INTRODUCTION

Alcohol dependence is one of the most common psychiatric diseases worldwide (Flensborg-Madsen et al., 2009; Hasin et al., 2007; Teesson et al., 2009), having a very high comorbidity with somatic disorders (Rehm et al., 2003), especially with hepatic and pancreatic diseases (Yang et al., 2008).

In some settings, alcohol-dependent patients do not receive treatment focused on their addiction (Hasin et al., 2007). If admitted for internal diseases, specialized addiction treatment is rarely available in some countries, even in those with highly developed healthcare systems like Germany (Arolt and Diressen, 1996; Arolt et al., 1995; Diehl et al., 2009). Therefore, alcohol-use disorders remain undetected and psychiatric comorbidities overlooked. The medication generally used for alcohol withdrawal at internal medicine wards, benzodiazepines, is standardized for all patients in most countries (Blondell, 2005; Mayo-Smith, 1997; Saiz and O’Malley, 1997; Weaver et al., 2006). Lesch and Walter (2009) propose that not all patients benefit from these standardized treatment plans. Regarding relapse prevention, sociological factors like age of onset, gender and the typology according to Babor or Cloninger are associated with different responses to pharmaceutical treatments (Leggio et al., 2009; Lesch and Walter, 2009; Walter et al., 2003). Smith et al. (2006) examined alcohol-dependent patients who either attended a liver unit or were admitted to a detoxification unit and concluded that these two patient groups require different approaches for intervention and treatment as they differ in the features of the alcohol dependence syndrome.

Thus, there is a need for the classification of patients in therapy-relevant subgroups, so the individual needs of each patient, from the addiction point of view as well as that of internal medicine, can be met.

The Lesch alcoholism typology (LAT), developed by psychiatrists to improve the long-term outcome of alcohol-dependent patients, has been in regular use in several countries for planning addiction treatment in psychiatric settings and for forensic and prognostic assessments (Hillemacher and Bleich, 2008; Leggio et al., 2009; Lesch and Walter, 1996; Lesch et al., 1988). The assessment with the LAT is also part of the routine diagnostic for patients with a history of alcohol dependence undergoing liver transplantation (LTX) at the Vienna General Hospital. Berlakovitch et al. (1994, 1999) published results for the long-term treatment outcomes of these patients, which demonstrated that there is a good long-term outcome.

There are significant differences between the distribution of the four different types according to Lesch in different therapeutic settings (homeless shelter, specialized addiction treatment unit, psychiatric department [Lesch and Walter, 2009]), but no data have been collected yet about the distribution of the types at gastroenterological wards, where many patients are admitted because of alcoholic liver disease (Arolt and Diressen, 1996; Arolt et al., 1995; Diehl et al., 2009). For this reason, it is of clinical interest to assess similarities and differences between alcohol-dependent patients admitted to gastroenterology or psychiatric wards.

Objectives

The aim of this study was the assessment and comparison of the clinical and biological status of two alcohol-dependent patient groups, those admitted to the gastroenterological department and those admitted to psychiatric department, to assist in defining treatment approaches for withdrawal and relapse prevention likely to be optimal in these groups using distribution of the four types according to Lesch.
PATIENTS AND METHODS

Men and women between the age of 18 and 65 who fulfilled the alcohol dependence criteria according to the ‘International Classification of Diseases’ tenth revision (ICD-10) and the ‘Diagnostic and Statistical Manual, text revised’ version IV (DSM-IV-TR) were included (APA, 2000; WHO, 1992). Exclusion criteria were lack of informed consent, current substance dependence other than alcohol or nicotine dependence according to ICD-10 and DSM-IV-TR and psychotic disorders.

In the period from January 2005 till November 2006, an assessment was made of consecutive patients with alcohol dependence according to ICD-10 and DSM-IV-TR admitted to the Vienna General Hospital, to a psychiatric ward specialized in the treatment of alcohol detoxification and treatment and to the gastroenterological ward that had a focus on liver diseases.

At the first day of their in-hospital stay, the standard laboratory parameters were assessed (serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, creatinine, gamma glutamyltransferase, mean corpuscular volume (MCV), amylase and prothrombin time.

To assess the severity of the liver damage, the ratio of AST/ALT and the MELD score (model for end-stage liver disease) were calculated. AST/ALT ≥2 suggests advanced alcoholic liver disease (Nyblom et al., 2004). The MELD score is calculated according to the serum bilirubin concentration, serum creatinine concentration and international normalized ratio (INR) and ranges from 6 (mild liver disease) to 40 (end-stage liver disease) points (Kamath et al., 2001; Srikurja et al., 2005).

All patients were clinically assessed by a psychiatrist using the LAT online program, a standardized structured interview assessing areas of alcohol dependence (the drinking history, family history positive/negative, onset of dependence, loss of control during the last 3 months prior to the current inpatient stay and alcohol-related disabilities; Lesch and Walter, 2009). A part of the LAT is the rating of lifetime experience of withdrawal states, coded as ‘none’, ‘mild’ (mild shaking and anxiety states) and ‘severe’ (three-dimensional tremor, severe sweating and severe vegetative symptoms and/or delusional states up to delirium tremens). The LAT was combined with a psychiatric exploration to evaluate psychiatric comorbidities according to ICD-10 and DSM-IV-TR. Using LAT, we classified all patients according to the Lesch typology based on the decision tree (Bleich et al., 2004; Hillemacher and Bleich, 2008; Kiefer and Barocka, 1999; Lesch et al., 1990; Pombo and Lesch, 2009; Walter et al., 2006; Table 1).

This decision tree assesses multidimensionally four different subgroups. If a symptom of Type IV can be found then the patient has to be defined as Type IV. If there are no
symptoms of Type IV but the patient has an affective disorder or suicidal behaviour independent from alcohol intake or withdrawal, this leads to the diagnosis of Type III. If there are no symptoms of Types IV and III, but there are severe withdrawal symptoms or withdrawal seizures then Type I has to be diagnosed. Type II patients, consuming alcohol to cope with states of anxiety, do not show any symptoms of Type IV, III or I.

These types are more comprehensive than the general diagnosis of alcohol dependence and have been used in basic research and medical withdrawal and relapse prevention treatment (Bleich et al., 2004; Hillemacher and Bleich, 2008; Kiefer and Barocka, 1999; Lesch et al., 1990; Pombo and Lesch, 2009; Walter et al., 2006). They are heterogeneous in terms of mechanism of craving and proposed therapy.

The LAT system recommends, based on 20 years of clinical experience and theoretical considerations, the choices for alcohol withdrawal as follows: benzodiazepines (Type I), tiapride and/or trazodone (Type II), γ-OH-butyrate (GHB) or trazodone (Type III) and GHB and carbamazepine (Type IV) (Hillemacher and Bleich, 2008; Lesch and Walter, 2009; Walter et al., 2006). As for medical relapse prevention, acamprosate (Types I and II; Lesch et al., 2001) and naltrexone (Types III and IV) proved to be effective (Kiefer et al., 2005).

The stability over time for these four types is especially strong for Types III and IV. Only Type II can develop, over a long time of abuse, to meet criteria of Type IV (e.g. polyneuropathy), symptoms of Type III (affective disorders) and only in rare cases Type I symptoms.

Ethics
This study is a subanalysis of the study ‘Genetic differences of alcohol-dependent patients according to the Lesch Typology’ for which ethical approval by the ethic commission of the Medical University of Vienna was obtained on 5 July 2004.

Statistics
Statistical analysis was performed with the software SPSS version 15.0, using standard deviation, T-test, U-test and χ² test as appropriate. All statistical tests were two-sided and a P-value of <0.05 was considered significant.

RESULTS

Patients’ sociodemography and pre-treatment experience
Eighty patients were included in this study, 44 at the psychiatric ward (15 women, 34%, 29 men, 66%) and 36 at the gastroenterological ward (14 women, 39%, and 22 men, 61%). There were no significant differences in gender and age (50 ± 10 years) between wards.

‘Usual living arrangements’ did not differentiate the two groups (e.g. at both departments ~50% of the patients were living with a partner and 50% were living alone). No significant differences could be found between the groups regarding a positive family history for alcohol dependence or a positive family history for other psychiatric diseases. The duration of pathologic drinking behaviour and the longest period of abstinence since the beginning of their alcohol dependence were not statistically different between the two patient groups (Table 2).

Previous medical treatment focusing on alcohol dependence and relapse prevention prior to the current in-hospital stay was more common in psychiatric patients [32 of 44 (72.7%)] than in gastroenterological patients [12 of 36 (33.3%)] (P < 0.05).

Somatic disease
As would be expected, the MELD score (P < 0.05) is significantly higher in the group admitted to the gastroenterological ward. Although AST and ALT were similar, the ratio AST/ALT was higher in the group admitted to the gastroenterological ward (P < 0.05). All other parameters reflecting alcohol intake, severity of liver and pancreatic disease were significantly higher (P < 0.05) in the gastroenterological patient group (Table 3).

Life-time rates of epilepsy independent of alcohol intake and withdrawal (2 of 44 [4.5%] at the psychiatric ward vs. 1 of 36 [2.8%] at the gastroenterological ward) as well as the rate of polyneuropathy (2 of 44 [4.5%] at the psychiatric ward vs. 3 of 36 [8.3%] at the gastroenterological ward) were not significantly different between the two groups.

Psychiatric factors
Mood disorders
At the psychiatric ward, 11 of the 44 (25%) patients showed a comorbidity with affective disorders according to ICD-10 (F32 and F33) and DSM-IV. At the gastroenterological ward, significantly fewer patients (P < 0.05) were diagnosed with an affective mood disorder (2 of 36; 5.6%). In their case history, 16 of 44 (36.4%) of the alcohol-dependent patients at the psychiatric ward reported suicidal tendencies. At the gastroenterological ward, this rate was lower (5 of 36, 13.9%; P < 0.05).

At the psychiatric ward, 23 of 44 (52.3%) consumed alcohol to reduce feelings of anxiety and 32 of 44 (72.7%) used alcohol to reduce the severity of depressive symptoms. At the gastroenterological ward, this was significantly less (7 of 36 (19.4%) for feelings of anxiety, 17 of 36 (47.2%) for the reduction in depressive mood; P < 0.05).

Alcohol dependency and severity of symptoms
Withdrawal states
Table 2. Duration of pathological drinking and longest period of abstinence

<table>
<thead>
<tr>
<th></th>
<th>Number of patients reporting pathological drinking behavior since over 5 years</th>
<th>Longest period of abstinence since the onset of alcohol dependence (over 6 months/up to 6 months/cannot be assessed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric ward</td>
<td>36/44 (81.8%)</td>
<td>23/20/1 (52.3%/45.5%/2.3%)</td>
</tr>
<tr>
<td>Gastroenterological</td>
<td>31/36 (86.1%)</td>
<td>16/16/4 (44.4%/44.4%/11.1%)</td>
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symptoms in their case history. Of the 44 patients, 11 (25%) experienced a strong severity degree with shaking, sweating, up to delusions (delirium tremens), and 28 of the 44 (63.6%) psychiatric patients reported only mild withdrawal symptoms with mild shaking and anxiety states. In contrast, on the gastroenterological ward, fewer patients reported any past alcohol withdrawal symptoms (19 of 36, 52.8%; \( P < 0.05 \)), but 10 of 36 (27.8%), a similar proportion to that of the psychiatric ward, reported severe withdrawal symptoms and/or delusional states up to delirium tremens.

At the psychiatric ward, only 2 of 44 (4.5%) reported previous alcohol withdrawal seizures, compared with 6 of 36 (16.7%) at the gastroenterological ward.

**Lesch typology**

Using the LAT instrument, significant differences \( (P < 0.05) \) were found in the distribution of the types according to Lesch. As expected, Type III was by far the most frequent one (22 of 44 [50%]) at the psychiatric ward, whereas Type II was the dominant one at the gastroenterological ward (19 of 36 [53%]; Fig. 1).

The distribution of the four types describes significant differences in comorbidity rates and cause of intake.

In the Lesch model, Type III patients mainly use alcohol to improve their depressive mood (23 of 27 [85.2%]) and against their withdrawal symptoms (15 of 27 [55.6%]). Type I patients use alcohol mainly to reduce their withdrawal symptoms (9 of 11 [81.8%]). Only a very small group of Type II patients use alcohol also against their mild withdrawal states (5 of 32 [15.6%]).

Type III and IV patients reported significantly higher \( (P < 0.05) \) suicidal tendencies (Type III: 13 of 27 [48.1%]; Type IV: 5 of 10 [50%]) than Type I and II patients (Type I: 1 of 11 [9.1%]; Type II: 2 of 32 [6.3%]).
There were no significant differences between the Lesch types regarding the drinking pattern, the amount of alcohol consumed prior to the current inpatient stay, the rate of loss of control or laboratory parameters (Table 5).

### DISCUSSION

As expected, alcohol-related liver diseases at the gastroenterological ward were more common and significantly more advanced as shown by the MELD score than at the psychiatric ward, although gender, age and the history of alcohol dependence were not different.

An important aspect in the case history of the patients is the medical treatment focusing on alcohol dependence prior to the current inpatient stay. It was significantly different between the two groups—72% of the psychiatric patients received prior outpatient or inpatient treatment for alcohol dependence in contrast to only 33.3% of the gastroenterological patients. This could, perhaps, be because patients who pass through the psychiatric service received specific addiction treatment earlier in life, resulting in periods of sobriety which therefore might slow the progression of those somatic diseases likely to be caused by a regular high alcohol intake. Illustrating that, Proudfoot and Teesson (2009) showed that in general practice alcohol-dependent patients with other psychiatric comorbidities have higher rates of medical service use than those without such disorders. We found that 25% of the patients in the psychiatric ward had an affective disorder according to DSM-IV and ICD-10, compared with only 5.6% of those in the gastroenterological ward. Thus, we can speculate that the significantly higher comorbidity rate of affective mood disorders among the psychiatric ward patients has led to greater healthcare utilization.

Other patterns of symptoms could also have led to earlier contact with addiction treatment services such as alcohol withdrawal symptoms and loss of control drinking: nearly 90% of the psychiatric patients, but only 50% of the gastroenterological patients reported that they had experienced alcohol withdrawal symptoms and 40.9% of the alcohol-dependent patients at the psychiatric ward reported frequent or permanent loss of control, compared with 16.7% at the gastroenterological ward (loss of control drinking may lead to social problems and consequent contact with services).

Perhaps, gastroenterological patients had the self-perception of being able to control the amount of alcohol consumed, which could represent a lack of ‘insight’ thus also delaying obtaining specific addiction treatment and therefore worsening the final prognosis, in terms of somatic disease.

Regarding the rate of psychiatric comorbidities, we observed that significantly more psychiatric patients than gastroenterological patients were suffering from affective disorders, as discussed above, and that the severity of the psychiatric diseases is higher among psychiatric inpatients, e.g. 36.4% of the alcohol-dependent patients at the psychiatric ward reported suicidal tendencies compared with 13.9% at the gastroenterological ward. Psychiatric treatment is strongly recommended for those gastroenterological patients who are suffering from affective comorbidities and/or are reporting suicidal tendencies (Arnot and Driessen, 1996; Arnot et al., 1995; Diehl et al., 2009).

### Medical withdrawal treatment

Benzodiazepines, the medication generally used for alcohol withdrawal at the gastroenterological wards (Blondell, 2005; Mayo-Smith, 1997; Saitz and O‘Malley, 1997; Weaver et al., 2006), need to be used with caution in alcohol-dependent patients for two reasons. First of all, patients with advanced liver disease and hepatic encephalopathy exhibit an increased sensitivity to the sedative effects of benzodiazepines (Aboucha and Butterworth, 2004, 2005; Butterworth, 2008; Jones et al., 1984, 1993; Mullen et al., 1990)—our gastroenterological patients had an average MELD score of 16.73, therefore indicating an advanced liver disease. Second, using benzodiazepines as withdrawal medication entails a risk of creating a benzodiazepine addiction. One subgroup of alcohol-dependent patients, Lesch Type II patients, shows a particular disposition towards addiction, caused by their premorbid personality structure (Lesch and Walter, 2009). Since more than 50% of the patients at the gastroenterological ward were Type II patients, this needs to be taken into account when prescribing withdrawal treatment.

Following these findings, the recommended medical withdrawal treatment at the psychiatric ward is either GHB alone or combined with carbamazepine (27 of 44 [61.4%]) and tiapride and/or trazodone (13 of 44 [29.5%]), but seldom benzodiazepines (4 of 44 [9.1%]). At the gastroenterological ward for the majority of patients, tiapride and/or trazodone (19 of 36 [52.8%]) is the recommended medication, followed by GHB alone. An additional advantage of GHB is that it depends little on the liver for its excretion. GHB may be also combined with carbamazepine (10 of 36 [27.8%]). Only for a small number of patients (7 of 36 [19.4%]), benzodiazepines are the proper choice. In this study, according to the recommendations emanating from the use of the Lesch typology, only one-quarter of these patients should be treated with benzodiazepines for withdrawal treatment, i.e. those who reported severe withdrawal symptoms and were diagnosed as Type I patients.

### Medical relapse prevention treatment

Regarding medication for relapse prevention, as mentioned above, Types I and II are probably treated most effectively with acamprosate, whereas naltrexone seems to be most beneficial for Types III and IV (Kiefer et al., 2005; Lesch et al., 2001).

Thus in our sample, 39% of the patients in the psychiatric ward and 73% of those in the gastroenterological ward should be treated with acamprosate and 61% of the patients in the

<table>
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<th>Drinking pattern, during the last 5 years (constant alcohol consumption/alternating N alcohol consumption)</th>
<th>Average alcohol consumption prior to current inpatient stay, self-reported (&lt;3 heavy drinking days per week/&gt;3 heavy drinking days per week)</th>
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<tr>
<td>Type I 11</td>
<td>9/2 (81.8%/18.2%) 8/3 (72.7%/27.3%)</td>
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<tr>
<td>Type II 32</td>
<td>20/12 (62.5%/37.5) 19/13 (59.4%/40.6%)</td>
</tr>
<tr>
<td>Type III 27</td>
<td>16/11 (59.3%/40.7%) 8/19 (29.6%/70.4%)</td>
</tr>
<tr>
<td>Type IV 10</td>
<td>6/4 (60.0%/40.0%) 8/2 (80.0%/20.0%)</td>
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</table>

A ‘heavy drinking’ day is defined as a day with alcohol consumption of six standard drinks or more (1 standard drink = 1/8 l wine or 0.3 l beer or 4 cl strong alcoholic beverage like vodka).
psychiatric ward with naltrexone. For 27% of the gastroenterological patients, naltrexone would be recommended based on the Lesch typology, but studies reported that naltrexone might be associated with worsening of liver disease in alcohol-dependent patients with advanced liver cirrhosis and therefore has no place in treatment of this patient group (Lucey, 2009). As a promising alternative, baclofen could be used for these patients; however, larger studies are still needed to evaluate the long-term effectiveness of baclofen (Addolorato et al., 2007).

By using naltrexone as standard relapse prevention treatment, one-third of the patients in the psychiatric ward and almost three-quarters of the gastroenterological patients would not receive the proper medical treatment option, increasing the danger of alcohol relapse and risking causing additional hepatic damage to the gastroenterological patients.

Because of the described somatic and psychiatric comorbidities of alcohol-dependent patients, a proper classification of patients is of high clinical relevance, since therapeutic approaches vary significantly. Scientific data are available showing that the Lesch typology is a useful evidence-based instrument to plan withdrawal and relapse prevention treatment (Leggio et al., 2009; Lesch and Walter, 2009; Walter et al., 2003). Following this treatment concept and considering the result that more than 50% of the patients admitted at the gastroenterological ward were Type II patients, it can be concluded that when treating alcohol-dependent patients at the gastroenterological ward the medical focus should be put on non-benzodiazepine anxiolytic treatment. Long-term psychotherapeutic outpatient treatment and acamprosate are needed for sufficient relapse prevention treatment in Type II (Lesch and Walter, 2009). As Type II patients show a mild long-term course with a very good long-term outcome when treated properly, this diagnosis could be considered as a positive prognostic factor in choosing LTX in patients with severe alcoholic liver disease.

Nevertheless, the sample size of this study is small and further trials would be needed with a larger number of patients at the gastroenterological ward to develop better treatment following the proposals developed by psychiatric research. As treatment concepts vary significantly among the European countries, it would be important to carry out these trials in different regions of Europe.

Conflict of interest statement. The online LAT is sold by the Austrian Society of Addiction Medicine (AUSAM) and O.M.L. is the current president of AUSAM. He does not receive financial benefits through sales of LAT. In relation to medications mentioned in this paper, he declares honoraria for advice to D&A Pharma and Laboratorio Farmaceutico C.T. S.r.l. The other authors have no conflict of interest with any commercial or other associations in connection with the submitted article.

REFERENCES


Srikurja W, Kyulo N, Runyon B et al. (2005) MELD Score is a better prognostic model than Child-Turcotte-Pugh score or Discriminant Function score in patientes with alcoholic hepatitis. *J Hepatol* 42:700–706.


