SEVERE ALCOHOL-INDUCED LIVER DISEASE AND THE ALCOHOL DEPENDENCE SYNDROME

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Abstract — Aims: To examine the hypothesis that patients who present in the UK to detoxification services differ from patients who present with severe alcohol-induced liver disease (ALD) with respect to severity of dependence on alcohol and other features of their drinking history. Methods: Levels of alcohol dependence were assessed in 34 patients with severe ALD, all of whom were cirrhotic, and 34 subjects from a residential alcohol detox centre in Southampton using the Severity of Alcohol Dependence Questionnaire (SADQ). During interview, various aspects of participants’ alcohol consumption were recorded, including total monthly consumption, whom they usually drank with and where, and, if applicable, what caused them to start drinking heavily. Social circumstances were also noted, including participants’ employment and marital status. Results: Among ALD patients, 58% scored none/mild on the SADQ, 32% moderate and 9% severe. In contrast, 76% of the detox group were graded severe and 34% moderate (P < 0.001). ALD patients were also significantly older, had lower scores on the Alcohol Use Disorders Identification Test, tended to drink less alcohol, were more likely to be in a stable relationship, were less likely to be unemployed and gave different reasons for starting to drink heavily. The ALD group were most likely to have started drinking heavily for social reasons, whereas subjects in the detox group were most likely to have started drinking heavily as a result of relationship or money problems. Conclusion: Patients attending a liver unit and patients admitted to a detoxification unit were separate but overlapping populations of alcohol misusers. Perhaps these two populations of alcohol misusers are likely to require different approaches for effective detection, intervention and treatment.

INTRODUCTION

At a time when the mortality from alcohol-induced liver disease (ALD) is generally dropping (La Vecchia et al., 1994) deaths from ALD in the UK are increasing dramatically (Chief Medical Officer, 2001) and have increased in young and middle-aged subjects 8-fold since the 1970s (Leon and McCambridge, 2006). The perception of the general public (and many health professionals) is that alcoholic cirrhosis develops only in patients who show features of the alcohol dependence syndrome (Smith et al., 2004). As liver doctors in Southampton, UK, our clinical impression is that patients with liver disease often do not have the features of the alcohol dependence syndrome but instead are heavy social drinkers with relatively controlled patterns of drinking.

In the 1940s, Jellinek (1960a, b) described five main types of ‘alcoholism’. He defined ‘β alcoholics’ as those who are not dependent on alcohol but who often succumb to medical conditions such as liver cirrhosis, whereas ‘γ alcoholics’ are highly physically dependent and often suffer behavioural problems and sociological complications. Jellinek (1960a, b) also noted differences in the reasons why these two groups drink heavily, hypothesizing that the tendency towards heavy drinking in β alcoholics was related to the customs within their social group, whereas γ alcoholism was characterized in part by drinking to relieve craving.

Although Jellinek (1960a, b) provided the theoretical framework for viewing drinkers presenting with the disease as a quite different population from drinkers presenting with dependence, there have been few studies of drinking patterns and attitudes in patients with ALD. Studies in this group are vastly outnumbered by the massive literature on alcohol dependence—and perhaps it is unsurprising that, for many people, they seem to amount to the same thing. Wodak et al. (1983) identified significant differences between a population of ALD patients and a population of patients recruited from an alcohol treatment centre for dependence, finding that only 18% of patients with ALD were severely dependent on alcohol compared with 56% of the treatment centre patients; 63% of the patients with ALD were classed as having no or only mild dependence. One smaller study from India, using male subjects only, found similar results (Sarin et al., 1988). There have also been a few studies in the liver transplant population, although these are open to the criticism that data could be biased by the desire of patients to be accepted into the transplant programme (Burra et al., 2000).

Unfortunately ALD usually develops silently, and the first indication of a problem is a presentation with acute gastrointestinal haemorrhage or alcoholic hepatitis, often both, with no warning signs of developing alcohol dependence. This first presentation with ALD is often fatal—in cases of variceal haemorrhage up to a quarter of patients may die (Brett et al., 2001; Harry and Wendon, 2002), and in alcoholic hepatitis up to a half of patients with severe disease may die (Mathurin et al., 1996). In view of the continuing increase in potentially preventable liver deaths in the UK, we set out to explore the hypothesis that heavy drinkers often develop ALD without the features of alcohol dependence and that dependent drinkers and liver patients may form different populations of heavy alcohol misusers that may require different approaches to detection and prevention.

METHODS

The study group consisted of 34 patients with severe ALD recruited in the Liver Unit at Southampton General Hospital. They were selected from patients consecutively seen for clinical purposes by the investigators, and were included if they...
had significant ALD and were capable of completing a detailed interview and giving informed consent. All subjects in this group had a biopsy-proven diagnosis of alcohol-induced liver cirrhosis. No pre-selection took place and all patients who consented to take part in the study were included in the subsequent analysis.

The control (detox) population were 34 patients known to have the alcohol dependence syndrome who had been admitted for residential detoxification at Two Saints Substance Misuse Service in Southampton. Subjects were considered suitable for interview if the substance of dependent use was alcohol and they were able to be interviewed and give informed consent. Subjects were excluded if they had a history of a liver problem or known liver disease, but no attempts were made to uncover sub-clinical liver disease—which in the absence of a liver biopsy cannot be completely excluded.

Subjects completed a questionnaire on basic demographic characteristics, including marital and employment status, and on alcohol intake, type of alcohol most frequently consumed, how much consumed, where consumed and with whom. At the end of the interview, when a rapport had been established, the Severity of Alcohol Dependence Questionnaire (SADQ) and Alcohol Use Disorders Identification Test (AUDIT) (Saunders et al., 1993) were administered. The SADQ was devised according to guidelines issued by a World Health Organization committee and is considered a valid and reliable method for rating alcohol dependence (Stockwell et al., 1983). It is a 20-item questionnaire with a maximum score of 60. A score of 31 or more indicates severe alcohol dependence, a score between 15 and 30 indicates moderate dependence and a score of <15 shows no dependence or only mild dependence.

Data was analysed using SPSS (http://www.spss.com/) software. One-way ANOVA was used to compare continuous variables with normal distributions, such as mean age, SADQ score and alcohol consumption. \( \chi^2 \) analysis was used to compare non-parametric data, such as unemployment levels and numbers drinking alone.

RESULTS

Of the patients in the ALD group, 23 (67%) had previously had ascites and 25 (73%) had oesophageal varices. There were no differences between the ALD (22 male/12 female) and detox (24 male/10 female) groups with respect to gender.

Levels of alcohol dependence as assessed using the SADQ were significantly different between the two groups (Fig. 1, \( P < 0.001 \)). Of the ALD group, 9% showed evidence of severe alcohol dependence on the SADQ, whereas 76% of the detox group showed severe alcohol dependence. More than half the ALD patients (58%) were graded none/mild on the SADQ, compared with none of the detox group.

There were a number of other significant differences between the ALD and detox groups. The ALD group was older (mean age 50 versus 40 years, \( P < 0.001 \)), drank less alcohol (mean 348 versus 571 U/30 days, \( P = 0.02 \)) and had started drinking at a later age than the detox group (Fig. 2, \( P < 0.005 \)).

Subjects with liver disease had significantly lower scores on the AUDIT screening tests for hazardous drinking (Fig. 3). There were no significant differences between the ALD and detox groups in terms of the preferred type of alcohol consumed, with 33% preferring spirits, 25% wine and 25% beer/lager; however, the detox group were significantly more likely to drink alone (73%), whereas the ALD group were more likely to drink with family, friends or work...
colleagues (51%, P < 0.005). The ALD patients were more likely to be married or in a stable relationship (41%) compared with the detox group (14%) and less likely to be unemployed (41%) compared with the detox group (73%).

We asked both groups to list the main reasons why they started to drink heavily and found some significant differences in the answers (P < 0.05, χ² analysis). Subjects with liver disease gave a wide range of reasons but were most likely to have started drinking heavily for social reasons, whereas subjects in the detox group were most likely to have started drinking heavily as a result of relationship or money problems.

**DISCUSSION**

We have confirmed that most patients with severe ALD do not have the features of the alcohol dependence syndrome, as assessed by the SADQ, compared with subjects presenting primarily with alcohol dependence. The very nature of the alcohol dependence syndrome means that patients are very unlikely to return to non-dependent patterns of drinking (Edwards et al., 1983, 1986; Taylor et al., 1985), and therefore we believe that it is highly unlikely that the ALD group had previously suffered from severe physical dependence and spontaneously reverted to non-dependent drinking patterns. Furthermore, the SADQ refers to the period when their drinking was heaviest. These data support those of Wodak et al. (1983), who found that 63% of their liver disease group had either mild or no evidence of alcohol dependence according to the SADQ, similar to levels of alcohol dependence reported by patients under assessment for liver transplantation (Rothenhausler et al., 2003).

Previous studies have not addressed whether there are, in addition, other qualitative differences between ALD patients and patients presenting with alcohol dependence. The other major findings of our study are that there are significant differences in terms of marital status and unemployment, where people drink and the reasons given for starting to drink heavily. Subjects in the detox group reported that their heavy drinking was often triggered by traumatic life events and/or feelings of depression, whereas, in the ALD population, heavy drinking was heaviest. These data support those of Wodak et al. (1983), who found that 63% of their liver disease group had either mild or no evidence of alcohol dependence according to the SADQ, similar to levels of alcohol dependence reported by patients under assessment for liver transplantation (Rothenhausler et al., 2003).

These data support the hypothesis that heavy drinkers can fall into one of two paths. The majority of patients presenting with alcoholic liver disease appear to be heavy controlled or social drinkers, leading relatively controlled lives, perhaps not feeling that their drinking is necessarily a major health issue until they present with end-stage liver disease, at which point the liver has been silently damaged to the extent that only 30% will be long-term survivors (Bell et al., 2004; Sorensen et al., 2003). Alternatively, if drinking spirals completely out of control as a result of dependence, or vice versa, then subjects are more likely to present at an earlier age. Previous studies also suggest that subjects with alcohol dependence survive longer, despite drinking more: around two-thirds will be long-term survivors (Edwards et al., 1983).

Wodak et al. (1983) suggested as an explanation for the fact that ‘only 15% of heavy drinkers develop chronic liver disease’ that dependent drinkers would be much more likely to present to health services and receive treatment or spontaneously stop drinking, thus avoiding liver disease. Many lines of evidence suggest that it is perfectly possible to continue drinking at a very high level and never develop clinically significant liver disease. In the seminal study by Griffith Edwards and colleagues (1983) of the 10-year outcomes of alcohol dependence, 68% of subjects had survived, and, of these, half were drinking in an uncontrolled fashion, but only one had a diagnosis of cirrhosis. However, the cause of death in the 18 patients who died was not stated, so some of these were also likely to have had liver disease. Similarly, autopsy and biopsy surveys have repeatedly shown that only 20–30% of lifelong alcoholics will ever develop cirrhosis (Levey, 1968; Lelbach, 1976; Bruguera, 1977). The explanation for this is most likely to lie in different genetic susceptibilities to the complex chronic liver toxicity of alcohol (Hrubec and Omenn, 1981; Sheron et al., 1993).

The high mortality of severe ALD at first presentation means that there are limited options for reducing deaths. There have been important advances in the acute management of variceal haemorrhage with the development of endoscopic therapy (Gimson et al., 1993) and percutaneous shunting (Richter et al., 1990; Jalan et al., 1995), but despite this the 1-year case fatality rate for alcoholic cirrhosis has remained unchanged at 38% since 1968 (Roberts et al., 2005). The proven effective measures of reducing alcohol availability and increasing taxation (Room et al., 2005) seem politically unfeasible in the UK at the present time. Our work suggests that detecting alcohol problems through the development of early features of alcohol dependence (Prime Ministers Strategy Unit, 2004) will miss many patients who will later die from ALD.

The Malmo Preventive Program (Peterson et al., 1985) aimed to reduce morbidity and mortality of ALD in heavy drinkers using serum gamma glutamyl transferase screening—a very non-specific measure of liver damage. Deaths were reduced by 50%, although the numbers were small, and morbidity was significantly reduced. We suggest that by adding newer and more specific assays (Tsutsumi et al., 1996; Tran et al., 2000; Stickel et al., 2001) together with strategies for the primary prevention of variceal haemorrhage (Lui et al., 2002) and specific psychological interventions, it may be possible to prevent unnecessary alcohol-related deaths in the future. Further clinical trials are much needed in this area.

**REFERENCES**


