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Exploring Caffeine Withdrawal Insomnia Using Insomnia Severity Index (Isi) Method: An Observational Study in Indian Rural Population

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Running title

Severity during Caffeine Withdrawal in Rural India

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KEYWORDS
Caffeine consumption, Insomnia, Caffeine withdrawal, Rural population, DSM-IV

ABSTRACT:

Purpose

The aim of this study was to assess the physical and mental changes in individuals from a rural Indian population before and after caffeine withdrawal. This study focuses on the behavioral effects, especially insomnia, after caffeine deprivation among participants consuming high levels of caffeine daily.

Methods

An observational cross-sectional study was conducted over a two-month period among 68 volunteers at Sanjivani Rural Education Society, Maharashtra, India. Participants were selected based on their daily caffeine intake, with inclusion criteria focusing on individuals consuming more than 400 mg of caffeine per day. Data on demographics and caffeine consumption were collected using a structured questionnaire. The Insomnia Severity Index (ISI) was used to assess changes in sleep patterns before and after 72 hours of caffeine withdrawal. A multiple correlation method was applied to analyze the

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relationship between caffeine intake and insomnia severity.

Result

Out of 68 participants, 84% (n=59) reported sleep disturbances during the caffeine withdrawal period, which was classified as substance-induced insomnia according to DSM-IV criteria. A multiple correlation analysis indicated a mild positive association ($R=0.22$) between high caffeine consumption and the severity of insomnia during withdrawal. These findings suggest that excessive caffeine intake significantly affects sleep quality, particularly during withdrawal periods.

Conclusion

The study identified a notable impact of high caffeine intake on sleep disturbances in a rural Indian population. The results emphasize the importance of moderating daily caffeine consumption to prevent insomnia and improve sleep hygiene. Individualized recommendations for daily caffeine intake are crucial for mitigating potential adverse effects on sleep and overall health.

Introduction

Coffee is one of the most popular beverages in the world (Cano-Marquina, 2013). Tea, a beverage made from the leaves of the tea plant, originated in ancient China and has gained worldwide popularity in recent years (Y.-J. Guo, 2017). Fifteen major compounds have been identified in coffee, divided into three groups: purine alkaloids (caffeine, theobromine, trigonelline, and niacin), polyphenols (chlorogenic acid, caffeic acid, quinic acid, ferulic acid, hydroxyhydroquinone, quercetin, phenylindarins), and secoisolpenol (secoisolene). Many bioactive substances, including polyphenols, pigments, polysaccharides, alkaloids, free amino acids, and saponins, have been found in tea leaves and their brewing process (Bi, 2016; L. Guo, 2016; Pan, 2017; Wang, 2017; Tang, 2019; Zhao, 2019). These active ingredients do not contain chlorogenic acid, quinic acid, and phenylindanes due to their intestinal absorption or higher fractional bioavailability than pharmacokinetic data. Due to thermal instability, chlorogenic acids break down almost completely into volatile phenolic compounds under intense conditions (Y.-J. Guo, 2017). According to the production process, tea can be divided into six groups: white tea, green tea, yellow tea, oolong tea, black tea, and dark tea. White and green tea are not fermented, while oolong, black, and dark tea are heavily fermented (Islam, 2018; Kujawska, 2016; Lv, 2017; Sanlier, 2018; Hilal & Engelhardt, 2007; Zheng, 2015). Several studies have shown that tea and its bioactive components have many health benefits, such as anti-oxidation, anti-inflammatory, anti-cancer, anti-cardiovascular, anti-diabetic, and anti-hyperlipidemia (Lorenzo; Gan, 2018; Li, 2016; Ramadan, 2017; Santamarina, 2015; Suzuki, 2016).

Coffee consumption is associated with an increased risk of many diseases, including diabetes, heart disease, neurodegenerative diseases, and cancer (Cano-Marquina, 2013). Drinking coffee has also been associated with a reduced risk of Parkinson's disease. Drinking more coffee has been shown to reduce the risk of Parkinson's disease in a dose-dependent manner (Wei, 2012). Caffeine is rapidly absorbed after consumption, 99% within 45 minutes. Peak plasma concentrations occur 15 to 120 minutes after oral ingestion and may be affected by the route of administration or other foods. When caffeine is absorbed, it is quickly converted to water in the body. However, caffeine is still lipophilic enough to easily cross all biological barriers, including the blood-brain barrier. The average half-life of caffeine in the plasma of healthy people is about 5 hours, but the half-life can be between 1.5 and 9.5 hours. This large variation in exposure half-life may be due to individual differences in excretion or due to individuals smoking (shortening half-life) or using oral contraceptives (prolonging half-life) (Ferré, 2008; Fisone, 2004).

The mechanism of action of caffeine involves intracellular calcium mobilization. Some effects of caffeine on skeletal muscle appear to be related to ionized calcium (Ca^{++}). Studies have shown that high doses of caffeine (1-10 mM) inhibit calcium uptake and

its storage in the sarcoplasmic reticulum of striated muscle and increase Ca++ translocation through the plasma membrane. Caffeine can increase the Ca++ sensitivity of myofilaments by binding to ryanodine receptors on calcium channels in muscles and cells. Although caffeine has been shown to release calcium from intracellular stores in bone and muscle, the initial concentration required to observe this effect (250M) is greater than that required for cardiovascular disease in vivo (50M). Therefore, the subcellular effect of caffeine may not be physiologically significant (Kerrigan & Lindsey, 2005). As with most drugs, caffeine has a long list of side effects, ranging from mild to severe or even fatal, usually related to dosage and individual sensitivity. Death from caffeine toxicity is usually associated with cardiac arrhythmias, hypotension, myocardial infarction, electrolyte disturbances, and aspiration.

In 1994, a study of hundreds of physicians in Minnesota and Vermont found that 94% recommended reducing or limiting caffeine intake for patients suffering from heartburn. Jeffrey Goldberg described the findings as "difficult" and noted that a workshop was held to review whether the evidence supports the recommendations. It's not uncommon for 94% of doctors to recommend something after a heart attack, such as beta-blockers or atrial fibrillation drugs, even if the results have been demonstrated in clinical trials. While there are many ways to measure the effects of caffeine on the heart, such as QRS duration and the time it takes for the ventricles to depolarize, there are also studies that focus on three types of arrhythmia, such as atrial fibrillation, premature ventricular complexes, and arrhythmias that can cause sudden cardiac death (Hughes, 1988).

More than 93% of the adult U.S. population consumes approximately 200 mg of caffeine per day (Sajadi-Ernazarova, 2023). In China, male and female caffeine intake was found to be 123 mg and 116 mg per day, respectively (Meredith, 2013). In Japan, 43% of the population consumes caffeine-related drinks. About 82% of the Russian population has a caffeine consumption habit (Martinchik, 2005). The Canadian population consumes an average of 400 mg/day of caffeine (Verster & Koenig, 2018). In the UAE, the per capita intake of caffeine is identified as 3.5 kg. In India, caffeine intake varies by state, and while exact data is unknown, the population in Maharashtra consumes approximately 200 mg of coffee and 150 mg of tea per day (Silverman, 1992). Yet currently, there is no existing research on caffeine withdrawal studies conducted in the rural Indian population. This study specifically focuses on examining the physical and mental changes in individuals before and after caffeine withdrawal for a given time period, based on strong evidence.

Methodology

An observational cross-sectional study was conducted at Sanjivani Rural Education Society, Maharashtra, India, over a period of two months. The study included 68 participants, who were selected based on their daily caffeine consumption. The primary objective was to examine behavioral and symptomatic changes in individuals after caffeine withdrawal. The participants were chosen using a simple random sampling method, with eligibility based on their caffeine intake. The inclusion criterion for the study was a daily intake of more than six cups of caffeinated beverages (exceeding 400 mg/day). This threshold was selected based on prior research, which has shown that consuming over six cups per day can lead to severe health issues such as dementia, depression, confusion, and bradycardia. Those consuming less than six cups of coffee or tea were excluded from the study, as such intake levels are generally considered safe. A data collection form was used to gather essential demographic information, including age, gender, weight, medical history, and daily coffee consumption. The participants were between the ages of 18 and 60, with data collected on their medical backgrounds to better understand the impact of high caffeine intake. Once the participants were enrolled and informed about the study, they were given time to decide whether they wanted to participate. Those who agreed provided signed informed consent. Behavioral changes were analyzed through a series of questions based on the Insomnia Severity Index (ISI) method (Williamson, 2020; Bastien, 2001).The primary focus of the study was to assess the changes in participants' behavior and symptoms before and after caffeine withdrawal. Participants underwent a 72-hour period without caffeine, during which their symptoms were monitored closely. To analyze the outcomes, the study employed multiple correlation analysis, using Equation No. 1, which was designed to assess the relationships between various symptomatic changes and the duration

of caffeine deprivation. Scatter plots were also generated to visually validate the associations between different variables. The study's findings were evaluated by analyzing the correlation between the variables (e.g., symptomatic changes) and the length of caffeine withdrawal. The use of statistical tools, such as multiple correlation and scatter plot analysis, enabled the researchers to assess whether there were significant behavioral and symptomatic changes in the participants after caffeine deprivation.

This study provides insights into the effects of high caffeine consumption and withdrawal, focusing on the associated behavioral changes, and contributes valuable data regarding the health implications of excessive caffeine intake.

Where...R = Correlation Coefficient (R= 0 - 0.25;

Mild Positive

association, R= 0.25 – 0.5;

Moderate Positive association, R= 0.5 - 0.9;

Strong positive association.)

Y = Independent Variable

$$R = \frac{\sqrt{r}2yx1 + r2yx2 - 2ryx1(ryx2)(rx1x2)}{\sqrt{1} - r2x1x2}$$

……………….Eq.no.1

Data Analysis

The data collected from the study participants was carefully categorized into discrete random variables, primarily focusing on the amount of caffeine intake. Each volunteer's score was derived from their responses to a questionnaire designed to assess symptomatic changes during the caffeine withdrawal period. For statistical purposes, a Multiple Correlation Statistical Method was applied using the formula detailed in Equation No. 1. In this method, two independent variables were utilized: (1) the daily caffeine intake (measured in cups), and (2) the hours of withdrawal. The dependent variable was the severity of insomnia, which was experienced by the participants during the withdrawal period.

The multiple correlation analysis allowed for a comprehensive understanding of the relationship between caffeine intake, the withdrawal period, and insomnia, as reported by the participants. The goal was to determine if higher levels of caffeine intake and longer withdrawal periods correlated with increased insomnia severity.

Result

A total of 68 volunteers were included in the study after meeting the predetermined inclusion and exclusion criteria. All volunteers provided informed consent and underwent a detailed briefing on the study's goals and methodology. The demographic details of the participants are summarized in Table 2. To measure the severity of insomnia before and after the caffeine withdrawal period, the Insomnia Severity Index (ISI) was employed. During the study, it was found that 84% of the participants (59 out of 68) reported difficulty sleeping during the withdrawal phase. This condition met the criteria for substance-induced insomnia, as per the DSM-IV diagnostic manual, demonstrating a notable effect of caffeine withdrawal on sleep patterns.

Statistical analysis using the Multiple Correlation Method revealed a mild but statistically significant positive correlation between caffeine intake, withdrawal duration, and insomnia severity. The R-value of 0.22 indicates that while the correlation is not strong, it is still significant enough to suggest that higher caffeine consumption, combined with longer withdrawal, leads to more severe insomnia symptoms.

$$R = \frac{\sqrt{(-0.1751)^2 + (-0.1647)^2 - 2(-0.1751)(-0.1647)(0.1653)}}{\sqrt{1 - (0.1653)^2}}$$

R = 0.22

Discussion

The study comprised 38 females (56%) and 30 males (44%), aged between 18-60 years. According to research by Jeffrey Goldberg, consuming more than 400ml of caffeine daily can lead to several adverse effects, including behavioural changes, insomnia, anxiety, depression, and cardiac arrhythmias. These findings align with our study's observations, where participants

consuming 6-8 cups of caffeine per day experienced increased insomnia severity.

The R-value of 0.22 from our correlation analysis supports the hypothesis that there is a positive association between daily caffeine consumption and insomnia during withdrawal. This result underscores the risks of excessive caffeine intake, particularly in relation to sleep disturbances. It also highlights the importance of moderating caffeine intake as a preventive measure for insomnia and other related conditions.

Conclusion

This study demonstrated a significant difference in caffeine intake among rural Indian participants, with higher consumption leading to noticeable effects on sleep. Many participants reported substance-induced insomnia, as defined by the DSM-IV, which emphasizes the need for careful management of daily caffeine intake. The results of the multiple correlation analysis further support the idea that individuals should adjust their caffeine consumption according to their lifestyle and personal tolerance to prevent sleep disturbances.

Limitations

One of the key limitations of this study is the small sample size (68 participants) and the limited study duration (2 months). To strengthen the findings, future studies should aim to expand the sample size and include participants from urban areas in India to gain a broader epidemiological understanding of caffeine withdrawal and its effects on sleep and behaviour. Further studies could also explore other lifestyle factors that may influence the impact of caffeine on sleep patterns and overall health.

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Author's contribution: Ajith JS and Vijay Bayaskar designed the study and reviewed the manuscript. Mate Vaishnavi and Wagh Bhagyashree written the manuscript, collected the data and did data anaylsis. Matre Vaibhav and Navale Samruddhi were designed the methodology. Supriya Bhagwat , Shubangi Khade , Swati Sandhan, Poonam Wajpei and Mahima Wadje edited the manuscript. On behalf of all the co-authors, I declared that the prepared manuscript is ready for publication.

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Table No.1: Various ingredients present in different amounts of caffeine

Item	Average (mg)	Range (mg)
Coffee (5-oz cup)a		
Brewed, drip method	120	90–150
Percolated	90	64–124
Instant	75	30–120
Decaffeinated	3	1–5
Espresso (6-oz cup)	240	180–300
Teas (loose or bags, 5-oz cup)		
1-minute brew	21	9–33
3-minute brew	33	20–46
Tea products		
Instant (5-oz cup)	20	12–28
Iced (12-oz glass)	29	22–36
Carbonated beverages	24	20–40
Colas and pepper drinks (12 oz)		
National brands, packaged	42	36–48
National brands, fountain	39	32–48
Store brands, packaged	18	5–29
Citrus drinks (12 oz)		
National brands, packaged	52	43–56
Store brands, packaged	38	26–52
Chocolate products		
Cocoa beverage (8 oz)	6	3–32
Chocolate milk beverage (8 oz)	5	2–7

Table No. 2: Mean of the demographic data of volunteers

Criteria	Mean
Gender	Male 51% Female 49%
More than 6 cups of caffeine intake	22.33
BMI	22.98kg/m^2