Severe Acute Alcoholic Hepatitis: An audit of medical treatment

Author: McCormick PA, O’Keeffe C

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 and retrospective studies steroid treatment in alcoholic hepatitis has failed to conclusively reduce mortality or retard the progression to cirrhosis. Steroids, enteral nutrition and more recently pentoxifylline are the most promising treatments. Enteral nutrition with high calorie intake may be beneficial. The role of steroids is still controversial. Early studies which examined the effects of steroids in acute alcoholic hepatitis showed conflicting results, with survival, improved in some but not in others. 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, 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%. Two randomised controlled trials using this criterion demonstrated improved survival in steroid treated patients. Although the evidence is not conclusive steroid treatment has been recommended for patients with severe acute alcoholic hepatitis and a discriminant function >32. In light of these results the aim of this study was to evaluate current treatment and outcomes in patients with severe alcoholic hepatitis.

Introduction

Patients admitted to hospital with severe alcoholic hepatitis have a poor prognosis with reported short-term mortality rates ranging between 20% and 50%. A clinical diagnosis of acute alcoholic hepatitis is often difficult to make. If there is any doubt a liver biopsy should be performed 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. 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)]

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

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%) of the group had cirrhosis present when compared with those with a DF value <32 (44% of the DF group vs 16% of DF <32). Cirrhosis was present in 12/19 (63%) of those biopsied: in 4/9 (44%) of those with a DF <32 and 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%). In our patients with the most severe disease appeared to respond best to steroids. This led to the development of the discriminant function (DF) value, 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%.

Two randomised controlled trials using this criterion demonstrated improved survival in steroid treated patients. Although the evidence is not conclusive steroid treatment has been recommended for patients with severe acute alcoholic hepatitis and a discriminant function >32. In light of these results the aim of this study was to evaluate current treatment and outcomes in patients with severe 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 was made if there was evidence of recent alcohol intake up to 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. 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:

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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.

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 unfavourably with other studies. In our study the group with a DF value >32 were more frequently cirrhotic when compared with those with a DF value <32. This suggests that patients with the highest DF scores (DF >32) 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 fulfilled criteria for steroid treatment. Of the 10 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. Features include hepatocyte ballooning and disarray with neutrophilic infiltration, steatosis, necrosis, fibrosis, cholestasis and Mallory 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. 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. 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 uncomplicated alcoholic cirrhosis without alcoholic hepatitis.
In 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 confounding variables were not properly communicated. 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 hemorrhage 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. There are several factors which may explain this finding. These include an increase in the severity of sepsis and a greater frequency of re-sternotomy in patients with 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.

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 and survival in alcoholic hepatitis. 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

<table>
<thead>
<tr>
<th>Details</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Male/Female</td>
<td>16/43</td>
</tr>
<tr>
<td>Age (years)</td>
<td>46.9 ± 1.6</td>
</tr>
<tr>
<td>Fever (&gt; 37°C)</td>
<td>15/43 (35%)</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>24/43 (56%)</td>
</tr>
<tr>
<td>Ascites</td>
<td>12.9 ± 9.5</td>
</tr>
<tr>
<td>White cell count</td>
<td>35/33 (15%)</td>
</tr>
<tr>
<td>Serum bilirubin (µmol/L)</td>
<td>95 ± 24</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>27 ± 10.0</td>
</tr>
<tr>
<td>Prothrombin time (secs)</td>
<td>22.2 ± 1.5</td>
</tr>
<tr>
<td>Discriminant function (DF) &gt;32</td>
<td>25/43 (58%)</td>
</tr>
<tr>
<td>Liver biopsy</td>
<td>19/43 (44%)</td>
</tr>
<tr>
<td>Steroid treatment</td>
<td>5/43 (12%)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Discriminant factor values (D.F.)</th>
<th>Mortality</th>
<th>P value vs 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Discriminant function (DF) &lt; 32</td>
<td>3/18 (17%)</td>
<td>0.035</td>
</tr>
<tr>
<td>2. DF &gt;32</td>
<td>8/25 (32%)</td>
<td></td>
</tr>
<tr>
<td>3. DF &gt;32 and no contra-indications to steroids</td>
<td>1/15 (6%)</td>
<td>0.029</td>
</tr>
<tr>
<td>4. DF &gt;32 + DF &gt;32 and no Contra-indications to steroids</td>
<td>5/33 (15%)</td>
<td>0.0096</td>
</tr>
<tr>
<td>5. DF &gt;32 and contra-indications to steroids</td>
<td>6/10 (60%)</td>
<td></td>
</tr>
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Correspondence:
Patricia A McCormick, St Vincents University Hospital, Elm Park, Dublin 4, Ireland
Phone: 01 2094248.
Fax: 01 2837724.

References:

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