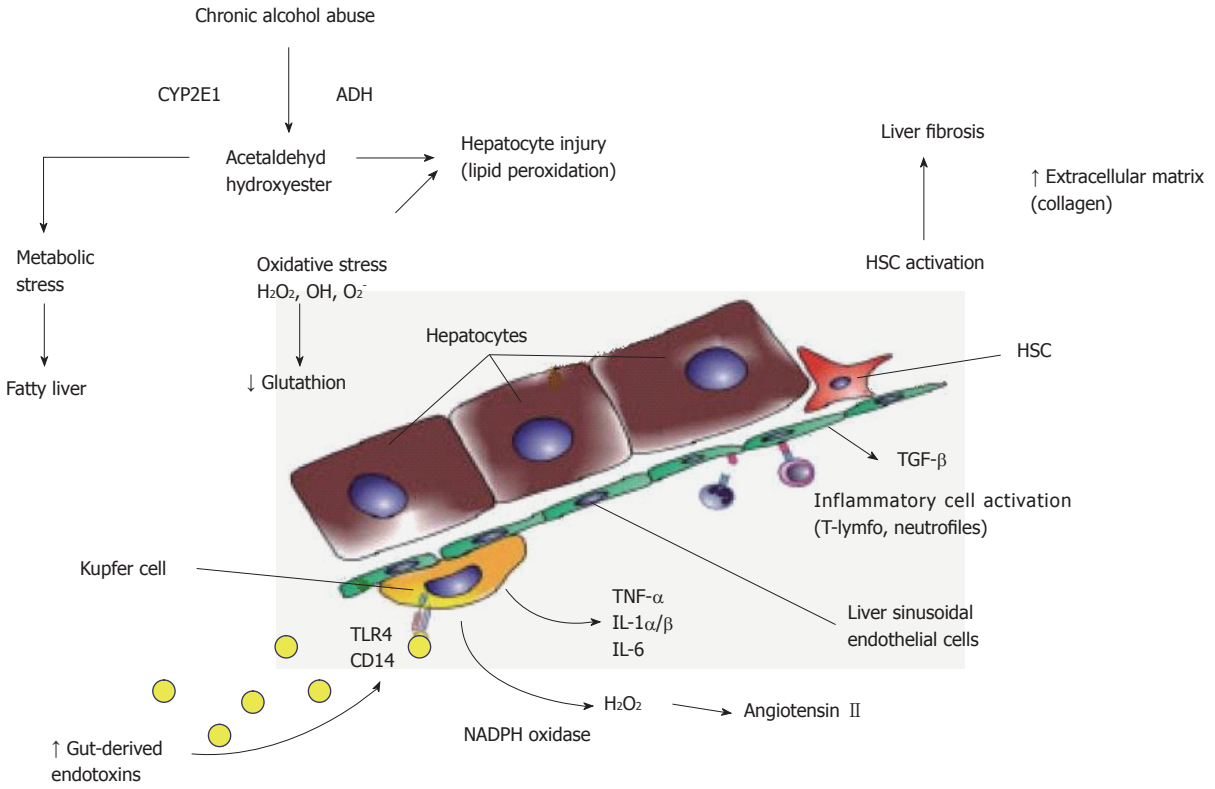

Figure 2 Pathogenesis of inflammatory changes in alcoholic liver disease[56]. ADH: Alcohol dehydrogenase; HSC: Hepatic stellate cell.

ETIOLOGY, PATHOGENESIS, NATURAL COURSE AND PROGNOSIS OF ALCOHOLIC LIVER DISEASE

The liver is the main organ of alcohol metabolism. Alcohol is metabolized in the liver in three ways: (1) by the enzyme alcohol dehydrogenase (ADH); (2) by cytochrome P-4502E1 (CYP2E1); and (3) by mitochondrial catalase. Only the first two pathways are of practical significance-ADH finds use in the degradation of limited quantities of alcohol, while alcohol-induced CYP2E1 takes place in excessive alcohol intake. Apart from the liver, ADH is also present in the gastric mucosa and the assumption is that individuals with low gastric ADH activity are more susceptible to alcoholic liver disease. This may also help to explain why women who have decreased gastric ADH activity[17] are more susceptible to developing alcoholic liver disease.

Both enzymes convert alcohol to acetaldehyde, which is in part responsible for the liver injury too. However, the process of liver injury is much more complex (Figure 2)-resulting from biochemical, genetic, cellular, immunological and humoral disorders in connection with the intake and metabolism of excessive quantities of alcohol. A major role is played there by oxidative stress (which is mainly due to alcohol-induced CYP2E1), by simultaneous shortage of antioxidants in the hepatocytes and, last but not least, by acetaldehyde alone and altered balance of many cytokines-mainly tumor necrosis factor (TNF)-α[18]. Changes in lipid metabolism and in adipose tissue also enhance the process of liver injury[19]. All above mentioned changes result in the injury of cell membranes and organelles (especially mitochondria). The mechanisms of hepatocytic damage due to excessive intake of alcohol show some similarity to changes seen in non-alcoholic steatohepatitis, except that the primary insult is different[20].

Individual susceptibility is another factor to take into account; moreover, any other liver involvement such as viral hepatitis[21] or metabolic disease adds to the risks of alcoholism, as does obesity and metabolic syndrome[22].

In fact, alcoholics were clearly shown to have an increased prevalence of HCV when compared with non-alcoholics and this combination synergistically accelerates liver injury[23]. As for alcohol influence on the liver, the caloric intake should also be taken in account. Increased caloric intake leads to excessive fat deposition and obesity in some patients and can aggravate the liver injury[24].

Of late, there has been an influx of information on correlations between genetic polymorphisms of alcohol-metabolizing enzymes and alcoholic liver disease[25]. The genetics of ALD development involves an inherited predisposition to alcohol dependence, as well as the resulting development of liver injury[26]. Family studies have established an important role of genetics in alcohol dependence. To date, only two genes, which are involved in alcohol metabolism, have shown significant involvement. The alcohol dehydrogenase ADH1B*1 allele was found to be associated with an approximately threefold increase in alcohol dependence and the aldehyde dehy-

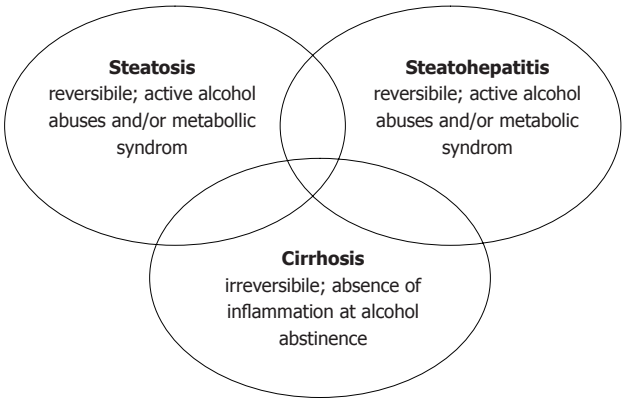

Figure 3 Spectrum of alcoholic liver disease.

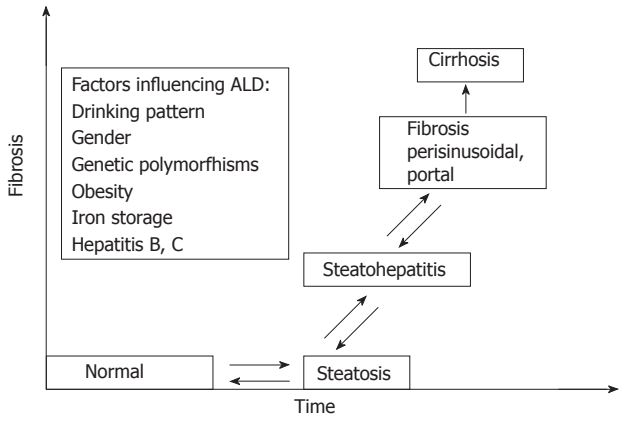

Figure 4 Dynamic process of alcoholic liver disease. ALD: alcoholic liver disease.

drogenase ALDH2*2 allele was found to be instrumental in a 10-fold reduction of the alcohol dependence risk[27]. This association was described in Asian populations[28]. Also reported have been links between alcohol dependence and certain genetic polymorphisms of genes for the GABA receptor or some other neuropeptides[29].

Although most heavy drinkers do develop fatty liver, only a minority progress to liver cirrhosis, suggesting that some other genetic or environmental factors are important for the disease progression. Evidence of genetic involvement in the progression of alcoholic fatty liver to advanced ALD comes from a twin study. The rate of alcoholic cirrhosis was described to be significantly higher in monozygotic twins than in dizygotic twins (16.9% *vs* 5.3%, respectively)[30]. A study of genes involved in alcohol metabolism (e.g., alcohol and aldehyde dehydrogenase and cytochrome P450 2E1) and genes associated with inflammation (e.g., TNF-α and interleukin-10) proved to be inconclusive, with several allelic associations detected but not verified in follow-up studies[31]. The Asian population's hypersensitivity to alcohol could be put down to polymorphisms of genes for the enzymes ADH and CYP2E1. Perhaps the most compelling genetic finding for advanced ALD risk involves the immune regulatory cytotoxic T lymphocyte antigen-4 gene, in which homozygosity for the A49G polymorphism was found to confer a significant risk of alcoholic cirrhosis (odds ratio 3.5) in Italians[32]. However, this finding has yet to be confirmed in follow-up studies.

Polymorphisms for TNF-α co-responsible for an increased risk of liver disease have been discovered in a similar way[33]. For the time being, though, we do not know how to make use of this new knowledge in routine practice.

Malnutrition is another clinical situation with an impact on the evolution of ALD. Heavy alcohol drinkers often lack proper diets or consume diets which are compromised in various nutrients, such as proteins, polyunsaturated fatty acids and vitamins[34].

Liver steatosis is the most frequent primary change in chronic alcohol abuse. Changes associated with alcohol metabolism may subsequently trigger an inflammatory reaction, resulting in alcoholic hepatitis or chronic liver disease (Figure 3).

Liver disease in alcohol abusers is more likely to take the form of chronic changes (steato-hepatitis and fibrosis), leading to cirrhosis later in life. The spectrum of histological findings can be described as a dynamic process[35] (Figure 4). Simple steatosis is reversible after a number of weeks of abstinence; steatohepatitis, a condition seen in only some alcoholics, is a fibrogenic process which can induce changes leading to cirrhosis. Steatohepatitis is also reversible, although a certain degree of fibrosis may persist. The reversibility of steatohepatitis or even fibrosis in humans is well documented by trials on the treatment of chronic hepatitis C[36] and experimentally on NASH models[37]. Steatohepatitis, in particular, often coincides with liver cirrhosis in active alcoholics and is a frequent cause of decompensation of cirrhosis[38].

Simple steatosis is regarded as a benign condition; nevertheless, given continued abuse, it too, can induce fibrogenesis[39]; in any case, up to 20% of the patients with simple steatosis are likely to develop fibrosis or cirrhosis within a period of ten years[40]. The prognosis of a patient with cirrhosis depends mainly on the presence of complications because of portal hypertension and continued abuse of alcohol. Abstainers with decompensated cirrhosis have a five year survival at a rate of 60% against the 30% survival rate in those who continue in the abuse[41].

Severe alcoholic hepatitis, although relatively rare, has a death rate of up to 50%. Identifying individuals with a high mortality risk is crucial in the management of acute alcoholic hepatitis. Multiple prognostic factors were studied over the last decade, including Child-Pugh classification (CTP), Maddrey score (bilirubin mg/dL + 4.6 × prothrombin time)[42] and others. The MELD score was found a more valuable model than CTP or the Maddrey score in the detection of high risk patients admitted with alcoholic hepatitis[43]. Alternatively, the more recent Glasgow alcoholic hepatitis score could be used[44]. A Glasgow score exceeding 9 points is associated with poor prognosis (Table 1).

Table 1 Glasgow alcoholic hepatitis score[44]

Parameter/score	1	2	3
Age (yr)	< 50	⩾ 50	-
Leucocytes (10^9/L)	< 15	⩾ 15	-
Urea (mmol/L)	< 5	⩾ 5	-
INR	< 1.5	1.5-2	> 2
Bilirubin (μmol/L)	< 125	125-250	> 250

The score is to be added to each parameter, the sum total being between 5 and 12 points. The value of 9 and higher implies poor prognosis in alcoholic hepatitis. **INR: International normalised ratio.**

CLINICAL MANIFESTATION AND LABORATORY FINDINGS

Patients with steatosis are usually symptom-free; they may have slightly elevated liver function tests and enlarged liver (both are often discovered accidentally during examination for other reasons).

In the stage of acute alcoholic hepatitis, there may be nausea, loss of appetite, gradual loss of weight, icterus and other symptoms of liver dysfunction (prolonged prothrombin time, hypoalbuminemia, ascites, and hepatic encephalopathy). Patients with alcoholic hepatitis usually show increased liver test results, including gamma-glutamyl transferase (GGT), hypergammaglobulinemia and enlarged liver.

Sonography is the basic imaging technique for liver examination. Liver biopsy, while not always necessary, can help to differentiate simple steatosis from steatohepatitis, fibrosis or incipient cirrhosis. Precise definition of the liver fibrosis stage is essential for management and prognosis in clinical practice. Recently, blood markers and instrumental methods have been proposed for non-invasive assessment of liver fibrosis[45]. However, there are still some doubts as to their implementation in clinical use. Non-invasive examination with transient elastography takes advantage of the fibrotic liver tissue ability to change the velocity of ultrasound propagation. The results of this method correlate well with the bioptically proved degree of fibrosis[46]. Similar results could be obtained from a combination of biochemical and clinical parameters of fibrosis. As for the clinical picture, the state of alcoholic liver cirrhosis shows no difference from cirrhosis of other etiology[38].

ASSESSMENT OF ACTIVE ALCOHOL ABUSE

Assessment of continued alcohol abuse in patients with alcoholic liver disease is essential for their treatment as well as prognosis. Those with alcoholic cirrhosis also make up a significant part of patients indicated for liver transplantation (30%-50%), bearing in mind that abstinence is an essential condition for considering this treatment. Continued alcohol abuse is evaluated on the basis of clinical history, psychological examination and laboratory testing. Thorough clinical and psychological examination is the crucial condition for alcohol abuse diagnosis. Regarding the clinical history, the diagnosis of alcohol abuse and dependence was substantially improved by implementation of simple methods such as a single question inquiring how often the maximum daily alcohol limit has been exceeded[47]. Other clinical screening tools such as the need to cut down, annoyed by criticism, guilty about drinking need for an eye-opener in the morning (CAGE), and the alcohol use disorders identification test (AUDIT-C) are also very easy to apply[48]. With the CAGE questionnaire, two positive answers indicate alcohol dependence with a sensitivity of more than 70% and specificity of more than 90%. The AUDIT-C screening thresholds for the detection of alcohol abuse are ⩾ 4 points for men (sensitivity 86%, specificity 89%) and ⩾ 3 points for women (sensitivity 73%, specificity 91%).

As for laboratory tests, continued abuse can be read from higher GGT values, increased AST/ALT ratio or an increased volume of red blood cells (MCV). In advanced liver cirrhosis, however, the values of hepatic enzymes fall short of sufficient sensitivity or specificity levels. More information about the actual abuse of alcohol can be derived from the percentage of carboxy-deficient transferrin estimation (%CDT) in serum or ethyl glucuronide in urine or hair[49]. A CDT value greater than 2.8% has a 79% sensitivity and 92% specificity for active alcohol abuse detection in patients with advanced cirrhosis[50].

PREVENTION OF ALD

Prevention of or treatment for alcohol abuse are crucial steps in the prevention of ALD[51]. Alcohol dependence is a chronic relapsing medical disorder which is treatable when efficacious medicines are added to enhance the effects of psychosocial treatment. Medication with, e.g., naltrexone and acamprosate showed mixed results in previous clinical trials[52]. Rősner *et al*[53] recently performed a meta-analysis to determine the efficacy and tolerability of acamprosate in comparison with placebo and other pharmacological agents. Almost 7000 patients in 24 double-blind randomised controlled trials were evaluated. Compared to placebo, acamprosate was shown to significantly reduce the risk of any drinking (RR 0.86) and to significantly increase the cumulative abstinence duration. The only side effect that was more frequently reported under acamprosate than with placebo was diarrhea. The authors of this Cochrane review conclude that acamprosate appears to be an effective and safe treatment strategy for supporting continuous abstinence after detoxification in alcohol dependent patients. Indeed, without a pharmacological adjunct to psychosocial therapy, the clinical outcome is poor, with up to 70% of patients resuming drinking within one year[54].

The prevention of liver injury in active alcohol abusers is not clinically applicable. For example, in an experiment, the addition to the diet of polyunsaturated fatty acids prevented alcohol-induced fatty liver and mitochon-

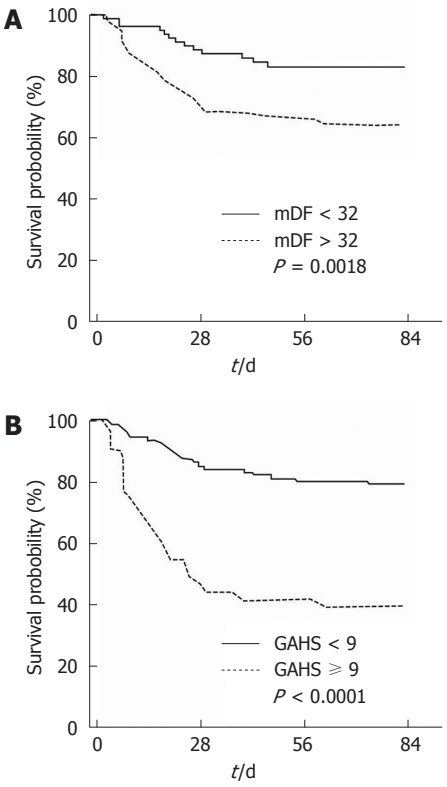

Figure 5 Kaplan-Meier survival analysis relative to the modified Maddrey discriminant function (mDF) (A) and the Glasgow alcoholic hepatitis score (GAHS) (B). The Glasgow score was developed on 241 patients and validated on 195 separate patients[44].

drial dysfunction in an animal model of ALD by protecting various mitochondrial enzymes, most likely through reducing oxidative/nitrosative stress[55]. The clinical use of similar medicaments would probably be always hampered by alcohol abusers´ failure to comply.

TREATMENT

Absolute abstinence is essential to consider any treatment for alcoholic liver disease. Even major changes, including cirrhotic restructuring, may show partial regression during total abstinence[56]. Portal hypertension declines and even regression of esophageal varices have been reported in abstainers. This, however, appears to have resulted from the remission of inflammatory changes and steatosis rather than from regressing fibrosis or cirrhosis. Sustained abstinence markedly improves the patient's prognosis in any phase of the liver disease[57], prevents the progression of the disease and fibrosis and, probably, also the development of hepatocellular carcinoma[58].

Pharmacotherapy of liver disease has but a supportive and rather dubious relevance. Treatment with silymarin, essential phospholipids or vitamin preparations was very popular in the past. Since an oxidative stress has been implicated in the pathophysiology of hepatic insult, the use of natural compounds with anti-oxidant properties represents an extremely popular therapeutic option for the treatment of liver disease. One such phytochemical, resveratrol, is remarkable as it is known as a major constituent of an alcoholic beverage, red wine. Resveratrol was shown to prevent liver injury by means of scavenging free radicals and inflammatory cytokines in experimental studies[59]. Its clinical utilization, though, is still far away. There are no conclusive data to prove the efficacy of any antioxidant medicaments for longer survival time or improved clinical conditions in the treatment of ALD. These are mostly cases of rather costly placebo. In contrast, dietary readjustment in the sense of sufficient energy intake and adequate supply of proteins is of value because malnutrition is a very poor prognostic factor in liver diseases[60]. What has been described as "liver diet" with increased supply of saccharides at the restriction of proteins and fats has no substantiation. Appropriate caloric intake with sufficient supply of proteins and polyunsaturated fats is important[34,61].

Severe alcoholic hepatitis has been treated with corticoids in many trials, with the best results in patients with hepatic encephalopathy, Maddrey score > 32 or Glasgow score > 9[62]. The Glasgow score is very simple to evaluate and its prognostic value is also greater than that of any other classification (Figure 5). The corticoid dose in that case is 40 mg prednisolone per day. The side effects of glucocorticosteroids must be also taken into consideration, as some patients on glucocorticosteroids experience adverse effects, mainly in the form hyperglycemia, Cushing's syndrome and increased risk of infection[63]. Despite the fact that the available trials are rather heterogeneous and some authors do not recommend the use of steroids in alcoholic hepatitis, recently published data emphasize the effect of corticosteroids on short-term survival of patients with severe alcoholic hepatitis[64], particularly in those with Maddrey score > 32.

Some trials and reviews of pentoxifylline (PTX) have shown a better risk/benefit profile than that of steroids and suggested that PTX could be a better first-line treatment in patients with severe AH. The efficacy of PTX in severe AH was first demonstrated by Akrividais *et al*[65] in 2000 on a group of 101 patients with severe AH. 24.5% of the patients who received PTX died during their index hospitalization, compared to a 46.1% mortality in the placebo group ($P = 0.037$). Remarkably, hepatorenal syndrome was the cause of death in 50% of patients on PTX compared to 91.7% of the HRS-related deaths in the placebo group ($P = 0.009$). According to the authors, the benefit appears to be related to a significant decrease in the risk of developing hepatorenal syndrome. In fact, renal dysfunction is frequent in patients with severe alcoholic hepatitis and, it seems, could be prevented with PTX[66].

Even in direct comparison with corticosteroids in a randomized trial, pentoxifylline was found to be superior to prednisolone for the management of severe alcoholic hepatitis regarding reduced mortality, improved risk-benefit profile and renoprotective effect[67]. Nevertheless, this observation should be confirmed on a larger cohort of patients[68]. A recent study by Lebrec *et al*[69] stopped short of confirming the effect of PTX on better survival but,

unlike a previous study, only Child-Pugh class C patients were included. However, the study did confirm a reduced risk of complications, such as bacterial infection, renal insufficiency, hepatic encephalopathy or gastrointestinal hemorrhage in patients treated with PTX compared to placebo.

Some centers recommend the use of PTX as the routine first line treatment of severe alcoholic hepatitis at a dose of 400 mg orally 3 times daily for a period of at least 4 wk[70]. They point to its safety, low cost and scope for long-term treatment. Significantly enough, the sweeping use of PTX as a first-line option is not generally recommended[71] and steroids should be used in patients with severe alcoholic hepatitis. Pentoxifylline could be used in patients with ineffectiveness or contraindications to steroids. The combination of pentoxifylline and steroids waits for clinical evaluation.

Biological treatment with anti- TNF-α antibodies fell short of expectations[72,73] so it can no longer be recommended for the management of alcoholic hepatitis[74].

Many studies with diverse conclusions have been published on the subject of nutrition and alcoholic hepatitis. In general, patients with alcoholic liver disease are frequently malnourished, a condition which worsens the prognosis[75]. However, the situation is not all that easy, as the spectrum of nutritional status in these patients may range from severe malnutrition to morbid obesity. The nutritional intervention on an outpatient basis depends on the degree of malnutrition, obesity and cooperation. In general, supplementation of multivitamins, folic acid and thiamine could be of value in chronic alcohol abuse, but data in the relevant literature are limited. Night-time nutritional supplements (approximately 700 kcal/d) may prevent muscle wasting and improve lean muscle mass in patients with liver cirrhosis[76] and should be considered, also relative to alcoholic hepatitis in patients with evidence of liver cirrhosis.

More data are available regarding the treatment of severe alcoholic hepatitis by enteral nutrition. The benefit of tube-feeding over the regular diet was demonstrated previously[77]. Patients on tube-fed nutrition had improved PSE scores, bilirubin and antipyrine clearance.

Many reviews and recommendations refer to a study by Cabre *et al*[78], which clearly demonstrated the efficacy of tube-fed nutrition. In their multi-center study, 71 patients with severe alcoholic hepatitis were randomized to receive 40 mg/d prednisolone or enteral tube feeding for 28 d and were followed up for 1 year. Mortality during the treatment was similar in both groups but during the follow-up significantly higher with steroids (37% *vs* 8%; $P = 0.04$), mainly because of infections with steroid treatment. The authors concluded that, unlike steroids, enteral nutrition had similar short-term mortality rates, improved 1 year mortality rates and reduced infectious complications. While some studies refrain from confirming any favorable effect of enteral feeding on survival, the implementation of tube-feeding in the treatment of acute alcoholic hepatitis is generally accepted[79]. There are only inconsistent data concerning the use of parenteral nutrition.

Despite the progress in the treatment of severe acute alcoholic hepatitis, the prognosis is still poor.

Alcoholic cirrhosis as such is treated in the same way as cirrhosis of other etiology; in particular, with adequate nutrition, bone disease prevention and prevention or treatment of liver cirrhosis complications (e.g., bleeding from esophageal varices, ascites, spontaneous bacterial peritonitis, hepatic encephalopathy)[80].

Quite a few medicinal products were tested for the treatment of alcoholic cirrhosis: antiphlogistics/propylthiuracil[81], colchicine[82], antioxidants/silymarin[83,84] and also phosphatidylcholine[85]. However, none of these were found to have a favorable effect on survival time and none are recommended for this particular indication any longer. Medicaments with a direct antifibrotic effect are still under evaluation[86].

Patients with advanced cirrhosis can be considered for liver transplantation, provided they are total abstainers[87]. In such cases, a five year post-transplantation survival can reach anything up to 85%[88].

CONCLUSION

Long-term intake of more than 30 g of absolute alcohol per day increases the risk of alcoholic liver disease; liver disease is nearly certain in long-term consumption in excess of 80 g of absolute alcohol per day. Alcoholic liver disease may take the chronic form (steatosis, steatohepatitis, fibrosis, cirrhosis) or that of acute hepatitis. Steatosis is fully reversible, which does not apply to the other conditions; cirrhosis is associated with a markedly shortened life expectancy. The results of laboratory testing in alcoholic liver disease usually include: increased GGT, AST/ALT ratio greater than 2 and increased MCV. Sonography will reveal enlarged liver and signs of steatosis. Absolute abstinence is an essential therapeutic precaution; no hepatoprotective treatment has been shown to improve the course of the disease. Likewise, there is no medicine that would demonstrably "protect" from the effects of alcohol.

The clinical course of severe alcoholic hepatitis could be improved with corticoids, enteral nutrition and pentoxifylline, although more clinical data are necessary to standardize or combine this treatment.

Patients with advanced cirrhosis should be considered for liver transplantation, provided they are verifiable abstainers.

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