



Serum Potassium in Alcohol Withdrawal Delirium: A Prospective Observational Study from a Rural Teaching Hospital in Central India.

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Abstract

Background: Hypokalemia is common in alcohol dependence, and low serum potassium has been reported among the clinical predictors of severe alcohol withdrawal. Whether serum potassium changes with the clinical course of alcohol withdrawal delirium has been examined in few Indian samples. **Methods:** Fifty consecutive men admitted with alcohol withdrawal delirium to the psychiatry ward of a rural tertiary care teaching hospital in central India were studied between November 2019 and June 2021. Diagnosis followed the International Classification of Diseases, tenth revision. Serum potassium was measured on the day of admission and again after clinical remission of delirium. Severity of delirium was rated with the Delirium Rating Scale-Revised-98. A paired t test compared admission and recovery potassium, and Spearman rho tested the association between serum potassium and Delirium Rating Scale-Revised-98 total score. **Results:** Mean age was 36.26 years (standard deviation, SD 9.89) and mean duration of alcohol use was 10.40 years (SD 4.40). Thirty-six participants (72%) drank daily. Thirteen (26%) were hypokalemic at admission. Mean serum potassium rose from 3.46 mmol/L (SD 0.31) at admission to 3.88 mmol/L (SD 0.35) at recovery, a mean increase of 0.42 mmol/L ($p < 0.001$). Among the 13 hypokalemic participants, delirium severity and serum potassium were not correlated ($\rho = -0.21$, $p = 0.470$). **Conclusion:** Serum potassium rose between admission and clinical recovery in men with alcohol withdrawal delirium. Admission potassium did not track delirium severity in this small sample, and the rise cannot be separated from the effect of treatment given during admission.

Keywords: Alcohol Withdrawal Delirium; Hypokalemia; Potassium; Alcoholism; Delirium.



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INTRODUCTION

Alcohol dependence affects 9.1% of the Indian adult population according to the National Mental Health Survey 2015-2016 [1]. Withdrawal begins 6 to 24 hours after a dependent drinker stops or reduces intake and produces a cluster of symptoms driven by autonomic hyperactivity [2]. Delirium tremens and withdrawal seizures sit at the severe end of this spectrum and occur in 5% to 10% of treatment-seeking patients with alcohol dependence [3]. Delirium tremens presents with acute onset, fluctuating inattention, disorientation and visual hallucination, together with tremor, tachycardia and raised blood pressure. Mortality is close to 5%, falling below 1% when the condition is recognised early and benzodiazepines are started promptly [4].

Because delirium is a medical emergency, markers that identify patients at risk of a severe course carry practical value. In a systematic review and meta-analysis, Goodson and colleagues identified a past history of delirium tremens, structural brain lesion, and severity of early withdrawal, older age, low platelet count, low serum potassium and low magnesium among the predictors of severe alcohol withdrawal [5]. Hypokalemia, defined as a serum potassium below 3.5 mmol/L, has been attributed in this setting to beta-adrenergic stimulation driving potassium into cells, a mechanism demonstrated experimentally by Clausen and Flatman [6].

Serum potassium is measured routinely on admission in almost every Indian hospital and costs little. If it moved with the clinical course of delirium, it would be an unusually accessible marker in a condition where prognostic information is scarce. We hypothesised that serum potassium would be lower during delirium than after its remission, and that the degree of hypokalemia at admission would relate to the severity of delirium. The aim of this study was to measure serum potassium

at admission and again at clinical recovery in consecutive admissions for alcohol withdrawal delirium, and to test its association with delirium severity.

MATERIALS AND METHODS

This was a prospective observational study conducted in the psychiatry ward of a rural tertiary care teaching hospital in central India between November 2019 and June 2021. The hospital serves a district in which the sale of alcohol is prohibited. Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Fifty consecutive admissions for alcohol withdrawal delirium were enrolled. The diagnosis was made by the treating consultant psychiatrist according to the International Classification of Diseases, tenth revision (ICD-10). No formal sample size calculation was carried out; the sample comprises every eligible admission during the study period.

The study was approved by the institutional ethics committee before enrolment began, and the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Declaration of Helsinki. Patients in delirium were unable to give consent, so written informed consent was obtained from the accompanying relative. All signed informed consent forms have been received and archived by the authors. Socio-demographic details, quantity and pattern of alcohol use and family history of alcohol use were recorded on a predesigned proforma. Serum potassium was estimated on venous samples drawn on the day of admission and repeated after clinical remission of delirium as judged by the treating consultant. Hypokalemia was defined as a serum potassium below 3.5 mmol/L.

Severity of delirium was rated with the Delirium Rating Scale-Revised-98 (DRS-R98), a clinician-rated 16-item instrument validated by Trzepacz and colleagues [7]. Three diagnostic items cover temporal onset, fluctuating course and the underlying physiological cause. A separate 13-item severity subsection rates disturbance of cognition, affect, language, motor activity and the sleep-wake cycle over the preceding 24 hours.

Statistical analysis: Data were analysed in SPSS version 21 (IBM Corp., Armonk, NY, USA). Continuous variables are summarised as mean and standard deviation (SD), categorical variables as counts and percentages. A paired t test compared serum potassium at admission with serum potassium at recovery. Spearman rho tested the association between serum potassium and DRS-R98 total score. A two-sided p value below 0.05 was taken as statistically significant.

RESULTS

It was observed from **Table 1** that all 50 participants were men. Mean age was 36.26 years (SD 9.89), and the largest single group, 20 participants (40%), was aged 30 to 39 years. Thirty participants (60%) were married, 24 (48%) had studied up to high school and 12 (24%) held a graduate or professional degree. Twenty-seven (54%) lived in rural areas. Thirty-seven (74%) were skilled or semi-skilled workers. Mean duration of alcohol use was 10.40 years (SD 4.40) and mean reported intake was 14.72 units per day (SD 4.30). Thirty-six participants (72%) drank daily and 14 (28%) drank in a binge pattern. Twenty-eight (56%) reported a family history of alcohol use.

Table 1: Socio-demographic characteristics and pattern of alcohol use (N = 50)

Characteristic	No. (%)
Age (in years)	
18-29 yrs	13 (26)
30-39 yrs	20 (40)
40-49 yrs	12 (24)
50-59 yrs	5 (10)
Mean (SD)	36.26 (9.89)
Marital Status	
Married	30 (60)
Single	15 (30)
Divorced	3 (6)
Separated	2 (4)
Religion	
Hindu	30 (60)
Buddhist	11 (22)
Muslim	9 (18)
Education	
Professional degree	2 (4)
Graduate	10 (20)
Diploma	2 (4)

High school	24 (48)
Middle school	11 (22)
Illiterate	1 (2)
Area of residence	
Rural	27 (54)
Semi-urban	15 (30)
Urban	8 (16)
Occupation	
Skilled worker	22 (44)
Semi-skilled worker	15 (30)
Semi-professional	11 (22)
Professional	1 (2)
Unemployed	1 (2)
Alcohol use	
Duration of use in years, mean (SD)	10.40 (4.40)
Duration more than 10 years	22 (44)
Intake in units per day, mean (SD)	14.72 (4.30)
Daily pattern of drinking	36 (72)
Binge pattern of drinking	14 (28)
Family history of alcohol use	28 (56)

[SD, standard deviation. Values are n (%) unless stated otherwise]

It was seen from **Table 2** that there were thirteen participants (26%) were hypokalemic at admission. Serum potassium rose by a mean of 0.42 mmol/L between admission and recovery ($p < 0.001$).

Table 2: Serum potassium at admission and at recovery (N = 50)

Time point	Mean (mmol/L)	SD	Mean difference	t	p
Admission	3.46	0.31	0.42 (0.33)	4.62	<0.001
Recovery	3.88	0.35			

[SD, standard deviation. Paired t test. The mean difference is reported with its standard deviation in parentheses]

As shown in **Table 3** that among the 13 hypokalemic participants, serum potassium and DRS-R98 total score were not correlated ($\rho = -0.21$, $p = 0.470$). Delirium Rating Scale-Revised-98 total score against serum potassium at admission among the 13 participants who were hypokalemic on admission.

Table 3: Serum potassium and delirium severity among hypokalemic participants (n = 13)

Variable	Mean (SD)	Spearman rho	p
Delirium Rating Scale-Revised-98 total score	27.30 (4.11)	-0.21	0.470
Serum potassium (mmol/L)	3.25 (0.12)		

[SD, standard deviation. Spearman rank correlation]

DISCUSSION

Serum potassium rose by a mean of 0.42 mmol/L between admission and clinical recovery in 50 men admitted with alcohol withdrawal delirium. Among those who were hypokalemic on admission, the degree of hypokalemia showed no relationship with the severity of delirium.

A rise in potassium accompanying clinical improvement is consistent with earlier work. Carl and Holzbach described hypokalemia and hypomagnesemia during alcohol withdrawal that reversed as withdrawal settled [8]. Wetterling and colleagues included low serum potassium among the clinical predictors of alcohol withdrawal delirium in a prospective sample [9].

Several mechanisms plausibly contribute. Plasma catecholamines rise during alcohol withdrawal, and beta-2 adrenoceptor stimulation moves potassium into cells without any change in total body potassium [6,10]. Poor nutritional intake, vomiting, diarrhoea, diuresis and reduced renal tubular reabsorption all lower serum potassium in people who drink heavily, and respiratory alkalosis from hyperventilation shifts potassium intracellularly as well [10]. These mechanisms differ in how quickly they reverse, which may be why serum potassium at a single time point is a blunt indicator.

The demographic profile of the sample is close to that reported in earlier Indian work. Behere found that 30 to 39 years was the most affected age band in a rural community survey in a dry district of central India [11]. Every participant here

was male. Mohan and colleagues reported that women in rural Indian communities who drink do so in small quantities, which makes severe withdrawal in women correspondingly rare [12]. Seventy-two percent of participants drank daily and 28% in a binge pattern, and severity of delirium did not differ between the two groups, in keeping with the observation of Grover and Ghosh that the pattern of consumption does not predict the development of delirium [13].

The absence of a correlation between admission potassium and DRS-R98 score should be read cautiously rather than as a negative finding. The correlation was tested in only 13 participants. Detecting a correlation of the magnitude observed here ($\rho = -0.21$) with 80% power at a two-sided alpha of 0.05 would require approximately 175 participants, so this study was never in a position to find it. The result is uninformative about the underlying association rather than evidence against it.

Limitations

The study was conducted at a single centre in an all-male sample, and there was no comparison group of patients with uncomplicated alcohol withdrawal, so it is not possible to say whether the observed potassium values are specific to delirium. The interval between admission and the repeat sample was not standardized and varied with the clinical course.

CONCLUSION

Most importantly, patients received benzodiazepines, intravenous fluids, thiamine and, where clinically indicated, electrolyte replacement between the two measurements. The rise in serum potassium therefore cannot be separated from the effect of treatment, and an observational design of this kind cannot distinguish the two. Serum magnesium was not measured, despite its recognized association with withdrawal severity. What this study establishes is that serum potassium in this population is low at admission and higher at recovery, in a rural Indian setting from which little such data exist. Whether it carries prognostic information will need a larger prospective sample, a comparison group of uncomplicated withdrawal, standardized sampling times and a record of electrolyte replacement given during admission. Given how cheaply serum potassium is measured, that question is worth settling.

Conflict of Interest

The authors declare that they have no conflict of interest.

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