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Case Report

# Investigating a Peculiar Case of Opioid Withdrawal Induced Tinnitus

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## ABSTRACT

**Background:** Tinnitus induced by various opioids has been documented; however, the inhibitory effect of opioids on tinnitus, exacerbation during withdrawal, and relief upon re-administration has not been previously described.

**Case presentation:** A 37-year-old male with a history of daily intravenous heroin use since age 15 presented with a new-onset constant static tinnitus in both ears, rated at 9 out of 10 in intensity. The tinnitus was alleviated by opioid use but returned after a few hours, necessitating repeated administrations. Buprenorphine reduced the intensity from 9 to 5 out of 10. The patient also reported auditory hallucinations and displayed psychiatric symptoms during the evaluation.

**Results:** Neurological examination revealed decreased tinnitus intensity when the patient opened his mouth widely. The psychiatric assessment indicated depressive and anxious symptoms, limited insight, and poor judgment.

**Discussion:** The present case suggests that tinnitus experienced during opioid withdrawal is opioid-dependent and can be eliminated by opioid administration. The reduction in tinnitus intensity when the mouth is opened widely suggests a central auditory hallucination mechanism related to micro-laryngeal movements. The opioids may exert their inhibitory effect on tinnitus through cortical modulation rather than direct effects on the auditory system. Investigating tinnitus in individuals with opioid dependence may identify a subgroup that could benefit from tinnitus-alleviating medications, potentially reducing the risk of opioid relapse.

**Keywords:** Opioid dependence; Tinnitus; Enantiopathy; Auditory hallucinations; Benzodiazepines; Heroin withdrawal

## INTRODUCTION

In adults, persistent tinnitus has a prevalence of 25% [1]. Myriad psychopharmacologic agents have been reported to induce tinnitus, including amitriptyline, fluoxetine, and baclofen. Conversely, withdrawal from duloxetine, venlafaxine, or benzodiazepines can induce tinnitus [2]. In addition, under a wide variety of conditions, benzodiazepine withdrawal has been observed to precipitate tinnitus, including those concurrently treated with methadone or buprenorphine [3-7].

Peradventure, the mechanism for benzodiazepine withdrawal-induced tinnitus may be its action as an allosteric modulator of Gamma-Aminobutyric Acid (GABA) receptors [8]. In a parallel fashion, benzodiazepine administration has been found to alleviate tinnitus [9,10]. Similarly, alcohol has been observed to reduce tinnitus and has been speculated to be a factor contributing to the development of alcohol dependence [11]. Many opioids have been reported to induce tinnitus [12]. The pathophysiology whereby opioids induce tinnitus has been postulated to include vasospasm or vasculitis-induced ischemia of the spiral modiolar artery inducing an ischemic cochlea, effects on hepatic metabolic enzymes, dysfunction of transporting protein receptors, and direct effects on cochlear opioid receptors. These opioid receptors are present in the inner and outer hair cells in the organ of Corti and spiral ganglion. Activation of opioid receptors inhibits calcium currents and thus

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adenylate cyclase, impairing neuromodulation and thus inducing sensorineural hearing loss and tinnitus [13]. Alternatively, opioids induce the release of endorphins which may exacerbate tinnitus through their actions on dynorphin receptors in the cochlear. Opioids may act on Type-I auditory dendrites of the lateral efferent olivocochlear system, inducing spontaneous discharge independent of the organ of Corti [14]. Opioid tinnitus induction may be perceived through its impact on spontaneous auditory nerve discharges. Such neural instability may be induced through the blockade of glutamate or opioids' impact on N-Methyl-D-Aspartate (NMDA) receptors within the cochlea [15]. Since opioids interact not only with opioid receptors but also with NMDA receptors, chronic use can lead to the downregulation of GABA receptors, upregulation of extracellular glutamate receptors, and increased activity of voltage-dependent calcium channels, causing hyperexcitability of auditory sensory receptors, culminating in tinnitus [16]. Opioid tinnitus induction may also occur through a reduction in GABA receptors and associated input of inhibitory neurotransmitters with disinhibition manifesting as tinnitus [17]. On the other hand, opioids' effect of inducing tinnitus may be through its neurotoxic impact on the auditory system, causing a release phenomenon with a reduction of hearing, disinhibiting tinnitus [18]. While methadone and other opioids have been reported to reduce tinnitus at high levels, opioid antagonists have also been reported to cause tinnitus [19]. Naloxone administration for opioid-induced sedation with associated tinnitus may be directly due to naloxone or may be due to naloxone-induced acute opioid withdrawal. This implies that opioids act not only to precipitate tinnitus but may also reduce tinnitus [20]. This is consistent with the finding that tinnitus occurs in 12% of individuals who withdraw from the opioid tramadol [21]. Such tramadol withdrawal tinnitus as part of buprenorphine induction further implies that opioids may inhibit or reduce tinnitus [22]. While naltrexone's actions to enhance tinnitus may be through the actions on the organ of Corti and primary auditory sensory pathway, it may function on the emotional component of tinnitus, impacting the mesolimbic system including the orbitofrontal cortex, posterior cingulate cortex, anterior cingulate cortex, and bilateral posterior hippocampus, all areas which are activated in those who suffer from tinnitus [23]. Despite this, publications discussing the opioid reduction of tinnitus limited attribution to local effects. Local buprenorphine analgesia applied to the superior cervical ganglion reduces tinnitus in 80% of those studied, possibly through inhibition of ganglionic transmission at postsynaptic receptors [24]. Opioid inhibition of tinnitus, exacerbation upon withdrawal, and relief upon re-administration has not been described. Such a case is presented.

## CASE PRESENTATION

This 37-year-old male presented with one gram of Intravenous (IV) heroin daily since age 15. Three years prior to admission, he discontinued heroin. Upon stopping the heroin, he noted a new onset of a constant static tinnitus AU, high and low pitched, 9 out of 10 in intensity, with ten being the most severe. He localized this static noise as "inside the center of my head. It impaired his hearing ability, and he had trouble understanding words and thus interacting with others. The noise was constant day and night, without diurnal variation. He found that opioids, including heroin one gram IV or morphine 125 mg IV, eliminated tinnitus. Less than 125 mg of morphine did not eliminate it. As soon as he injected the opioid, the tinnitus resolved. After opioid injections, he found that the tinnitus returned 6-8 hours later and thus required recurrent injections. Buprenorphine 8 mg, thrice a day, reduced tinnitus from 9 out of 10 to 5 out of 10 in intensity.

Other than opioids, nothing made it better or worse. There was no ear pain associated with this. Six months prior to admission, he started using heroin in order to stop the ringing in the ear.

After eight days in-patient, without any opioids, the tinnitus disappeared. Independent of this static noise, he also has auditory hallucinations. He has heard these hallucinations for many years, consisting of someone calling his name, voices talking, whispering, and the phone ringing. These are independent of opioid-related tinnitus and do not occur with opioids or on opioid withdrawal.

## RESULTS

The neurological examination results indicate abnormalities related to the eighth Cranial Nerve (CN VIII) and the patient's auditory functions. The calibrated finger rub auditory screening test showed a typical result, signifying that the patient's hearing sensitivity is within the expected range (AU 70). The Weber test yielded a negative result, which means that the patient heard sounds equally in both ears, indicating an average finding. Similarly, the rinne test showed a negative (standard) result, implying that air conduction was not significantly better than bone conduction.

One interesting observation from the neurological examination is the relationship between the patient's tinnitus and their jaw position. When the patient opened their mouth widely, the intensity of the tinnitus decreased from 9/10 to 5/10. This suggests a potential link between the patient's jaw movement and tinnitus, indicating that their jaw position might influence the condition.

To further assess the patient's mental health and emotional well-being in light of the neurological findings, a psychiatric evaluation was conducted by a board-certified neurologist. The key findings from this evaluation are summarized in the table below (Table 1).

These findings collectively suggest possible symptoms of depression and anxiety in the patient, which may warrant further assessment and intervention by mental health professionals.

The neurological examination indicated abnormalities related to the eighth cranial nerve, while the psychiatric evaluation highlighted possible signs of depression and anxiety in the patient. Considering both neurological and psychological aspects, a comprehensive approach to their care would be essential for an accurate diagnosis and appropriate management.

**Table 1:** Abnormalities observed in the psychiatric evaluation.

| Aspect | Assessment |
|---|---|
| Orientation | X3 |
| Appearance | Disheveled |
| Suicidal thoughts | Present |
| Affect | Sad and congruent |
| Eye contact | Poor |
| Cooperative | Yes |
| Abnormal movements | None |
| Attention | Intact |
| Speech | Hypoverbal |
| Mood | Depressed and anxious |
| Thought process | Slow |
| Judgment | Poor |
| Insight | Limited |

## DISCUSSION

The concept where one disease acts to ameliorate another disorder, yclept enantiopathy, is widely described among neurological diseases. These include bradyphagia for Burning Mouth Syndrome (BMS), upper respiratory infection for BMS, cerebellar hemorrhage for stereotypy, nasal congestion for phantosmia, anosmia for palinageusia, alcohol dependence for both cataplexy and essential tremor [25]. Parkinson's disease-induced hyposmia for snatiation, heroin dependence for quetiapine-induced restless leg syndrome, chemosensory dysfunction for gustatory rhinitis, and both COVID-19 and head trauma induced hyposmia for odor induced migraines. In the current case, heroin withdrawal precipitating tinnitus and elimination with heroin or other opioids strongly suggests that the tinnitus is opioid dependent. This was self-observed in the subject as he identified it as one of the motivators to relapse on heroin to eliminate tinnitus. The reduction in tinnitus with the mouth wide open would be consistent with the sound not being derived from the auditory apparatus but rather as a variant of central psychosis auditory hallucinations ascribed to micro-laryngeal movements. Cortically mediated mouth opening inhibits micro-laryngeal movements and, thus, auditory hallucinations. This suggests that his tinnitus and verbal auditory hallucination are mediated through the exact mechanism. The opioids may inhibit tinnitus through their cortical effects rather than otological effects [26].

## CONCLUSION

This case report presents a unique and previously undocumented phenomenon of tinnitus induced by opioid use, its exacerbation during withdrawal, and its relief upon re-administration of opioids. It highlights the importance of considering opioid dependence as a potential cause of tinnitus in specific individuals. The mechanism behind opioids' inhibitory effect on tinnitus remains complex, with the possible involvement of cortical modulation rather than direct effects on the auditory system. The implications of this case report are noteworthy, as it suggests that investigating tinnitus in individuals with opioid dependence could identify a subgroup that may benefit from tinnitus-alleviating medications. Such interventions could potentially reduce the risk of opioid relapse and improve the overall well-being of these individuals. However, further research is required to gain a deeper understanding of the underlying mechanisms and explore potential therapeutic options for tinnitus in opioid dependence.

In conclusion, this case report sheds light on an intriguing relationship between opioid use, withdrawal, and tinnitus. The findings open new avenues for investigating tinnitus management strategies in individuals with opioid dependency, potentially offering a novel approach to address tinnitus and opioid-related concerns.

## ETHICS APPROVAL

The patient provided informed consent.

## CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient to publish this case report.

## REFERENCES

1. Bauer CA. Tinnitus. N Engl J Med. 2018;378(13):1224-1231.
2. Fornaro M, Martino M. Tinnitus psychopharmacology: A comprehensive review of its pathomechanisms and management. Neuropsychiatr Dis Treat. 2010;6:209-218.
3. Busto U, Sellers EM, Naranjo CA, Cappell H, Sanchez-Craig M, Sykora K. Withdrawal reaction after long-term therapeutic use of benzodiazepines. N Engl J Med. 1986;315(14):854-859.
4. Bayón AR, de Sagrario MT, Sampedro FG. Auditory hallucinations in cognitive neurology. Neurologia. 2017;32(6):345-354.
5. Lintzeris N, Nielsen S. Benzodiazepines, methadone and buprenorphine: interactions and clinical management. Am J Addict. 2010;19(1):59-72.
6. Quinlan J, Cox F. Acute pain management in patients with drug dependence syndrome. Pain Rep. 2017;2(4):39-34.
7. O'Brien CP. Benzodiazepine use, abuse, and dependence. J Clin Psychiatry. 2005;66(Suppl 2):28-33.
8. Laskey C, Opitz B. Tinnitus associated with benzodiazepine withdrawal syndrome: A case report and literature review. Ment Health Clin. 2020;10(3):100-103.
9. Jufas NE, Wood R. The use of benzodiazepines for tinnitus: systematic review. J Laryngol Otol. 2015;129(S3):S14-22.
10. Vahdatinia R, Keane J, Troncoso V, Goldstein LB. Tinnitus: Diagnosis and treatment options. Heighpubs Otolaryngol Rhinol. 2017;1(1):53-59.
11. Keshavan MS, David AS, Steingard S, Lishman WA. Musical hallucinations: a review and synthesis. Cogn Behav Neurol. 1992;5(3):211-223.

12. Saifan C, Glass D, Barakat I, El-Sayegh S. Methadone induced sensorineural hearing loss. Case Rep Med. 2013;2013:56-61.
13. Oroei M, Peyvandi AA, Mokhtarinejad F. Opioid drugs and sensorineural hearing loss. Addict Health. 2018;10(1):64.
14. Sahley TL, Nodar RH. A biochemical model of peripheral tinnitus. Hear Res. 2001;152(1-2):43-54.
15. Sahley TL, Hammonds MD, Musiek FE. Endogenous dynorphins, glutamate and N-methyl-d-aspartate (NMDA) receptors may participate in a stress-mediated Type-I auditory neural exacerbation of tinnitus. Brain Res. 2013;1499:80-108.
16. Kratzer U, Schmidt WJ. Caroverine inhibits the conditioned place aversion induced by naloxone-precipitated morphine withdrawal in rats. Neurosci Lett. 2003;349(2):91-94.
17. Thabit MN, Fouad N, Shahat B, Youssif M. Combined central and peripheral stimulation for treatment of chronic tinnitus: a randomized pilot study. Neurorehabil Neural Repair. 2015;29(3):224-233.
18. Rawool V, Dluhy C. Auditory sensitivity in opiate addicts with and without a history of noise exposure. Noise Health. 2011;13(54):356.
19. Shaw KA, Babu KM, Hack JB. Methadone, another cause of opioid-associated hearing loss: a case report. J Emerg Med. 2011;41(6): 635-639.
20. Barsan WG, Seger D, Danzl DF, Ling LJ, Bartlett R, Buncher R, et al. Duration of antagonistic effects of nalmefene and naloxone in opiate-induced sedation for emergency department procedures. Am J Emerg Med. 1989;7(2):155-161.
21. Senay EC, Adams EH, Geller A, Inciardi JA, Muñoz A, Schnoll SH, et al. Physical dependence on Ultram®(tramadol hydrochloride): Both opioid-like and atypical withdrawal symptoms occur. Drug Alcohol Depend. 2003;69(3):233-241.
22. Terasaki D, Klie K. Tramadol withdrawal in the setting of buprenorphine induction: A case report. J Addict Med. 2020;14(3): 264-266.
23. Beebe Palumbo D, Joos K, De Ridder D, Vanneste S. The management and outcomes of pharmacological treatments for tinnitus. Curr Neuropharmacol. 2015;13(5):692-700.
24. Franz B, Collis-Brown G, Altidis P, Altidis B, Cummings N. Cervical trauma and tinnitus. Int Tinnitus J. 1998;4(1):31-33.
25. Nasrallah HA, Schroeder D, Petty F. Alcoholism secondary to essential tremor. J Clin Psychiatry. 1982;43(4):163-164.
26. Bick PA, Kinsbourne M. Auditory hallucinations and subvocal speech in schizophrenic patients. Am J Psychiatry. 1987;144(2): 222-225.