Austin Journal of Gastroenterology

Austin Publishing Group

Open Access Full Text Article

Review Article

Alcoholic Liver Disease: a Review

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Received: May 31, 2014; **Accepted:** June 23, 2014; **Published:** June 25, 2014

Introduction

Alcoholism results in approximately 2.5 million deaths worldwide annually, representing 4% of all mortality. Although a variety of comorbidities and accidental injuries occur in patients with alcoholism, liver injury is the most common cause of alcoholism-related mortality. Liver injury caused by the alcohol abuse is called alcoholic liver disease (ALD), and it is classified into alcoholic steatosis (fatty liver), alcoholic hepatitis, and alcoholic liver cirrhosis. In this review, we summarize the epidemiology, etiology, clinical characteristics, biochemical markers, images, histology, and therapeutic options for each of these situations. The information provided will help physicians to understand ALD and thus contribute to better patient care.

Alcoholic Liver Disease (ALD)

ALD encompasses alcoholic steatosis, alcoholic hepatitis, and alcoholic liver cirrhosis, depending on the severity of the histological damages, liver functions, etc. There is also a risk of hepatocellular carcinoma in ALD patients. The incidence of ALD is relatively low compared with that of alcoholism [1]. This disparity is likely because of the various genetic and environmental factors that may be associated with the etiology of ALD. For example, variations in ethanol metabolism are associated with the incidence of ALD, and the risk of ALD is higher in women than in men [2]. In addition, metabolic syndrome [2,3], diabetes [3], and viral hepatitis [2,4,5] have been reported to be associated with ALD, and studies to identify specific genes and factors that contribute to a predisposition for ALD are ongoing [1].

Although it is controversial and situations are different in each country, the only definitive treatment for ALD is liver transplantation (LT). In general, in order to be considered for LT, at least 6 months of proven abstinence is necessary [6]. Because abstinence improves overall survival, supportive and nutritional therapies are also important [7-9]. The supportive therapies for abstinence include psychological and pharmacological therapies. Psychological therapies promoting abstinence include twelve-step facilitation therapy, cognitive-behavioral therapy, and motivational enhancement therapy [10,11]. In addition, family support is an essential component in the overall management of individuals with ALD.

The pharmacological therapies include disulfiram, naltrexone, baclofen, and acamprosate. Disulfiram is an acetaldehyde dehydrogenase inhibitor that causes accumulation of serum acetaldehyde after drinking alcohol, causing unpleasant sensations [12]. However, it also has toxic effects on the liver, because of which it is not often administered in patients with ALD [12]. Naltrexone is an opioid receptor antagonist that decreases alcohol cravings by blocking the central pleasurable effects of alcohol [13]. Baclofen is a gamma-aminobutyric acid-B agonist that has also been reported to be effective for decreasing alcohol intake, although the effect is controversial as per the negative results from a randomized-controlled trial conducted in US [14]. Acamprosate has also been reported to help decrease alcohol dependence although its mechanisms are unknown [15]. For all the above-mentioned drugs, there are limited data on efficacy in patients with advanced liver disease; therefore, further studies and assessments are necessary. Nutritional therapy is also important to manage ALD. It helps reverse muscle wasting, weight loss, vitamin deficiencies, and trace element deficiencies associated with ALD [16].

ALD is commonly classified into three stages: alcoholic steatosis, hepatitis, and liver cirrhosis. However, all three stages can sometimes be observed in the same liver as they are classified by the histological changes that occur with continued alcohol abuse. Thus, ALD can be diagnosed with the history of excessive alcohol intake with exclusion of other etiologies, such as viral hepatitis and nonalcoholic steatohepatitis [2]. The characteristics of three stages are summarized in Table 1. Alcoholic steatosis is the earliest manifestation of ALD and can be reversed with abstinence. With the continuous uptake of the alcohol, steatosis progresses to the status of chronic hepatitis, and finally to the cirrhosis. The significance increase of alcohol complicated with the inflammatory changes, may also lead to the severe alcoholic hepatitis that has a severe mortality. Clinical symptoms showed severity in the cirrhotic status and they are same as the ones found in the liver cirrhosis patients with other etiologies. Among those symptoms, gastrointestinal bleedings from esophageal, gastric varices and portal hypertensive gastroenteropathy are potentially life-threatening. Endoscopic ligation, sclerotherapy and balloon-occluded retrograde transvenous obliteration (BRTO) may be necessary for either prevention or emergent treatment [17]. ALD is histological characterized by microvesicular fat accumulation and inflammation with neutrophil infiltration [18]. The continuous inflammation results in micronodular regenerative nodules, which can be seen by various imaging modalities and serve to differentiate ALD from cirrhosis resulting from other etiologies [19]. Changes in serum biochemical parameters can be observed with increasing severity of inflammation and cirrhotic changes, contributing to liver dysfunction and portal hypertension. The severity of each stage and the indication for therapeutic options can be assessed by using several scoring systems, including the Child–Pugh score [20] and the MELD score (model for end-stage liver disease) [21]. The therapeutic options include LT, which is the only definitive treatment for ALD; however

Citation: Kamimura K, Abe H and Aoyagi Y. Alcoholic Liver Disease: a Review. Austin J Gastroenterol. 2014;1(2): 1006.

Table 1: Classification of Alcoholic Liver Disease.

	Steatosis	Hepatitis	Cirrhosis
Points	The status is reversible with abstinence.	Active inflammatory process with predominantly neutrophic infiltration.	The stage irreversible and cause liver failure and cancer.
Clinical Findings	Asymptomatic. Incidental diagnosis.	Jaundice, pyrexia, hepatomegaly. Acute hepatic dysfunction.	Vascular spider, palmar erythema, gynecomastia, ascites, gastrointestinal bleeding from esophageal/gastric varices, protal hypertensive gastroenteropathy, encephalopathy.
Biomarker	Mild elevations of liver enzymes.	Elevation of liver enzymes depend on the levels of inflammation.	Low hepatic reserve (hypoalbuminemia, prolonged prothrombin time), low platelet counts.
Images (CT, US)	Fatty infiltration	Significant hepatomegaly, focal or massive necrosis.	Cirrhotic changes, atrophic liver, nodular lesions, collateral vessels, tumors
Histology	Micro- and macro-vesicular fat accumulation within hepatocytes, no fibrosis.	Neutrophilic infiltration, ballooning degeneration of hepatocytes, necrosis, steatosis, and eosinophilic inclusions (Mallory body)	Liver fibrosis, micronodular regenerating lesions.
Therapeutic Options	Abstinence, Nutritional support	Corticosteroids, Pentoxifylline, GMA, LT	LT, management of various complications of cirrhotic liver.

Liver enzymes include gamma-glutamyltranspeptidase, aspartate aminotransferase, alanine aminotransferase, and bilirubin.
CT: Computed Tomography
US: Ultrasonography
GMA: Granulocytes/Monocytes Apheresis
LT: Liver transplantation

proven abstinence for at least 6 months is generally necessary to be considered for eligibility even if the scores indicate LT as a best option [6]. As mentioned above, the abstinence and nutritional support are important for the treatment of alcoholism, including the support of hypoproteinemia in cirrhotic patients. Severe alcoholic hepatitis (SAH) is an acute inflammatory response to endotoxins, resulting in leukocytosis, neutrophil infiltration in the liver, severe hepatic injury, renal failure, hepatic encephalopathy, and pneumonia [22,23]. Although corticosteroids have been used to control the inflammatory response, the outcome varies and no standardized therapy has been established. Efforts have been made to find novel therapeutics to treat cytokinemia, including the increased levels of TNF-α, IL-6, IL-8, and neutrophil elastase. Such potential treatments include anti-TNF-α antibody [24], pentoxifylline [25], and granulocytes/monocytes apheresis (GMA) [23,26,27]. Although the results of clinical trials for anti-TNFα antibody [24] and pentoxifylline [25] varied among themselves did not demonstrate any significant therapeutic effect, further efforts are necessary to evaluate the efficacy of GMA [27]. As Horie et al. reported, SAH patients with WBC counts >10,000/μl showed a higher mortality rate than patients with a lower WBC count. Therefore, it seems reasonable to treat these cases with GMA [26]. In fact, they have shown that treatment with GMA resulted in a 100% survival rate in patients with a WBC count >10,000/μl [26]. All cases treated with GMA to date are summarized in Kamimura's paper [27] with details of their two cases.

Conclusion

ALD is a disease consisting of various stages of liver injury and its progression can be prevented by abstinence. Although LT is the only definitive treatment, other therapeutic options summarized in this review are being assessed and are likely to help to improve the prognosis of the disease.

References

1. Gao B, Bataller R. Alcoholic liver disease: pathogenesis and new therapeutic targets. Gastroenterology. 2011; 141: 1572-1585.
2. Orman ES, Odena G, Bataller R. Alcoholic liver disease: pathogenesis, management, and novel targets for therapy. J Gastroenterol Hepatol. 2013; 28: 77-84.
3. Taniai M, Hashimoto E, Tokushige K, Kodama K, Kogiso T, Torii N, et al. Roles of gender, obesity, and lifestyle-related diseases in alcoholic liver disease: Obesity does not influence the severity of alcoholic liver disease. Hepatol Res. 2012; 42: 359-367.
4. Schmidt CS, Schön D, Schulte B, Lüth S, Polywka S, Reimer J. Viral hepatitis in alcohol-dependent inpatients: prevalence, risk factors, and treatment uptake. J Addict Med. 2013; 7: 417-421.
5. Zhang M, Wu R, Jiang J, Minuk GY, Niu J. The presence of hepatitis B core antibody is associated with more advanced liver disease in alcoholic patients with cirrhosis. Alcohol. 2013; 47: 553-558.
6. Murray KF, Carithers RL. AASLD practice guidelines: Evaluation of the patient for liver transplantation. Hepatology. 2005; 41: 1407-1432.
7. Pessione F, Ramond MJ, Peters L, Pham BN, Batel P, Rueff B, Valla DC. Five-year survival predictive factors in patients with excessive alcohol intake and cirrhosis. Effect of alcoholic hepatitis, smoking and abstinence. Liver Int. 2003; 23: 45-53.
8. Borowsky SA, Strome S, Lott E. Continued heavy drinking and survival in alcoholic cirrhotics. Gastroenterology. 1981; 80: 1405-1409.
9. Muntaner L, Altamirano JT, Augustin S, González A, Esteban R, Guardia J, et al. High doses of beta-blockers and alcohol abstinence improve long-term rebleeding and mortality in cirrhotic patients after an acute variceal bleeding. Liver Int. 2010; 30: 1123-1130.
10. Matching Alcoholism Treatments to Client Heterogeneity: Project MATCH posttreatment drinking outcomes. J Stud Alcohol. 1997; 58: 7-29.
11. Jaurigue MM, Cappell MS. Therapy for alcoholic liver disease. World J Gastroenterol. 2014; 20: 2143-2158.
12. Björnsson E, Nordlinder H, Olsson R. Clinical characteristics and prognostic markers in disulfiram-induced liver injury. J Hepatol. 2006; 44: 791-797.
13. Rösner S, Hackl-Herrwerth A, Leucht S, Vecchi S, Srisurapanont M, Soyka M. Opioid antagonists for alcohol dependence. Cochrane Database Syst Rev. 2010; 12: CD001867.
14. Garbutt JC, Kampov-Polevoy AB, Gallop R, Kalka-Juhl L, Flannery BA. Efficacy and safety of baclofen for alcohol dependence: a randomized, double-blind, placebo-controlled trial. Alcohol Clin Exp Res. 2010; 34: 1849-1857.
15. Rösner S, Hackl-Herrwerth A, Leucht S, Lehert P, Vecchi S, Soyka M. Acamprosate for alcohol dependence. Cochrane Database Syst Rev. 2010; 8: CD004332.
16. McClain CJ, Barve SS, Barve A, Marsano L. Alcoholic liver disease and malnutrition. Alcohol Clin Exp Res. 2011; 35: 815-820.

17. European Association for the Study of Liver. EASL clinical practical guidelines: management of alcoholic liver disease. J Hepatol. 2012; 57: 399-420.

18. MacSween RN, Burt AD. Histologic spectrum of alcoholic liver disease. Semin Liver Dis. 1986; 6: 221-232.

19. Okazaki H, Ito K, Fujita T, Koike S, Takano K, Matsunaga N. Discrimination of alcoholic from virus-induced cirrhosis on MR imaging. AJR Am J Roentgenol. 2000; 175: 1677-1681.

20. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. Br J Surg. 1973; 60: 646-649.

21. Freeman RB, Wiesner RH, Harper A, McDiarmid SV, Lake J, Edwards E, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl. 2002; 8: 851-858.

22. Lucey MR, Mathurin P, Morgan TR. Alcoholic hepatitis. N Engl J Med. 2009; 360: 2758-2769.

23. Horie Y, Yamagishi Y, Ebinuma H, Hibi T. Therapeutic strategies for severe alcoholic hepatitis. Clin Res Hepatol Gastroenterol. 2011; 35: 738-744.

24. Boetticher NC, Peine CJ, Kwo P, Abrams GA, Patel T, Aqel B, et al. A randomized, double-blinded, placebo-controlled multicenter trial of etanercept in the treatment of alcoholic hepatitis. Gastroenterology. 2008; 135: 1953-1960.

25. Parker R, Armstrong MJ, Corbett C, Rowe IA, Houlihan DD. Systematic review: pentoxifylline for the treatment of severe alcoholic hepatitis. Aliment Pharmacol Ther. 2013; 37: 845-854.

26. Horie Y. Granulocytapheresis and plasma exchange for severe alcoholic hepatitis. J Gastroenterol Hepatol. 2012; 27: 99-103.

27. Kamimura K, Imai M, Sakamaki A, Mori S, Kobayashi M, Mizuno K, et al. Granulocytapheresis for the treatment of severe alcoholic hepatitis: a case series and literature review. Dig Dis Sci. 2014; 59: 482-488.

Austin J Gastroenterol - Volume 1 Issue 2 - 2014
ISSN : 2381-9219 | www.austinpublishinggroup.com

Citation: Kamimura K, Abe H and Aoyagi Y. Alcoholic Liver Disease: a Review. Austin J Gastroenterol. 2014;1(2): 1006.