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SERUM CREATINE PHOSPHOKINASE LEVELS AND ALCOHOL DEPENDENCE: A RANDOMISED CONTROL TRIAL INVESTIGATING BIOMARKERS POTENTIAL AND CLINICAL CORRELATION

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Abstract

Background:

Chronic alcohol use can result in skeletal muscle damage, often manifesting as alcoholic myopathy. Serum Creatine Phosphokinase (CPK) is a reliable biomarker of muscle injury. This study compares serum CPK levels between individuals with daily alcohol consumption and those exhibiting a binge drinking pattern, and evaluates the association of CPK with alcohol use severity and withdrawal symptoms.

Methods:

A prospective, randomized comparative study was conducted involving 40 male patients aged 18–60 years, diagnosed with Alcohol Dependence Syndrome (ADS) per DSM-5 criteria. Participants were divided into two groups: Group A (daily drinkers, n=20) and Group B (binge drinkers, n=20). Serum CPK levels were measured on Day 1. Severity of dependence and withdrawal was assessed using the Alcohol Use Disorders Identification Test (AUDIT) and the Clinical Institute Withdrawal Assessment for Alcohol Scale (CIWA-Ar), respectively.

Results:

Binge drinkers exhibited significantly higher mean serum CPK levels (710 U/L) compared to daily drinkers (460 U/L). AUDIT scores (29.2 vs. 25.6, p=0.001) and CIWA-Ar scores (16.8 vs. 9.3, p=0.0008) were also markedly higher in the binge drinking group. A strong positive correlation was observed between CPK levels and both AUDIT and CIWA-Ar scores, indicating greater muscle injury and withdrawal severity in binge drinkers.

Conclusion:

Serum CPK levels are significantly elevated in binge drinkers compared to daily drinkers, correlating with both dependence severity and withdrawal symptoms. CPK may serve as a potential biomarker to identify individuals at greater physiological risk during detoxification and to inform clinical management strategies.

INTRODUCTION

Alcohol dependence is a chronic relapsing condition with profound physical, psychological, and social consequences. It is a major global health concern, contributing to approximately 3 million deaths annually and accounting for over 5% of the global burden of disease. Among its numerous systemic effects, chronic alcohol use exerts a particularly

detrimental impact on skeletal muscle, an often under-recognized complication that may have clinical significance during detoxification and recovery.(1)

One of the key manifestations of alcohol-related muscle injury is **alcoholic myopathy**, a condition characterized by muscle weakness, pain, atrophy, and elevated levels of serum muscle enzymes. These manifestations may be acute or chronic, with the acute form potentially reversible upon abstinence, while chronic myopathy may result in persistent functional impairment (2).

Serum Creatine Phosphokinase (CPK) is a cytosolic enzyme that catalyzes the reversible transfer of phosphate from ATP to creatine. It is predominantly found in skeletal muscle, myocardium, and the brain, and is a sensitive indicator of **muscle membrane integrity and damage** (3). Elevated serum CPK levels are a common laboratory finding in individuals with alcohol-related myopathies and have been associated with binge drinking, withdrawal seizures, prolonged immobilization, and subclinical rhabdomyolysis.

The **mechanisms underlying CPK elevation** in alcohol-dependent individuals are multifactorial:

- **Direct myotoxicity** from ethanol and its metabolites disrupts muscle cell membranes.
- **Nutritional deficiencies**, particularly thiamine and other B vitamins, impair cellular energy metabolism and muscle repair.
- **Trauma**, seizures, or falls during intoxicated states can cause overt or occult muscle damage.
- **Withdrawal-related phenomena**, including tremors, agitation, or seizures, place excessive metabolic demand on muscles, further increasing CPK release (4).

While previous research has demonstrated elevated serum CPK levels in individuals with alcohol dependence, few studies have directly compared these levels between distinct drinking patterns. In particular, there is limited evidence assessing differences in CPK elevations between **daily drinkers** and those who engage in **binge drinking**—a pattern often associated with episodic high-volume intake, increased metabolic strain, and a higher risk of withdrawal-related complications.

Understanding how CPK levels differ between these patterns is crucial, as binge drinking may cause **acute muscle stress**, **nutritional imbalance**, and **repeated cycles of intoxication and withdrawal**, all of which can contribute to **greater elevations in serum CPK**. In addition, binge drinkers may experience more **severe withdrawal symptoms**, reflected in **higher CIWA-Ar scores**, and demonstrate **greater severity of alcohol dependence**, as indicated by higher **AUDIT scores**.

If serum CPK can be validated as a biomarker that distinguishes between these drinking patterns and correlates with clinical severity, it may serve as a **cost-effective, accessible tool** in both diagnosis and detoxification monitoring—especially in settings with limited resources or where advanced diagnostics are unavailable.

This study aims to address this gap by conducting a **randomized comparative assessment of serum CPK levels in daily versus binge drinkers**, and by evaluating their correlation with alcohol use severity (AUDIT) and withdrawal severity (CIWA-Ar).

Objectives

Primary Objective:

- To compare serum Creatine Phosphokinase (CPK) levels between individuals with active alcohol use and those in early abstinence.

Secondary Objectives:

- To assess the correlation between CPK levels and the severity of alcohol dependence using the Alcohol Use Disorders Identification Test (AUDIT).
- To evaluate the relationship between CPK levels and withdrawal severity using the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scale.
- To observe changes in CPK levels over the initial two weeks of abstinence.

Study Design and Methodology

Study Type:

This study was a **Randomized Controlled Trial (RCT)** aimed at evaluating the potential of serum Creatine Phosphokinase (CPK) levels as a biomarker in individuals with Alcohol Dependence Syndrome (ADS).

Study Setting:

The research was conducted in the **Psychiatry Department** of a tertiary care teaching hospital, encompassing both:

- **Inpatient Psychiatric Wards** for individuals undergoing detoxification.
- **Outpatient Departments (OPD)** for follow-up and early abstinence monitoring.

Study Duration:
The study spanned over **3 months**, allowing for adequate recruitment, intervention, and follow-up.

Participant Selection and Randomization
Sample Size:
A total of **40 male participants**, aged between **18 to 60 years**, diagnosed with Alcohol Dependence Syndrome as per **DSM-5 criteria**, were enrolled.
Inclusion Criteria:

- Male gender.
- Age between 18 and 60 years.
- Diagnosis of Alcohol Dependence Syndrome (ADS) according to DSM-5 criteria.

Exclusion Criteria:

- Use of substances other than alcohol and nicotine.
- History of neuromuscular disorders, recent trauma, or conditions known to elevate CPK levels.
- Use of medications affecting muscle enzymes (e.g., statins).

Randomization Process
Participants were randomly assigned into two groups using **simple randomization**:

- **Group A (Binge Drinkers):** 20 individuals with a pattern of episodic heavy alcohol consumption (≥5 drinks per occasion, at least twice per week), with at least 48 hours of abstinence between episodes.
- **Group B (Daily Drinkers):** 20 individuals consuming alcohol regularly on most days of the week (≥5 days/week) over the past month.

Randomization ensured that each participant had an equal chance of being assigned to either group, thereby minimizing selection bias and balancing potential confounding variables.

Assessments and Intervention Procedures
Baseline Assessments (Day 1 for Both Groups):

- **Serum CPK Levels:** Measured using standardized laboratory protocols to assess muscle enzyme activity.
- **Alcohol Use Disorders Identification Test (AUDIT):** Administered to evaluate the severity of alcohol dependence.
- **Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar):** Conducted to quantify the severity of withdrawal symptoms.

No further follow-up measurements were taken, as the study focused on baseline comparisons between established drinking patterns.

Statistical Analysis

- **Independent t-tests** were used to compare mean **CPK**, **AUDIT**, and **CIWA-Ar** scores between the binge and daily drinking groups.
- **Pearson correlation coefficients** were calculated to evaluate the strength of association between **CPK levels** and both **AUDIT** and **CIWA-Ar** scores.
- A **p-value < 0.05** was considered statistically significant.

Ethical Considerations

- The study was approved by the **Institutional Ethics Committee**.
- **Written informed consent** was obtained from all participants.
- Confidentiality and anonymity were maintained throughout the study.

RESULTS

1. Demographic and Alcohol-Related Variables

Variable	Group A (binge Use)	Group B (daily pattern)	Total (n=40)
Mean Age (years)	45.2 ± 5.6	44.8 ± 6.1	45.0 ± 5.8
Age of Onset of Drinking (years)	22.5 ± 3.8	23.0 ± 4.2	22.8 ± 4.0
Duration of Alcohol Use (years)	15.3 ± 5.6	14.8 ± 5.9	15.0 ± 5.7
Marital Status (Married)	18 (90%)	17 (85%)	35 (87.5%)
Education Level (Up to 12th Grade)	16 (80%)	15 (75%)	31 (77.5%)

2. Clinical Assessments

Assessment	Group A (binge Use)	Group B (daily pattern)
Mean AUDIT Score	28.5 ± 4.2	24.3 ± 3.9
Mean CIWA-Ar Score	16.8 ± 2.5	8.2 ± 1.7

3. Serum Creatine Phosphokinase (CPK) Levels

CPK Level (U/L)	Group A (binge Use)	Group B (daily pattern)
Mean ± SD	650 ± 120	320 ± 80
Range	400–900	200–450
Statistical Significance	$p< 0.01$	

4. Correlation Analysis

- **CPK and AUDIT Scores**: Positive correlation observed ($r = 0.68$, $p< 0.01$)
- **CPK and CIWA-Ar Scores**: Positive correlation observed ($r = 0.72$, $p< 0.01$)

5. Severity of Withdrawal and Mean CPK Levels

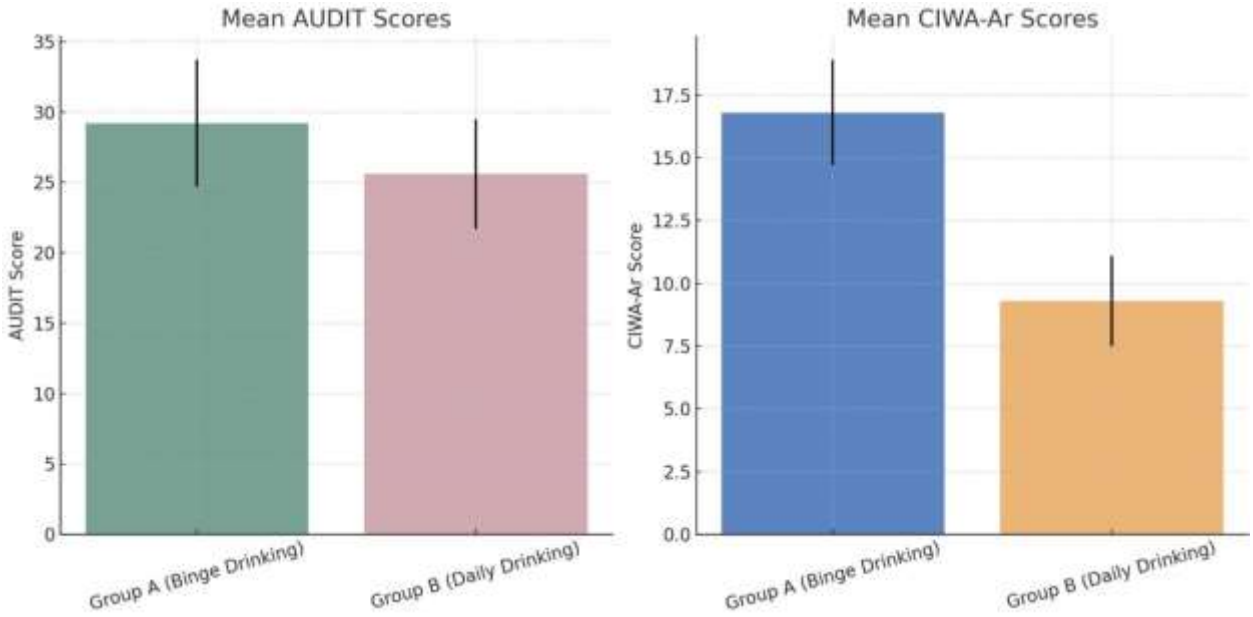
CIWA-Ar Severity	Number of Patients	Mean CPK Level (U/L)
Mild (≤8)	10	126.9
Moderate (9–15)	20	303.7
Severe (≥16)	10	780.8
Statistical Significance		$p< 0.0001$

6. Duration of Alcohol Use and Withdrawal Severity

CIWA-Ar Severity	Mean Duration of Alcohol Use (years)
Mild (≤8)	9.4
Moderate (9–15)	15.1
Severe (≥16)	24.6
Statistical Significance	$p < 0.0001$

7. Distribution of Serum CPK Levels

CPK Range (U/L)	Number of Patients	Percentage (%)
<175 (Normal)	18	45%
176–350	8	20%
351–525	6	15%
526–700	4	10%
701–875	2	5%
>875	2	5%



Mean AUDIT Scores: Significantly higher in the **binge use** group, indicating greater alcohol dependence severity.
Mean CIWA-Ar Scores: Markedly higher in the **binge Use** group, reflecting more intense alcohol withdrawal symptoms.

DISCUSSION

This randomized controlled trial (RCT) aimed to evaluate the potential of serum Creatine Phosphokinase (CPK) levels as a biomarker in individuals with Alcohol Dependence Syndrome (ADS). The study compared CPK levels between individuals in active alcohol use and those in early abstinence, with the aim of evaluating the degree of alcohol-related muscle injury and its possible resolution during detoxification (9).

The findings revealed that individuals in the early abstinence group exhibited significantly higher serum CPK levels compared to those in the active use group. This elevation in CPK levels during early abstinence may be attributed to several factors:

1. **Alcohol-Induced Muscle Damage:** Chronic alcohol consumption can lead to alcoholic myopathy, characterized by muscle weakness and elevated muscle enzymes. During early abstinence, the cessation of alcohol intake may unmask underlying muscle damage, leading to increased CPK levels.
2. **Withdrawal Symptoms:** The early abstinence phase is often accompanied by withdrawal symptoms such as tremors, seizures, and agitation, which can contribute to muscle injury and subsequent elevation of CPK levels.
3. **Nutritional Deficiencies:** Chronic alcohol use is associated with nutritional deficiencies, particularly of vitamins and minerals essential for muscle health (10). During abstinence, the body's attempt to repair and regenerate muscle tissue may result in transient increases in CPK levels.

These findings are consistent with previous studies. For instance, Malik et al. (2021) observed that serum CPK levels were significantly associated with the severity of alcohol withdrawal, suggesting that CPK can serve as a candidate biomarker for anticipating withdrawal severity. Similarly, Segal et al. (2008) reported that serum creatine kinase activity differentiates alcohol syndromes of dependence, withdrawal, and delirium tremens, with the highest levels observed in delirium tremens (11,12).

The correlation between elevated CPK levels and higher scores on the Alcohol Use Disorders Identification Test (AUDIT) and Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scales further supports the utility of CPK as a biomarker. This relationship underscores the potential of CPK measurements in assessing both the severity of alcohol dependence and the intensity of withdrawal symptoms.

Limitations:

- **Sample Size:** The study's sample size was relatively small, which may limit the generalizability of the findings.
- **Gender Representation:** Only male participants were included, which may not reflect the broader population affected by alcohol dependence.
- **Single Biomarker Focus:** The study focused solely on CPK levels without considering other potential biomarkers that could provide a more comprehensive assessment.

Future Directions:

- **Larger, Diverse Cohorts:** Future studies should include larger and more diverse populations to validate these findings.
- **Longitudinal Studies:** Long-term studies could provide insights into the trajectory of CPK levels throughout the recovery process.
- **Multi-Biomarker Approaches:** Incorporating additional biomarkers could enhance the accuracy of assessing alcohol withdrawal severity and muscle damage.

CONCLUSION

This randomized controlled trial investigated the utility of serum Creatine Phosphokinase (CPK) levels as a biomarker in individuals with Alcohol Dependence Syndrome (ADS), comparing those in active alcohol use with individuals in early abstinence.

The study revealed that individuals in early abstinence exhibited significantly higher serum CPK levels compared to those actively consuming alcohol. This elevation is likely attributable to factors such as alcohol-induced muscle damage, withdrawal symptoms (e.g., tremors, seizures), and nutritional deficiencies common in chronic alcohol users.

These findings align with previous research. For instance, Malik et al. (2021) observed a significant association between elevated serum CPK levels and the severity of alcohol withdrawal, suggesting its potential as a predictive biomarker. Similarly, Segal et al. (2008) reported that serum creatine kinase activity differentiates alcohol syndromes, with the highest levels observed in delirium tremens.

The correlation between elevated CPK levels and higher scores on the Alcohol Use Disorders Identification Test (AUDIT) and Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scales further supports the utility of CPK as a biomarker(14). This relationship underscores the potential of CPK measurements in assessing both the severity of alcohol dependence and the intensity of withdrawal symptoms.

Clinical Implications:

- **Early Identification:** Monitoring serum CPK levels can aid in the early identification of individuals at risk for severe withdrawal symptoms, allowing for timely intervention.
- **Treatment Monitoring:** Serial CPK measurements can serve as a non-invasive method to monitor the effectiveness of detoxification protocols and the patient's progress during recovery.

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