Severe Acute Alcoholic Hepatitis: An audit of medical treatment
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Abstract

Despite advances in treatment, severe alcoholic hepatitis is still associated with a high mortality rate of 30% to 40%. Nutritional support and steroids in selected patients are believed to improve prognosis. In controlled trials steroids have been beneficial in patients with a discriminant function (DF) value >32 or spontaneous hepatic encephalopathy. The aim of this study was to investigate current practice and outcomes in the treatment of acute alcoholic hepatitis. We retrospectively studied patients admitted to our unit with acute alcoholic hepatitis over a 4 year period. Forty−three patients with acute alcoholic hepatitis were admitted between 1994 and 1997. Overall mortality was 26% (11/43). Only 5 patients were treated with steroids of whom 1 died (mortality 20%). Liver biopsy was available in 19/43 of whom 12/19 (63%) had underlying cirrhosis in addition to alcoholic hepatitis. Mortality was higher in patients with a discriminant function of greater than 32 but not significantly so (32%: 8/25 vs 17%: 3/18 p = 0.31). A discriminant function of greater than 32 and contra−indications to steroid use was the best predictor of mortality (60% 6/10 P = 0.0096) compared to patients not fulfilling these criteria In this study overall mortality was comparable with published reports. Of interest was the relatively low liver biopsy rate and the fact that steroids were used in only a minority of eligible patients. We found that mortality was concentrated in a subgroup of patients with a discriminant function value >32 and contra−indications to steroids. These criteria appear to identify a high−risk subgroup of patients. If confirmed, experimental treatments need to be targeted at this group to improve the overall prognosis of acute alcoholic hepatitis.

Introduction

Patients admitted to hospital with severe alcoholic hepatitis have a poor prognosis with reported short−term mortality rates of >40%[1−5]. Despite this and the high prevalence of the disease, no therapeutic measure has been shown conclusively to reduce mortality or retard the progression to cirrhosis. Steroids, enteral nutrition and more recently pentoxifylline are the most promising treatments[6]. Enteral nutrition with high calorie intake may be beneficial[7−10]. The role of steroids is still controversial[11,12]. Early studies which examined the effects of steroids in acute alcoholic hepatitis showed conflicting results, with survival, improved in some[1,13,14] but not in others[2−5,15−19]. It was noted that patients with the most severe disease appeared to respond best to steroids. This led to the development of the discriminant function (DF) value[20], a mathematical formula to identify patients who may respond to steroids. A discriminant function value greater than 32 or spontaneous encephalopathy is believed to identify a group of patients with a two−month mortality rate of 50%[21]. Two randomised controlled trials using this criterion demonstrated improved survival in steroid treated patients[20−22]. Although the evidence is not conclusive steroid treatment has been recommended for patients with severe acute alcoholic hepatitis and a discriminant function > 32[23,24]. In light of these results the aim of this study was to evaluate current treatment and outcomes in patients with severe acute alcoholic hepatitis.

Methods

Using the Hospital In−Patient Enquiry (HIPE) data for the years 1994 to 1997 inclusive, cases of alcoholic hepatitis were identified. Patients were included if there was a clinical or biopsy diagnosis of acute alcoholic hepatitis. A clinical diagnosis of acute alcoholic hepatitis was diagnosed if there was a history of heavy alcohol consumption up to within 4 weeks of admission, jaundice and one or more of the following: fever, leucocytosis > 12,000/mm3 with polymorphonuclear predominance, hepatomegaly, transaminase level raised greater than twice normal, and other causes of liver disease including viral hepatitis, drugs, autoimmunity etc were excluded[10]. The charts were reviewed and data was collected regarding patient demographics, relevant clinical features and liver function tests. The use of steroids or contraindications to their use was noted. Liver biopsies were reviewed. The DF value was calculated in each case as follows:

D.F. = 4.6 x [prothrombin time − control (in sec)] +[serum bilirubin (in mmol/l)17.1]

Mortality rates at 30 days were calculated as a marker of short−term outcome.

Statistics: Unless otherwise stated data are expressed as mean + standard error of the mean. Comparison between groups was made using the Chi−squared 2−tailed Fisher exact test.

Results

In the period between 1994 and 1997 62 admissions with alcoholic hepatitis were identified in 54 patients. Data was unavailable in 2 cases. Thirteen patients were excluded because review of the notes suggested the diagnosis of alcoholic hepatitis was incorrect. Forty three admissions in the remaining 39 patients were studied. Demographic data, clinical features and laboratory parameters for the group are shown in Table 1.

Almost two−thirds of our patients were female. The mean age of presentation was 46.9 years. One third had encephalopathy on presentation and 58% had a DF value of >32. 12% of the group received steroids. Nineteen (44%) patients had a liver biopsy (see Table 2). 13 of these were performed during the acute illness giving a contemporary biopsy rate of 30%. Four had had a previous biopsy and 2 of those who died before 30 days had a post mortem biopsy performed. Half of the cases with a DF <32 (9/18) and 10/25 (40%) of those with a DF >32 had a biopsy performed. Cirrhosis was present in 12/19 (63%) of those biopsied: in 4/9 (44%) of those with a DF <32 as compared with 8/10 (80%) of those with a DF >32.

Of the 25 where the DF was greater than 32 steroids were contraindicated in 10. Steroids were used in 5 patients of whom one died (mortality rate 20%). Of the 10 patients in whom steroids were not contraindicated but not used, one died (mortality rate 10%). Steroids were contraindicated due to infection in 10 patients and 2 of these also had gastrointestinal haemorrhage. Two patients had spontaneous bacterial peritonitis. Five had pneumonia, of whom one also had central venous catheter sepsis and another had both central venous line sepsis and a urinary tract infection. Three had clinical features that were felt to be consistent with sepsis but no source was identified. Six of these ten patients died (mortality rate 60%).

Eleven patients died within 30 days giving an overall short−term mortality rate of 26% (Table 2). In 18 cases (42%) the DF was less than 32. No patient in this group received steroids and 15/18 survived to 30 days giving a short−term mortality rate of 17%. In 25 cases (58%) the DF was greater than or equal to 32. Eight died resulting in a mortality rate of 32%. The difference in mortality rates between these two groups was not statistically significant (p = 0.31). Patients with a discriminant function greater than 32 and a contraindication to steroids had a significantly greater mortality than patients with a discriminant function less than 32 (p = 0.035), a discriminant function greater than 32 and no contra−indications to steroids (p = 0.028) or compared to the latter two groups combined (p = 0.0096) (see Table 2).

Discussion

This study confirms that acute alcoholic hepatitis is a severe illness with high in−hospital mortality. One in three of our patients with a DF >32 died as compared to one in six with a DF <32. Our overall short−term mortality rate at 26% compares favourably with other studies. A recent multicentre UK study found a mortality of 50% in 241 patients with a DF greater than 32[25]. In our study the group with a DF value >32 were more frequently cirrhotic when compared with those with a DF value <32. A high DF value may therefore identify cirrhotic patients who as a consequence of their cirrhosis have a poorer outcome. Although the diagnosis of alcoholic hepatitis is based on histological criteria only 30% of our patients underwent liver biopsy during the acute illness. In terms of treatment a minority of patients fulfilling criteria for steroid treatment actually received steroids. The highest mortality (60%) occurred in patients who fulfilled criteria for steroid treatment but had contraindications to their use.

Although it has characteristic clinical features, alcoholic hepatitis is a histological diagnosis[26]. Features include hepatocyte ballooning and disarray with neutrophilic infiltration, steatosis, necrosis, fibrosis, cholestasis and Mallorys hyaline. However, as in our study, most cases are diagnosed clinically. Although the clinical syndrome is easily recognised some authors have claimed that liver biopsy is confirmatory in only 70% of patients with a clinical diagnosis and a discriminant function greater than 32[22]. Patients without histological alcoholic hepatitis would not be expected to benefit from steroid treatment, which may be deleterious in this situation.

A higher biopsy rate would be desirable in order to establish the diagnosis with certainty and allow appropriate treatment. Transjugular liver biopsy now offers a relatively safe and effective means of accessing liver histology even in the presence of coagulopathy and/or ascites[27]. The benefits of treating acute alcoholic hepatitis with steroids have not been proved conclusively but there is no rationale for steroid use in the treatment of decompensated alcoholic cirrhosis without alcoholic hepatitis.

In[8] our study only 20% of patients received steroids where indicated by a DF value >32. Forty per cent of those with DF >32 had no apparent contraindication to steroids but did not receive them. The reasons for not treating with steroids in this group were not clear. It may be that concerns regarding infection or other[8] contraindications to steroid use were not documented, or that the decision was based on an overall clinical appraisal of the individual patients condition. Most patients with alcoholic hepatitis have a neutrophil leucocytosis and/or a low grade pyrexia. Repeated cultures and possibly a trial of empirical antibiotics may be necessary to exclude sepsis in this patient group. This process takes time and may militate against early use of steroids.

In the present study we found that the mortality rate (60%) was highest in cases with a DF value >32 and in whom there was a contraindication to steroids, either infection, gastrointestinal haemorrhage or both. The mortality rate in this group was significantly higher than in those where steroids were not contraindicated. More than 50% of our total mortality occurred in this group. These two factors may identify a sub-group of patients at high risk for whom new therapies are needed. This should be confirmed in an independent data set. Patients with proven sepsis and/or variceal bleeding are excluded from most therapeutic trials in alcoholic hepatitis[6,10]. While this is understandable, more than half the deaths in our study happened in this group. It we are to improve prognosis further specific therapy for this group will be required. It appears logical that steroids may be deleterious in patients with sepsis or bleeding and alternative therapies will probably be needed.

In summary, alcoholic hepatitis is a life-threatening condition with a high mortality. Liver biopsy is desirable to confirm the diagnosis but appears to be under utilised.

Steroids are used in only a minority of eligible patients. Whether this is due to concerns about efficacy or other factors is not clear. Of interest is the potential value of the DF value in association with a contraindication to steroids as an indicator of severe disease and poor prognosis. Medical treatments are unlikely to have a major impact on mortality overall unless they can be used in this group.

Table 1 Summary of patient details. Forty three patients with acute alcoholic hepatitis

Male/Female	16/43
Age (years)	46.9 + 1.6
Fever (> 37C)	15/43 (35%)
Encephalopathy	14/43 (33%)
Ascites	24/43 (56%)
White cell count	12.9 + 9.5
Serum bilirubin (_mol/L)	195 + 24
Serum albumin (g/L)	27.8 + 1.0
Prothrombin time (secs)	22.2 + 1.5
Discriminant function (DF) > 32	25/43 (58%)
Liver biopsy	19/43 (44%)
Steroid treatment	5/43 (12%)

Table 2 Overall mortality according to discriminant factor values (D.F.). Significance values between groups are for comparisons with group 5. There was no significant difference in survival between groups 1 and 2: p = 0.31

		Mortality	P value vs 5
1.	8Discriminant function (DF) < 32	3/18 (17%)	0.035
2.	DF >32	8/25 (32%)	
3.	DF > 32 and no contra-indications to steroids	2/15 (13%)	0.028
4.	DF < 32 + DF >32 and no Contra-indications to steroids	5/33 (15%)	0.0096
5.	DF >32 and contra-indications to steroids	6/10 (60%)	

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