

## Opioid Drugs and Sensorineural Hearing Loss

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### Letter to Editor

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Almost from the 4<sup>th</sup> century B.C, the opioids have been consumed for analgesic and sedative effects in the recreational and religious ceremonies. Today, opioids are being prescribed for the treatment of acute and chronic painful conditions, of course, it is controversial in chronic noncancerous pain due to making tolerance and dependency. The opioid drugs have been chemically provided from different alkaloids of raw opium for medical use. Commonly abused opioid drugs consisted of heroin, morphine, opium, methadone, codeine, tramadol, oxycodone, and hydrocodone. Globally, it is estimated that about 35 million individuals aged 15-65 years old misuse opioids that in comparison with cannabis and amphetamine, is less common. Opioid drugs are major public health concerns, as it has potentially adverse effects on health consequences.<sup>1</sup> There are multiple complications with opioid use. One of the common complications is the opioid overdose. This public health concern has increased in the recent years. Opioid overdose occurs in the individuals who use opioids for treatment of chronic pain, and/or use them along with sedative drugs, in addition to family members of individuals in the passion of opioid drugs. This phenomenon is not always fatal; but can lead to various well-known complications. These non-lethal complications include functional impairment of central and peripheral nervous system, as well as gastrointestinal, respiratory, and cardiovascular system, and psychological disorders.<sup>2</sup>

Sensorineural hearing loss is an unusual reported one. In recent years, there have been remarkable numbers of occurring of hearing loss (suddenly, or rapidly progressive) associated with opioid overdose, especially in the young patients. The majority of cases has bilateral hearing loss reported after using heroin, morphine, methadone, propoxyphene, hydrocodone, and oxycodone along with acetaminophen. Hearing

loss is reversible in some individuals that improves with administration of corticosteroids and pentoxifylline. The cochlear implant is required in irreversible cases. Some patients in addition to hearing loss have tinnitus and vertigo. There are differences among these reports in terms of the route of consumption (oral, inhalation, and intravenous injection), the amount of drug, and duration of use.<sup>3</sup>

### The proposed mechanisms of opioid-induced hearing loss

The pathophysiology of opioid-associated hearing loss has been remained unknown yet. Several theories have proposed to explain the effect of opioid drugs on the hearing system. The most commonly proposed theories are ischemic cochlear secondary to vasospasm or vasculitis of the branch of the spiral modiolar artery, genetic variation in liver metabolic enzymes, transporting proteins and receptors, and direct effect of opioids on opioid receptors.

The cochlear structure is very susceptible to hypoxia. Animal studies have indicated opioids stimulate production and release of endothelin-1 as an endogenous vasoconstrictor. This factor binds to endothelin receptor (ET-A) on smooth muscle cells of the spiral modiolar artery, and leads to vasospasm and cochlear ischemia.<sup>3</sup>

Genetic polymorphism may be a predisposing factor in occurring opioid-induced hearing loss, like hearing loss secondary to aminoglycosides. Allelic variants in liver metabolizing enzymes, and mutations of the gene due to the  $\mu$ -opioid receptor (OPRM1) may be explained in various responses to opioid drugs in individuals.

Blood-labyrinth barrier has the main role for maintaining homeostasis of inner ear fluid. This barrier permits to transport molecules based on the molecular weight. According to differences in the molecular weight of opioid drugs, inter-person variation in transport channels may

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contribute to occurring hearing loss in some opioid users.<sup>4</sup>

Another proposed mechanism is the effect of opioids on special receptors in the inner ear. Opioid receptors [ $\mu$ -opioid receptors (MOR),  $\kappa$ -opioid receptor (KOR), and  $\delta$ -opioid receptor (DOR)] are present in various body systems including the central and peripheral nervous system. The stimulation of them can induce analgesia, euphoria, dependency, respiratory depression, bradycardia, and urinary retention. The majority of opioids that abused or depended are MOR-agonist. Multiple experimental studies have demonstrated the presence of the opioid receptors in the inner ear. These receptors are in inner and outer hair cells, supporting cells of the organ of Corti, spiral ganglion, and nerve fibers. The presence of MOR in the cochlea of human has been certainly unidentified. The activation of MOR can inhibit calcium, current with inhibition of adenylate cyclase in mammalian models. Endogenous opioid peptides (endorphin and enkephalin) have likely important role in auditory neuromodulation. It is possible that activation of MOR by exogenous opioid may impair auditory neuromodulation, and lead to hearing loss.<sup>5,6</sup> However, efforts should be made to demonstrate the pathogenesis of hearing loss after opioid overdose.

Based on World Health Organization report, the prevalence of disabling hearing loss has the upward trend in recent decades and the global prevalence has been estimated about 15 percent of the adults over 18 years.<sup>7</sup> Hearing loss is the fifth disease in the global burden of disease, that it has a higher rank than some chronic diseases such as chronic obstructive pulmonary disease, dementia, and diabetes. The profound hearing loss can negatively effect on quality of life through reducing interpersonal communication, family

and social role and health.<sup>8</sup> The individuals with mild hearing loss are not always safe and they may induce with increasing risk of functional deficits. This deficit can be exacerbated in the context of environmental noise.

The opioid overdose of young people is common in recreational activities that have noise exposure. In fact, this population can expose with two potential risk factors for hearing loss, opioid and noise. By neglecting this threat, it can induce remarkable prevalence of hearing loss in the age lower than presbycusis age. Furthermore, considering the increase of opioid use in general population and extensive use of methadone for maintenance treatment in addiction treatment clinics, it is necessary to do explanatory studies to cover the gap between hearing research and the role of ototoxicity of opioid drugs, especially synthetic or semi-synthetic drugs. Therefore with obtaining strong evidence, it can be very helpful in early detection of this symptom, prevention of hearing impairment, avoiding from inappropriate prescribing of these drugs by physicians, and restricting over-the-counter sales of opioids. In addition, it is important to improve physicians' awareness about this problem; in patients who are visited for sudden sensorinural hearing loss, it might be a result of opioid abuse, so the physicians should ask from patients about their recent opioid consumption as prescription or recreational use.

It is certain that the capacity of international health organizations, health policymakers, researchers, and other stakeholders should be employed to provide a new and special approach to this subject.

### Conflict of Interests

The Authors have no conflict of interest.

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