

Psychology and Mental Health Care

Jaison Joseph *

Open Access Review Article

Disulfiram Therapy for alcohol dependence in the Indian Context: - What Does the Literature Say?

Jaison Joseph 1*, Deepika C Khakha 2

- ¹ Lecturer, Department of Psychiatric Nursing, College of Nursing, Pt. B.D. Sharma University of Health Sciences, Rohtak 124001 India.
- ² Nursing Advisor, Dte. GHS, Ministry of Health and Family Welfare, New Delhi, India.
- *Corresponding Author: Jaison Joseph, Lecturer, Department of Psychiatric Nursing, College of Nursing, Pt. B.D. Sharma University of Health Sciences, Rohtak 124001 India.

Received date: April 14, 2023; Accepted date: May 01, 2023; Published date: May 08, 2023

Citation: Joseph J., Deepika C. Khakha, (2023), Disulfiram Therapy for alcohol dependence in the Indian Context: - What Does the Literature Say?, *Psychology and Mental Health Care*, 7(1): **DOI:**10.31579/2637-8892/214

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Abstract

Disulfiram is relatively the oldest molecule and one of the current medications for treating alcohol dependence. It is found to be a cheap prophylactic agent for treating alcohol dependence for the past many years. Many factors influence acceptance and adherence to disulfiram treatment based on various contexts. Interestingly, physical and psychiatric complications related to disulfiram treatment were reported as a predictor for poor drug adherence. There is convincing evidence to suggest that supervised disulfiram still has a major role in alcohol de-addiction treatment. Further, it is worth noting that disulfiram is the cheapest pharmacoprophylactic drug for alcohol dependence putting its importance on people living in low and middle-income countries. The present review elucidates the status of disulfiram therapy for alcohol dependence in the Indian context.

Keywords: disulfiram; alcohol; India

Introduction

The burden and problems due to alcohol dependence are well documented at the global level. The pharmacological treatment for alcohol dependence is growing with empirical trials of both older and novel agents. Disulfiram is relatively the oldest molecule and one of the current medications for treating alcohol dependence. It is found to be a cheap prophylactic agent for treating alcohol dependence for the past many years [1]. Disulfiram is usually prescribed for middle-aged male alcohol-dependent subjects with somewhat intact social stability and supervisory system after obtaining written informed consent. The common Disulfiram ethanol reactions (DER) are flushing, sweating, nausea, vomiting, palpitations, dyspnoea, tremors, confusion, restlessness, drowsiness, and hypotension which may develop within 5-15 minutes of alcohol intake. The general side effects in the absence of alcohol consumption include headache, general weakness, and dizziness [2]. The following medications must be avoided while on disulfiram treatment: - alcohol-containing syrups, sedatives such as diazepam, anti-diarrhoeal such as metrogyl, cardiac medication such as digitalis, anti-epileptic such as phenobarbitones, anti-tubercular medications such as rifampicin, isoniazid, anti-coagulants such as warfarin, anti-depressants such as depsonil. Further, avoid the following food and cosmetic items during the disulfiram therapy as it may lead to DER (sausages, shaving lotions, vinegar, etc) [3].

Many factors influence acceptance and adherence to disulfiram treatment based on various contexts. Interestingly, physical and psychiatric complications related to disulfiram treatment were reported as a predictor for poor drug adherence. Furthermore, researchers pointed out that the adverse effects could be dose-specific inculcating the need for regular follow-up for patients undergoing this therapy [4]. Many studies have been conducted for the efficacy and status of disulfiram in the alcohol deaddiction setting. There is convincing evidence to suggest that supervised disulfiram still has a major role in alcohol de-addiction treatment. Further, it is worth noting that disulfiram is the cheapest pharmacoprophylactic drug for alcohol dependence putting its importance in people living in low and middle-income countries [5]. The present review elucidates the status of disulfiram therapy for alcohol dependence in the Indian Context.

Disulfiram for preventing alcohol relapse in the Indian Context: - Evaluation of Efficacy trials & observational studies

A series of open-label trials compared the efficacy of disulfiram with acamprosate, naltrexone, and topiramate among hundred alcohol-dependent men attending a routine clinical practice in India.

Findings of these studies have the opinion that eighty-eight percent of patients on DSF remained abstinent compared to 46% with acamprosate [6]. Furthermore, eighty-six percent of the patients remained abstinent throughout the study with disulfiram compared to 44% with naltrexone [7]. In addition, they noted that 90% of the DSF patients remained abstinent as compared to 56% with topiramate [8]. All these studies are published in the year 2004-2008 and no other clinical trials and the follow-up period ranged from 9 -12 months. The findings demonstrated that disulfiram is superior for preventing relapse in the Indian alcohol deaddiction setting. From these findings, it can be assumed that this 'oldfashioned drug' appears to be a cost-effective molecule in the relapse prevention of alcohol dependence as compared to other anti-craving agents. Prasad S et al. (2000) reported that 81.7% (58/71) of outpatient patients attending a tertiary care centre from South India maintained total alcohol abstinence during follow-up at six months of disulfiram treatment [9]. In an observational study, Sidana A (2007) reported superior alcohol abstinence rates for disulfiram as compared to other pharmacological agents during 6-12 months among subjects in the Northern Indian setting.

Disulfiram Ethanol Reactions in India: - What Does the literature say?

Murthy KK (1997) reported the occurrence of mood disorder among 6 of 52 patients treated for alcohol dependence syndrome with a dose of 500 mg/day of disulfiram treatment [10]. An observational study by Sreenivasan and his colleagues (1994) evaluated 158 outpatients on daily oral disulfiram (250 mg/day) and revealed that 7 subjects experienced psychosis during the follow-up period [11]. Strikingly, a study from South India (Palatty, 2011) reported 76.5% adherence (60 days) to disulfiram therapy in which 45% (23/51 subjects) didn't complain of any ADR and 27.4% had drowsiness, 21.4% tiredness, 7.8% skin manifestation [11]. The critical analysis by Joseph J (2019) identified that psychiatric adverse events and de novo convulsions were the common adverse reactions to disulfiram treatment without alcohol challenge in the Indian setting. The authors noted that delusion of persecution and auditory hallucination were the major symptoms of psychosis followed by catatonia and delirium-like reactions in the Indian setting. The other disulfiram-induced adverse effects were hypertension, dermatitis, and peripheral neuropathy [12].

A recent study identified that 69 of 614 patients reported adverse drug reactions (ADRs) who received disulfiram for the treatment of alcohol use disorders [13]. Gastrointestinal disorders were the most common ADRs (n = 37, 53.6%), followed by nervous system disorders (n = 22, 31.9%), skin and subcutaneous tissue disorders (n = 16, 23.2%), psychiatric (n = 16, 23.2%), respiratory, (n = 11, 14.5%), and musculoskeletal and connective tissue disorders (n = 5, 7.2%).

Future directions

Even after many decades of invention, disulfiram remains one of the mainstay medications in alcohol dependence and a frequently used deterrent agent in alcohol de-addiction settings in India. Further, disulfiram is an economical and low-cost drug, however, cost-effectiveness needs to be rigorously evaluated. There is evidence that Indian patients report psychiatric side effects more often, posing a

research avenue of investigation regarding the biological mechanism of action of disulfiram in the Asian populations [14].

Conflicting Interests: The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article

Funding: The authors received no financial support for the research, authorship, and/or publication of this article.

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DOI:10.31579/2637-8892/214

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