Case Report

Clozapine Dependence: a case report

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ABSTRACT

Clozapine has been used widely in the management of treatment resistant schizophrenia. There have been some studies that have demonstrated withdrawal symptoms on stopping clozapine and patients who develop a dependence both physical and psychological on the drug. Here we report a case of 22-year-old male patient who suffering from alcohol dependence, had a history of substance abuse and developed a dependence on Clozapine.

Key words: dependence, Clozapine, psychotropics.

(Received – 27th December 2022, Peer Review completed – 11th March 2023, Accepted – 20th March 2023)

INTRODUCTION

Psychotropic is a canopy term which describes any drug that affects behaviour, mood, thoughts, or perception [1]. Dependence can be a bodily response to a substance, and this often occurs if you rely on medications to control a chronic medical condition [1]. The benefits of psychotropics are well known yet they should be prescribed with caution and drug dependency must be kept in mind [2]. This risk is well accepted about benzodiazepines, and it appeared useful to study the potential risk for antidepressants, neuroleptics and thermoregulatory agents [2]. Psychological dependence is more predominant as compared to physical dependence in case of psychotropics [2]. Prevention of drug dependency is most often achieved by informing and educating the patient, limiting the duration of drug use, making regular follow ups for re-evaluation of symptoms and of drug indication [2]. Studies have been conducted that demonstrate co-occurring psychotropic dependence and mental illness being prevalent among criminal offenders, but little is known about risk factors and prevalence for these co-occurring disorders in community corrections population [3]. To shed light on the same, we report a case of clozapine dependence in a 22-year-old man.

CASE REPORT

A 22 years old right handed Hindi speaking Muslim unmarried male, educated till 3rd standard, rickshaw driver by occupation resident of Titwala, Kalyan came with his mother with chief complaints of irritability, angry, abusive behaviour, suspiciousness that people are talking ill about him, hearing of voices inaudible to others, increased consumption of tablet clozapine on daily basis. All the above complaints were since 2-3 months prior to presentation and had increased since three days prior to visiting us.
The patient was unable to cut down on alcohol consumption and had been consuming alcohol since the past 5 years. He had last consumed alcohol 3 days prior to visiting us and had consumed 1.5 litres of country liquor at that time. He has been consuming tobacco for 10 years, having 20-25 packets of gutka per day. He

increased consumption of Clozapine from one tablet (100mg) to six tablets a day (600mg/day). He had been consuming the same till 7 days prior to visiting us.

He was a known case of psychiatric disorder taking medication from the hospital and currently was on Olanzapine – 30mg/day in divided doses, Clozapine 150mg at night, Lorazepam 2mg at night, Acamprosate 333mg thrice a day and Topiramate 25mg twice a day (Acamprosate and Topiramate were given to reduce alcohol craving and help him quit alcohol while Clozapine and Olanzapine were for his psychotic symptoms and Lorazepam was given for sleep at night)

He was admitted in Sion hospital from for 20 days. He was discharged with 60% improvement in symptoms on the above medicine. Patient claims that since discharge he was talking Clozapine 100mg 2 tablets thrice a day (6 tablets per day) since his discharge. After taking two tablets of clozapine, within 1-2 hours he would experience decreased irritability, decreased suspiciousness that someone is going to harm him, a sense of euphoria and a "free mind" as described by him. After taking Clozapine 100mg 2 tablets in the morning he would go out of his house and roam around places in his friend's vehicle and would come home only to take food and medications. Side effects in the form of increased salivation was noted. From the first day after discharge, he would take 6 tablets of tab clozapine in a day which remain constant throughout. If he would not take clozapine at the scheduled time in the same dose, he would have increased irritability, angry abusive behaviour, hearing of voice inaudible to others, hearing of azan (Islamic call for prayer) and would have suicidal ideation. The medication prescribed to him for 15 days would finish in 5-6 days and then would force his mother to go to the hospital and get the prescription for medication. If family members would not agree to his demands, he would be irritable and be angry and abusive. Since past 7 days he was not taking Clozapine due to its unavailability, and he started drinking alcohol 1-2 quarter of country liquor. He claims that he had also taken Clozapine with alcohol but claims no alteration in the effect compared to when taking Clozapine alone. Since the past three days prior to presentation, he was not able to procure alcohol and all the symptoms described above had aggravated like decreased sleep, hearing of voice inaudible to others, seeing things not seen by others "people trying to kill him", increased irritability and angry abusive behaviour. Due to increased irritability he tried to hang himself, but the act was prevented by family members. We admitted him as an inpatient and started treatment.

Patient started consuming cannabis at the age of 12 years. At first, he would smoke ganja rolled in rizla paper along with friends. at first, he used to get high with few puffs of smoking ganja. His consumption gradually increased in frequency and quantity with time as he was not able to achieve the usual high, he earlier used to get. he used to consume 2-3 Pudi of ganja daily. Last consumption was 6 years ago.

There was a history of Benzodiazepine consumption in the form of Alprazolam 1mg 4-5 tablets daily for 14 years. Last consumption was 6 years ago.

He also had a history of opioid consumption in the form of Corex cough syrup once a week. A bottle shared between 2-3 friends. Last consumption was 6 years ago.

Due to multiple substance use, he was admitted in rehabilitation centre in year 2016 after which he claims to have stopped the consumption of cannabis, benzodiazepines, and cough syrup.

There has been a history of lying, stealing, and gambling. After 2016 he claims to have started alcohol use in the form of 0.5 quarter with friends in a party. After that he started daily consumption of alcohol one quarter a day. His consumption gradually increased in quantity as he was not able to get the usual high, he earlier used to get. He would consume 4-6 quarters of alcohol daily.

He also shifted from whiskey to country liquor due to the unavailability of money to buy whiskey. History of eye-opening drinking present. History of drinking and driving present. History of alcohol withdrawal symptoms like decreased sleep, decreased appetite, tremulousness of hand and feet when not taking alcohol. Past admissions at a rehabilitation centre 3 times once in a 2016, 2021 and 2022.

He had a history of a police complaint registered against him 4-5 months ago, as he ran away with his girlfriend (was in a live in relationship for a week) to get married. She was 17-year-old. At police station due to increased irritability, he slashed his wrist and forearm with a slash in the abdomen and neck under the influence of alcohol. He was rushed to the hospital and later the police complaint was withdrawn.

His alcohol pattern increased after this incident. He started drinking 4-6 quarter per day. History of aggressive and threatening behaviour for money towards mother present. He started having decreased sleep,

hearing of voice inaudible to others, suspiciousness over his older brother, tremors. For above complaints he was admitted in Sion hospital and was later discharged claiming improvement.
No history of other significant major medical and surgical illness.
Family history of alcohol use by father in a dependent manner.
His birth and development history were normal. He had a history of decreased interest in academics, truancy, conduct issues in school and dropped out of school after 5th standard.
He has been gambling since the age of 13 years whenever he needed money. He is the youngest of the three siblings with poor financial support and fair social support. His premorbid personality was stubborn, impulsive, irresponsible and novelty seeking was present.
On mental status examination he was conscious cooperative and communicative. He had normal built, appropriate dressing and grooming. His eye-to-eye contact was initiated and maintained. His attention was aroused and sustained. Rapport was established and mood was conveyed as irritable. His affect was mood congruent and stable. His thoughts were continuous, coherent, and relevant. Delusion of persecution against brother was present. Suicidal ideation was present and auditory hallucination present in the form of "hearing of azan". He was oriented to time place and person. Test judgement was normal while personal and social were impaired. He had grade III insight. The patient was better in 2 weeks and discharged without Clozapine in his medication list.

DISCUSSION

Clozapine remains to be the standard for treating resistant schizophrenia [4]. However, clozapine is associated with several side-effects that complicate the use of the drug. In a study it was observed that clozapine induced a clear somatic withdrawal sign after chronic treatment [5]. Although there have been many demonstrations of clozapine causing tolerance, dependence, and withdrawal, very little is known about the underlying mechanisms for the same [6]. Thus, it was suggested to characterise the clozapine withdrawal symptoms in animal models; to determine the neurochemical mechanisms involved and to determine the antipsychotics are able to supress clozapine dependence and withdrawal [6].
It has been demonstrated in studies that there may be a variety of withdrawal reactions such as autonomic nervous system symptoms, psychosis, gastrointestinal tract, and serotonin discontinuation symptoms when the drug is discontinued which may further result in the dependence [7]. Dependence can result in a subsequent overdose which can increase the mortality and cause side effects like intracranial haemorrhage lethargy, tachycardia, myosis, confusion, agitation, coma, dysarthria, delirium, jerks, and hypotension [8].
To tackle this dependence from developing, a slow up-titration of clozapine is recommended to reach the optimal dosage [9]. Prevention of drug dependency can be achieved by different ways. Patient education is the most essential. This can be further supplemented by informing the patient, limiting the duration of drug use, and making regular follow ups for re-evaluation of symptoms and of drug indication [9].
In this case report we presented a patient with clozapine drug dependence. He had physiological dependence more than physical and wanted to obtain the central nervous system clinical effects of the drug such as reduced irritability, suspiciousness, and a sense of euphoria, so he kept adding the dose by himself. It is important for physicians to know the optimal dosage, titration, symptomatology, and compliance of the patient to correctly identify and tackle the drug dependence. Clinicians need to be vigilant to the possibility of Clozapine dependence.

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Acknowledgements – Nil
Conflict of Interest – Nil
Funding – Nil