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RESEARCH ARTICLE

SILDENAFIL INDUCED PSYCHOSIS: A RARE CASE REPORT

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Abstract

Sildenafil citrate is a commonly used medication for the management of erectile dysfunction. Previous studies have reported psychiatric side effects of this medication. So far, there has been paucity of literature. We present the case of a 42-year-old male, without a known psychiatric history, who developed psychotic symptoms following initiation of sildenafil. We also tried postulating a mechanism by which this may occur. This report highlights the importance of watchful observation for the occurrence of this rare but serious side effect. Further studies are needed to know the exact mechanism that causes sildenafil-induced psychosis.

Introduction:-

Sildenafil citrate is a commonly used medication for the management of erectile dysfunction (ED) Its mechanism implies selective inhibition of phosphodiesterase type 5(PDE5), whose function is hydrolysis of cyclic guanosine monophosphate (cGMP) in the corpus cavernosum [1]. This results in the increase in the levels of intracellular cGMP and hence relaxation of penile smooth muscles, dilatation of arterioles, increased blood flow, causing penile erection [2]. Notable side effects of sildenafil include headache, visual disturbances, flushing, stomach discomfort, back and muscle pain [3]. Neuropsychiatric adverse effects, including sleeplessness, abnormal dreams, lightheadedness, depression, behavior changes, and nervousness, have also been reported in previous studies [4]. So far, however, there have been paucity of literature in sildenafil induced psychosis. Hence, psychiatrists and physicians should be mindful of the possibility of this side effect. Though rare, this serious side effect results in impairment in quality of life even in the presence of satisfactory response. Here we present a patient, without any previous psychiatric history,who developed psychotic symptoms following initiation of sildenafil. We also postulate a mechanism by which this may occur. This report lay emphasis on the importance of close monitoring for the occurrence of rare but serious side effects of Tadalafil.

Case report

A 42-year-old male was referred to our hospital with the complaints of self muttering, speaking abusive words, suspicious over his wife that she is in romantic relationship with someone else, hearing of voices of god. The duration of the psychotic symptoms was 3 days when his family noticed that he sometimes talked to himself and is not eating well. He also had complaints of sleep disturbance, anger outbursts, was trying to run away from house. There were no symptoms consistent with low mood, decreased interest in work, increased activity and he did not have any previous episodes of psychotic or mood symptoms. The patient relatives deny for any history of exposure to toxic chemicals, head trauma, seizures, or other medical conditions that could cause psychosis. He was recently diagnosed with mild erectile dysfunction (International Index of Erectile Function score 20) [5] and had been

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prescribed sildenafil 50 mg as a single dose, no more than once a day, 1 hour before sexual intercourse over the past 3 weeks. He did not use any other medications while using sildenafil. He did not have a history of smoking, alcohol or illicit drug abuse. There was no family history of psychiatric disorders. Birth and early development were apparently within normal limits. He was illiterate and belonged to lower socioeconomic status and was working in a factory. His family described him as an extroverted, hardworking, and responsible person. On mental status examination, he was alert and oriented to place, time, and person. His physical examination, including a thorough neurological and genitourinary assessment, was unremarkable. All routine blood tests, including complete blood count (CBC), fasting blood glucose, hemoglobin A1c, lipid profle, electrolytes, renal and liver function tests, thyroid function tests, vitamin B12, folic acid, and vitamin D levels, and an electrocardiogram were within normal limits. Tests for syphilis, human immunodefciency virus (HIV), and hepatitis B and C as well as toxicology screening were negative. Magnetic resonance imaging was performed to rule out space-occupying lesions or vascular infarcts. After ruling out the other medical causes, on the basis of the clinical presentation and investigations, provisional diagnosis of sildenafil-induced psychotic disorder according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria was considered. Sildenafil was discontinued, and oral form of risperidone was prescribed at 2 mg/day. Surprisingly, all of the psychotic symptoms remitted only 1 week after the initiation of risperidone, and subsequently he was discharged after 10 days of hospitalization. Pt was regularly followed up and one month after hospital discharge, the patient reported no psychiatric symptoms and risperidone was tapered off gradually in 2 weeks. Follow-up visits during the next 12 months revealed no recurrence of the symptom.

Discussion:-

Psychiatric complications of medications have been important and challenging issues for the doctors as well as patients [6]. In this paper, we report a psychotic episode associated with the use of sildenafil in a patient without previous psychiatric history. Although various other side effects of sildenafil such as aggression, low mood, abnormal dreams and nervousness, and suicidal attempt have been published so far [7], there is deficit in literature about sildenafil-induced psychosis. Baggot et al reported a relapse of mixed episode with paranoia in a bipolar patient treated with sildenafil and the symptoms improved with discontinuation of sildenafil and prescription of antipsychotics. The pathophysiology underlying psychotic disorders was found excess of NO-stimulated cGMP due to the inhibition of PDE which is consider to directly result in relapse [8]. In another study by Özdemiroğlu et al. reported a Parkinson patient who developed psychotic symptoms when panax ginseng and sildenafil were added to the ongoing pramipexole treatment. Although a link between sildenafil and psychosis has been suggested in this article, concomitant medications such as ginseng and pramipexole were other possible causes of psychotic symptoms. Besides, the patient had Parkinson's disease, which is associated with a predisposition to psychosis [9]. In terms of pathophysiology, there is some evidence available to suggest a possible association between sildenafil and psychotic symptoms. As mentioned earlier, the main pharmacological action of sildenafil is the inhibition of the cGMP-specifc PDE5. PDE5 is present in the smooth muscles of the systemic vasculature and cerebral neurons and vessels [10]. Inhibition of cGMP degradation by selective PDE5 raises nitric oxide (NO) levels by increasing the ratio of nitrite to nitrate and by stimulating transcription of mRNA for nitric oxide synthase (NOS) [11]. NO is a key component in many processes occurring in the nervous system such as regulation of synaptic plasticity [12], neurotransmission [13], and development of nervous tissue [14], NO one one side has protective actions on neurons but on the other hand, in the high, unregulated mode, it has neurotoxic efects [15]. NO is involved in cerebrovascular diseases, seizures, neurodegenerative disorders, and pain [16]. Previous studies have also been done relating the association between NO and psychotic disorders (17, 18) Accordingly, it can be said that other PDE5 inhibitors such as tadalafil, vardenafil can also cause such symptoms through a similar mechanism. Nonetheless, in reviewing the literature, we found no reports on other PDE5inhibitors causing psychotic symptoms.

Conclusion:-

In our case, there was a close temporal relationship between the use of sildenafil and emergence of psychotic symptoms. Furthermore, discontinuation of the sildenafil led to quick and full recovery from psychotic symptoms. These data strongly support a causative role for sildenafil in the development of psychotic symptoms. This case highlights the importance of watchful observation for the occurrence of this rare but serious side effect of Sildenafil. Therefore, this case report should be considered as an exploratory study and future studies can further refine other possible mechanisms that until now have not been recognized.

Declaration of patient consent:-

The authors certify that they have obtained appropriate patient consent form. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest;-

There are no conflicts of interest.

References:-

1.Krishnappa P, Fernandez-Pascual E, Carballido J, Martinez-Salamanca JI. Sildenafil/Viagra in the treatment of premature ejaculation. Int J Impot Res.2019;31(2):65–70.
2.Andersson K-E. PDE5 inhibitors—pharmacology and clinical applications 20 years after sildenafil discovery. Br J Pharmacol. 2018;175(13):2554–65.
3.Kontaras K, Varnavas V, Kyriakides ZS. Does sildenafil cause myocardial infarction or sudden cardiac death? Am J Cardiovasc Drugs. 2008;8(1):1–7.
4. Sathyanarayana Rao T, Kumar V, Raman R, Andrade C. Prolonged, longstanding, ultra-high-dose abuse of sildenafil. Indian J Psychiatry. 2015;57(3):311–2.
5. Rosen RC, Riley A, Wagner G, et al. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dys - function. Urology. 1997;49:822–30.
6. Borhannejad F, Shariati B, Naderi S, Shalbafan M, Mortezaei A, Sahe - bolzamani E, et al. Comparison of vortioxetine and sertraline for treat - ment of major depressive disorder in elderly patients: a double-blind randomized trial. J Clin Pharm Ther. 2020;45(4):804–11.
7. Giuliano F, Jackson G, Montorsi F, Martin-Morales A, Raillard P. Safety of sildenafil citrate: review of 67 double-blind placebo-controlled trials and the postmarketing safety database. Int J ClinPract. 2010;64(2):240–55.
8. Baggott J, Singh AN. Sildenafil-induced relapse in bipolar disorder: is nitric oxide the mechanism? Int J Neuropsychopharmacol. 2004;7(4):525.
9. Ozdemiroglu F, Karakus K, Memis C, Kocabas O, Akyildiz U, Sevincok L. Psychotic symptoms following sildenafil and panax ginseng treatment in a pramipexole induced manic patient with Parkinson's disease: a case report. J Mood Disord. 2016;6(2):82.
10. Lin C-S, Lin G, Xin Z-C, Lue T. Expression, distribution and regulation of phosphodiesterase 5. Curr Pharm Des. 2006;12(27):3439–57.
11. Liu X, Peyton KJ, Wang X, Durante W. Sildenafil stimulates the expres - sion of gaseous monoxide-generating enzymes in vascular smooth muscle cells via distinct signaling pathways. BiochemPharmacol. 2012;84(8):1045–54.
12. Chakroborty S, Kim J, Schneider C, West AR, Stutzmann GE. Nitric oxide signaling is recruited as a compensatory mechanism for sustaining synaptic plasticity in Alzheimer's disease mice. J Neurosci. 2015;35(17):6893–902.
13. Yamamoto K, Takei H, Koyanagi Y, Koshikawa N, Kobayashi M. Presynaptic cell type-dependent regulation of GABAergic synaptic transmission by nitric oxide in rat insular cortex. Neuroscience. 2015;284:65–77.
14. Cossenza M, Socodato R, Portugal CC, Domith ICL, Gladulich LFH, Encarnação TG, et al. Chapter fve—nitric oxide in the nervous system: biochemical, developmental, and neurobiological aspects. In: Litwack G, editor., et al., Nitric oxide. London: Academic Press; 2014. p. 79–125.
15. Džoljić E, Grbatinić I, Kostić V. Why is nitric oxide important for our brain? Funct Neurol. 2015;30(3):159–63.
16. Asiimwe N, Yeo SG, Kim M-S, Jung J, Jeong NY. Nitric oxide: exploring the contextual link with Alzheimer's disease. Oxid Med Cell Longev. 2016; 2016:7205747.
17. Flatow J, Buckley P, Miller BJ. Meta-analysis of oxidative stress in schizo - phrenia. Biol Psychiatry. 2013;74(6):400–9.
18. Nasyrova RF, Ivashchenko DV, Ivanov MV, Neznanov NG. Role of nitric oxide and related molecules in schizophrenia pathogenesis: biochemical, genetic and clinical aspects. Front Physiol. 2015;11(6):139.