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APPROACH AND PRESCRIBING MEDICATIONS USED FOR ALCOHOL USE DISORDERS – A RETROSPECTIVE CHART-BASED STUDY ON INPATIENTS

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Abstract

Background: Alcohol use disorders (AUDs) are an important cause of death and disability across all regions of the world and age groups. Morbidity and mortality due to alcohol-related disorders can be minimised by correctly identifying and treating patients presenting to a hospital. This study attempted to investigate the prescribing patterns of pharmacological management of patients presenting to various departments of a tertiary care hospital, as well as across the spectrum of alcohol withdrawal. **Material and Methods**: This retrospective chart-based study was conducted at a tertiary care teaching hospital in Southern India. A total of 120 case sheets from patients admitted for alcohol use were screened for this study. A total of 104 case sheets from patients with problematic alcohol use disorders were recruited and studied. **Results**: We found significant associations between the nature of withdrawal, diazepam equivalent dose, detox done, drug of choice, adequacy of detox regimen**,** and index contact ($p < 0.05$). No significant association was found between the nature of complicated withdrawal and the duration of thiamine supplementation. We did not observe a significant difference in the duration, quantity, and last use of alcohol, diazepam equivalent dose per day, dosage of thiamine per day, or duration of thiamine supplementation between individuals with uncomplicated and complicated withdrawal states. **Conclusion**: We conclude that liaisons between departments should improve the management of cases of alcohol use disorder in a better way. This will subsequently lead to a significant change in the prescription pattern of medications which includes both detoxification regimen and thiamine supplementation.

INTRODUCTION

Alcohol use disorders, or alcoholism, are problematic patterns of alcohol use that result in clinically significant impairment or psychological distress. Alcohol use disorders are responsible for 3 million deaths worldwide annually and 5.1 million Disability Adjusted Life Years.[1] It which increased from 4.5% in 2000. Global Burden of Diseases study estimated that globally, alcohol use was the seventh leading cause of death and Disability Adjusted Life Years (DALY) in the world.[2] It caused 2.2% and 6.8% of age-standardised deaths in females and males respectively. In individuals age group 15-49 years, alcohol caused death in 3.8% of females and 12.2% of males. In individuals aged > 50 years, cancers caused alcohol-related deaths in 27% of females and 19% of males. Female-attributable DALYs at 15-49 years were 2.3% and 8.9%, respectively.

India has a higher disease burden owing to alcohol use disorders. The NIMHANS National Mental Health Survey estimated the prevalence of alcohol use disorder to be 4.6% (9.1% in males vs. 0.5% in females). The treatment gap is reported to be 86%.[5] A study by Balasubramani et al. identified three major hotspots known for problematic alcohol use in our country: North Eastern states, Eastern Peninsular States comprising Chhattisgarh, Orissa Jharkhand, and Telangana, and South Indian states comprising Kerala and Tamil Nadu. The prevalence of alcohol use disorders is high in Tamil Nadu.[4] In a study by Thirumagal et al. in rural Tamil Nadu, 39% of married men in rural sites spreading across 5 states had used alcohol in the past year, of which 8.49% were identified as problem drinkers.[5]

Diagnosis of alcohol use disorders

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Three or more of the following should have occurred together for at least one month or, if persisting for less than one month, should have occurred together repeatedly for 12 months. A strong desire or sense of compulsion to take the substance; impaired capacity to control substance-taking behaviour in terms of onset, termination, or levels of use, as evidenced by the substance being taken in larger amounts or for a longer period than intended; or by persistent desire or unsuccessful efforts to reduce or control substance use. A physiological withdrawal state occurs when substance use is reduced or ceased, as evidenced by characteristic withdrawal syndrome. Evidence of tolerance to the effects of a substance, such that there is a need for significantly increased amounts of the substance to achieve intoxication or desired effect, or a markedly diminished effect with continued use of the same amount of substance. Preoccupation with substance use is manifested by important alternate pleasures or interests being given up or reduced because of substance use, or a great deal of time being spent in activities necessary to obtain, take, or recover from the effects of the substance. Persistent substance use, despite clear evidence of harmful consequences, is evidenced by continued use when the individual is aware or may be expected to be aware of the nature and extent of harm.

The complications of chronic alcohol use include liver cirrhosis, various cancers, various cardiac ailments such as myocardial ischaemia and infarction, elevated blood pressure, coronary artery disease and arrhythmias, cerebrovascular accidents, and road traffic accidents.[6-8] Due to the huge burden of alcohol use disorders and alcohol-related disorders and the large treatment gap, a pertinent question is, what is the prevalence of patients with alcohol use disorders who present to a tertiary care centre in a city being identified and treated adequately?

Aims and Objectives

The primary aim of this study was to assess the frequency of cross-referrals made to psychiatry, either from emergency or general medicine units. To study the presentation patterns in various departments and assess prescription patterns in inpatients with alcohol use disorders. The secondary objective of the study was to assess the pattern and adequacy of detoxification therapy and to assess the adequacy of thiamine supplementation.

MATERIALS AND METHODS

This retrospective chart-based study was conducted at a tertiary care teaching hospital in southern India. A total of 120 case sheets from patients admitted for alcohol use were screened for this study. A total of 104 case sheets from patients with problematic alcohol use disorders were recruited and studied. The information was collected and tabulated.

Inclusion Criteria: Patients who fulfilled criteria for alcohol dependence syndrome by the treating physician

Exclusion Criteria: patients who had alcohol use (not in dependence pattern)

Statistical Analysis

The Epi Info software was used to statistically analyse the results. Continuous variables were described as means and standard deviations, whereas categorical variables were analysed using the chi-square test.

RESULTS

In our study, we identified that of the 66 individuals with alcohol use disorder attending either the casualty or general medicine department, only 63.6% (n=42) were referred to the psychiatry department. There was no significant difference between the two departments in referring individuals with alcohol dependence syndrome to the psychiatric department.

Of the 104 patients whose records were studied, 100 showed withdrawal symptoms. Among the 100 individuals with withdrawal symptoms, 28 had complicated withdrawal symptoms and 72 had uncomplicated withdrawal symptoms. Patients who had complicated withdrawal presented mainly to the General Medicine department (n=22, 78.57%), followed by the Department of Casualty (n=4, 14.29%), and then to the Psychiatry department (n=2, 7.14%). Patients who had uncomplicated withdrawal presented predominantly to the psychiatry department (n=34, 47.22%), followed by the department of general medicine (n=30, 41.66%), and then casualties (n=8, 11.11%). We found a significant association between the nature of withdrawal and index contact ($X^2=18.144$, $p=0.001$).

On comparing the individuals with uncomplicated withdrawal, 100% and 64.7% of the individuals who visited the casualty (n=8) and psychiatry (n=22) departments received a diazepam equivalent dose of <20 mg per day, whereas 53.3% (n=16) of individuals who visited the general medicine department received a diazepam equivalent dose of more than 20 mg/day, which was found to be statistically significant ($p=0.005$).

Detoxification

Collectively, only 88 of 104 patients required detoxification. Of these 88, 100% (n=12) of the patients who presented to the casualty received detox therapy, whereas 89.5% and 77.8% of patients who presented to the Department of Psychiatry (n=34) and general medicine (n=42) received detox therapy, respectively, showing a trend towards significance ($X^2=6.517$, $p=0.038$).

Regarding the choice of benzodiazepines, chlordiazepoxide (n = 56, 53.8%) was preferred over lorazepam (n=30, 28.8%) or diazepam (n=2, 1.9%), but we only demonstrated a trend towards

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significance (p=0.05). Sixteen patients did not require Detox treatment with benzodiazepines. [Table 1]

Upon testing the adequacy of the detoxification treatment, 33.3% of patients treated in the casualty (n=4) did not receive adequate detoxification treatment, although treatment was offered to everyone who attended the casualty. This was found to be statistically significant when compared with 84.2%, 60%, and 75% of the individuals who received adequate treatment in the respective departments of psychiatry (n=32), general medicine (n=38), and casualty (n=8) (X2=11.924, p=0.018).

In the management of uncomplicated withdrawal, there is a significant association between index contact and the adequacy of the detox regimen. In particular, 88.2% (n=30) of individuals visiting the departments of psychiatry were identified to undergo an effective detox regimen which was statistically significant compared to the individuals with uncomplicated withdrawal visiting either casualty (n=2, 25%) or general medicine (n=2, 6.7%) departments (p=0.009). We could not demonstrate a similar association between index contact and complicated withdrawal. [Table 2]

Of the 104 patients, 98 (94.2%) received thiamine supplementation. A total of 97% (n=64) of the patients treated by physicians received thiamine supplementation compared to 89.5% (n=34) of the patients treated by a psychiatrist. We did not observe any significant association between the treatment consultant and thiamine supplementation. However, Psychiatrists (63.2%) tended to give thiamine supplementation for a longer duration, that is, more than 5 days, as compared to physicians (12%), and this was statistically significant (X2=29.488, p<0.001).

Thiamine supplementation was administered to all 28 (100%) patients with complicated withdrawal, and 66 out of 72 (92%) patients experienced uncomplicated withdrawal. However, no significant association was identified between thiamine supplementation and state of withdrawal. Among individuals with complicated withdrawal, only 50% and 25% of patients with alcoholic hallucinosis and withdrawal seizures, respectively, received thiamine supplementation for more than 5 days. Surprisingly, none of the patients with DT received thiamine for > 5 days. No significant association was found between the nature of complicated withdrawal and the duration of thiamine supplementation (Table 3).

Only 100 patients, whose case records were studied, had withdrawal symptoms. 72 had uncomplicated withdrawal, and 28 had complicated withdrawal. [Table 3]

We could not demonstrate a significant difference in the duration, quantity, last use of alcohol, diazepam equivalent dose per day, dosage of thiamine per day, or duration of thiamine supplementation between individuals with uncomplicated and complicated withdrawal states. [Table 4]

75% of the patients who had uncomplicated withdrawal had been adequately treated with detox therapy, whereas 78% of those who had complicated withdrawal had been treated adequately with detox therapy. However, no significant association was established between the nature of withdrawal and the adequacy of the detoxification regimen. No significant association was established between the nature of withdrawal and the equivalent dose of diazepam. In addition, more than 50% of patients had been treated with a lower dose of benzodiazepine, that is, a diazepam equivalent dose of < 20 mg. This was true for patients with both complicated (n=16, 57.1%) and uncomplicated (n=44, 61.1%) withdrawal, but it was not found to be statistically significant.

No significant association could be established between the treating consultant, nature of withdrawal, and other dependent variables, such as the detox regimen and choice of benzodiazepine. We could also not demonstrate any significant association between the nature of withdrawal among all patients and complicated withdrawal with dependent variables such as adequacy of the detox regimen and duration of thiamine supplementation. We also could not identify any significant association between the treating consultant and the adequacy of the detox regimen, diazepam equivalent dose, or thiamine supplementation. [Table 5]

Table 1: Comparison of various parameters between index contact

		Index Contact			P value
		Casualty	General Medicine	Psychiatry	
Psychiatry referral	No	4(33.3%)	8(66.7%)	-	0.809
	Yes	20(37%)	34(63%)	-	
With drawl state	Complicated withdrawal (n=28)	4 (33.3%)	22 (40.7%)	2 (5.3%)	0.001
	Nil (n=4)	0	2 (3.7%)	2 (5.3%)	
	Uncomplicated withdrawal (n=72)	8 (66.7%)	30 (55.6%)	34 (89.5%)	
Diazepam equivalent dose	≤ 20	8 (100%)	14 (46.7%)	22 (64.7%)	0.005
	> 20	0	16 (53.3%)	12 (35.3%)	
Detox done	No	0	12 (22.2%)	4 (10.5%)	0.038
	Yes	12 (100%)	42 (77.8%)	34 (89.5%)	
Drug of Choice	Chlordiazepoxide (Librium)	10 (83.3%)	26 (48.1%)	20 (52.6%)	0.049
	Diazepam	0	0	2 (5.3%)	
	Lorazepam (Ativan)	2 (16.7%)	16 (29.6%)	12 (31.6%)	
	NA	0	12 (22.2%)	4 (10.5%)	

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Table 2: Association of index contact between adequacy of detox regimen and with uncomplicated withdrawal

		Index Contact			P value
		Casualty	General Medicine	Psychiatry	
Clinical Adequacy	NA	0	12 (22.2%)	4 (10.5%)	0.018
	No	4 (33.3%)	4 (7.4%)	2 (5.3%)	
	Yes	8 (66.7%)	38 (70.4%)	32 (84.2%)	
Uncomplicated withdrawal		**Casualty**	**General Medicine**	**Psychiatry**	**P value**
Clinical Adequacy	NA	0	10 (33.3%)	2 (5.9%)	0.009
	No	2 (25%)	2 (6.7%)	2 (5.9%)	
	Yes	6 (75%)	18 (60%)	30 (88.2%)	

Table 3: Association of consultant between thiamine supplementation and DTHS

		Physician	Psychiatrist	P value
Thiamine supplementation	No	2 (3%)	4 (10.5%)	-
	Yes	64 (97%)	34 (89.5%)	
DTHS	≤ 5	58 (87.9%)	14 (36.8%)	<0.001
	> 5	8 (12.1%)	24 (63.2%)	

Table 4: Comparison of duration, quantity and last use of alcohol among individuals with different withdrawal states

	Uncomplicated withdrawal	Complicated withdrawal	P value
Duration of alcohol use (days)	18.31±9.39	18.07±10.20	0.805
Quantity of alcohol use (ml)	395.28±246.02	392.86±214.53	0.846
Last use of alcohol (days)	5.42±11.11	3.57±4.77	0.875
Dosage per day DZM Equ. (mg)	22.75±15.63	25.38±15.16	0.304
Dosage of thiamine per day (mg)	124.24±43.18	150±74.54	0.144
Duration of thiamine supplementation (days)	4.39±3.17	3.71±2.05	0.507

Table 5: Association of withdrawal state between adequacy of detox regimen and Diazepam equivalent dose

		Withdrawal state			P value
		Uncomplicated withdrawal (n=72)	Complicated withdrawal (n=28)	Nil (n=4)	
Clinical Adequacy	NA	12 (16.7%)	2 (7.1%)	2 (50%)	0.245
	No	6 (8.3%)	4 (14.3%)	0	
	Yes	54 (75%)	22 (78.6%)	2 (50%)	
Diazepam equivalent dose (mg)	≤ 20	44 (61.1%)	16 (57.1%)	2 (50%)	0.866
	> 20	28 (38.9%)	12 (42.9%)	2 (50%)	

DISCUSSION

The presence of withdrawal symptoms is one of the criteria used to diagnose alcohol dependence syndrome. Approximately 50% of the patients have withdrawal symptoms. In this study, 100 out of 104 had withdrawal symptoms. 28 patients presented to the hospital with symptoms of complicated withdrawal, which is consistent with earlier studies showing a prevalence of perceptual disturbances of around 25%, withdrawal seizures of 10% and delirium tremens of 5%.[9-12]

Thiamine supplementation

Biochemical deficiency of thiamine red blood cell transketolase is found in 58% of patients suffering from chronic liver disease, more in alcoholic patients rather than non-alcoholic patients.[13] Thiamine deficiency is responsible for mild neurological and psychiatric symptoms like confusion, memory disturbance and reduced sleep, to severe complications like encephalopathy, ataxia, heart failure, muscle atrophy, even death.[14,15]

Thiamine and its enzyme, Thiamine Pyrophosphate, are deficient in patients suffering from alcohol dependence syndrome, and at their worst, they are prone to deficiency diseases, most notably Wernicke-Korsakoff syndrome. Oral thiamine supplementation is adequate for preventing major neurological complications. High-dose oral thiamine 200 mg/day for one week restores TPP levels.[13,16-18] Thompson et al. suggested treatment with thiamine in three groups of patients: patients suffering from confusion, ataxia, ophthalmoplegia, memory disturbance, hypothermia, patients suffering from delirium tremens, and hypoglycaemia receiving glucose.[19] However, for patients with impending Wernicke's encephalopathy, a higher dose of parenteral thiamine may be required due to subclinical changes in the brain due to chronic alcohol use.

Nearly 90% of the individuals who reported to the psychiatry department had uncomplicated withdrawal, unlike the general medicine department which had approximately 40% of individuals reporting complicated withdrawal. Despite a major difference in the presentation of the withdrawal state between the departments, psychiatrists tend to give thiamine supplements for at least 6 days which is significantly higher than that of General Physicians who provide at most 5 days of thiamine supplementation and treat predominantly complicated alcohol withdrawal states. In our study, we found that thiamine supplementation was inadequate, as per the existing evidence. Patients with clinical Wernicke-encephalopathy must be prescribed 500 mg thiamine in 100 ml NS TDS for

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3-5 days, followed by 250 mg IM once a day for a further 3-5 days or more if no response is seen, and then orally administered 100 mg TDS. Patients with subclinical Wernicke's encephalopathy or those who drink excess alcohol must be prescribed 100-200 mg thiamine IM/IV for three days, followed by 100 mg orally daily. Patients with a high risk of Wernicke's encephalopathy (250 mg) daily for 3-5 days, followed by 300 mg orally daily.[13,20,21]

Detox therapy

Detoxification therapy is the treatment of choice for patients with psychoactive substance withdrawal. This ensures smooth withdrawal, providing the required medication, along with vitamins and other supportive therapies. The choice of agent for the treatment of acute withdrawal effects, including complicated withdrawal, includes benzodiazepines, such as chlordiazepoxide, diazepam, and lorazepam. This has to be continued along with vitamin supplementation, adequate nutrition, hydration and management of comorbidities.[22,23]

In this study, 16 patients were not treated with any benzodiazepines, as they had mild withdrawal symptoms and minimal risk of delirium or seizures. This is in keeping with Mayo-Smith and Saitz and O Malley who described a treatment regimen for alcohol withdrawal syndrome.[24,25] In this study, chlordiazepoxide was the benzodiazepine of choice (56), followed by lorazepam (30), and diazepam (2). This is replicated in another study done in India.[26]

A symptom-triggered regimen (STR) can be administered in a relatively stable inpatient setting based on patients' withdrawal symptoms and CIWA scores, resulting in a reduced dosage of benzodiazepine (diazepam equivalents). The fixed tapering dose regimen (FTDR) uses the concept of administering benzodiazepine at predetermined tapering levels and is more useful for outpatient treatment of alcohol withdrawal syndrome. One drink or 10 g of alcohol is usually prescribed as 5 mg diazepam (25 mg chlordiazepoxide or 1 mg lorazepam). These doses were gradually tapered and stopped in 7-10 days.[27] The adequacy of benzodiazepine was determined by the amount of benzodiazepine administered in diazepam-equivalent doses as per the alcohol consumption of the patient and the number of days. Patients suffering from complicated withdrawal syndrome (alcoholic hallucinosis, delirium tremens, or alcohol withdrawal seizures) require a higher dose of benzodiazepines for their condition. Mayo-Smith et al. recommended that control of agitation in patients with DT can be achieved with parenteral short-acting benzodiazepines, in adequate doses to maintain light somnolence during the DT phase.[28]

In this study, 75% of patients who had uncomplicated withdrawal were adequately treated with detox therapy. 78% of those who had complicated withdrawals were treated adequately for detox, and this was not clinically significant. In addition, the majority of patients were treated with a lower dose of benzodiazepine (diazepam equivalent 20 mg) than patients who received a higher dose. This was true for patients with both complicated and uncomplicated withdrawals and was not statistically significant.

CONCLUSION

We conclude that liaisons between departments should improve the management of cases of alcohol use disorder in a better way. This will subsequently lead to a significant change in the prescription pattern of medications which includes both detoxification regimen and thiamine supplementation.

Limitations

The follow-up of these inpatients after discharge was not studied; hence, long-term outcomes were unknown, and it would be difficult to predict who relapsed and who remained abstinent. However, non-pharmacological methods have not yet been studied.

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