



Oxymetazoline Toxicity: A Systematic Review of Case Reports and Clinical Presentations.

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ABSTRACT

Oxymetazoline is a common over-the-counter nasal decongestant. But if it is misuse it can result in severe toxicity and adverse effects. This systematic review aims to summarize the clinical presentation and characteristics of oxymetazoline toxicity based on case reports in the literature. With a summary of the clinical presentation and a focus on the typical signs and symptoms of this illness, this systematic review offers a thorough examination of case reports on oxymetazoline toxicity. The research can help medical practitioners identify and treat cases of oxymetazoline poisoning and further our understanding of the condition. It is necessary to conduct more study to look at potential risk factors, cures, and long-term effects connected to oxymetazoline toxicity.

Keywords: Oxymetazoline, Decongestant, Vasoconstrictor, Tachycardia, Rebound Congestion, Hypertension

Introduction

Oxymetazoline, the imidazole derivative, is an alpha-adrenergic agonist [1, 9]. The oxymetazoline brand Afrin was first sold as a prescription medication in 1966. It became available as an over the counter drug in 1975. It has vasoconstrictor and decongestive properties that gives relief from nasal congestion. Due to which it is widely used as a non-prescribed nasal decongestion [4]. Nasal congestion can be caused by the conditions like perennial and allergic rhinitis, Hay fever and sinusitis.

Oxymetazoline acts by triggering alpha-adrenergic receptors in the blood arteries of the nose, which causes vasoconstriction [1, 2]. Nasal congestion is relieved as a result of the constriction's decreasing blood flow to the nasal mucosa and congestion. It gets absorbed through the mucosa of the nose when it is used as a nasal spray or drop. The first signs of action generally appear within a few minutes. Its effects might last ranging from a few minutes to many hours. It breaks down in the liver before being eliminated. The main metabolic route involves oxidation followed by conjugation among them. The metabolites are then eliminated through the urine.

Clinically the use of oxymetazoline is to provide short-term relief from nasal congestion brought on by conditions including the common cold, sinusitis, and allergies. As it reduces nasal tissue swelling, which can help with stuffiness relief and breathing improvements.

Though oxymetazoline is generally considered to be safe if consumed as prescribed, it is extremely important to follow the suggested dosage and usage time [1, 3, 11]. When nasal symptoms get worse after stopping medication due to prolonged or frequent use, a condition called rebound congestion is caused. Oxymetazoline frequently leads to discomfort or pain in the nose, sneezing, dryness, and moderate irritation if any side effects appears, it's crucial to keep the drug out of your mouth and eyes, and to stop using it.

It is specially recommended that without contacting a medical expert, oxymetazoline is not advised for those with specific medical concerns, such as high blood pressure, heart disease, diabetes, thyroid abnormalities, or prostate issues. Additionally, because it raises the possibility of negative side effects or drug interactions, it's vital to avoid using certain drugs or substances simultaneously, such as monoamine oxidase inhibitors (MAOIs) or other nasal decongestants.

In order to limit our exposure to these substances and to prevent or reduce the possibility that a medical condition or other adverse health outcome would occur. It is important to review case reports to gain insights into the adverse effects and toxicity profile of oxymetazoline. Safety regulators, legislators, and others can use the essential data and knowledge that toxicology provides.

Methodology

Case reports of oxymetazoline poisoning were chosen based on pre-established inclusion and exclusion criteria after an extensive search of computerized databases was undertaken using appropriate keywords. Details on the patient's demographics, clinical characteristics, diagnostic standards, therapeutic modalities, and results were taken out and studied. The included case reports' reliability was also evaluated.

Adverse effects and risk factors

Common side effects are nasal burning, stinging, dryness or sneezing. It can also cause headaches or dizziness. Nervousness, shakiness or trembling, blurry vision, trouble sleeping or drowsiness, increased runny or stuffy nose are the symptoms of overdoses.

Cardiovascular Effects: Oxymetazoline may result in gastrointestinal uptake, particularly when administered at greater dosages or for longer periods of time. Cardiovascular symptoms include raised blood pressure, tachycardia (rapid heartbeat), palpitations, and maybe arrhythmias might ensue from this [1, 4, 5]. Oxymetazoline should only be used with precaution and under medical guidance by those with pre-existing cardiovascular issues or those who are taking drugs that alter blood pressure [9].

Effects on the Central Nervous System: Oxymetazoline may occasionally have effects on the CNS (central nervous system) due to its systemic intake. These include possible symptoms including tremors, headaches, nervousness, anxiety, and dizziness. Although rare, excessive systemic absorption or drug abuse can result in serious CNS side effects [4, 5].

Allergic Reactions: Despite being uncommon, oxymetazoline can occasionally cause allergic responses in some people. From minor irritation of the skin, rash, or itching to increasingly serious responses including swelling on the face, tongue, and throat, as well as trouble breathing, and anaphylaxis, symptoms can range from moderate to severe. If an allergic response is believed to have occurred, quick medical attention must be obtained.

Rebound congestion: If used more than 3-4 days in a row can make nasal congestion worse called as rebound congestion in the form of rhinitis medicamentosa [3].

Eye and mouth Irritation: Oxymetazoline can irritate the eyes and mouth if it comes into touch with them unintentionally. To reduce the chance of discomfort, it's crucial to keep your hands away from these regions and to completely wash them after application.

Patients may get physically addicted to oxymetazoline. It can raise blood pressure. When taken with medicines that are used to treat depression leads to the condition such as hypertension.

The Food and Drug Administration (FDA) places oxymetazoline in category C, indicating risk to the fetus cannot be ruled out. Accidentally ingested causes many adverse effects. In the event of possibly, life threatening overdose (such as hypertensive crisis). Especially in children, an overdose can quickly cause severe central nervous system depression and cardiovascular adverse effects.

Summary of Case Reports

Case Report 1:

In 1989, a 22 year old male was died from a blow to the head. His body was examined for the presence of drugs. In this examination, a postmortem liver extract contained two similar chemicals. One of these was confirmed as xylometazoline, a nasal decongestant. And other turned out to be a recently unidentified imidazole metabolite of xylometazoline which was concluded by mass spectrometry [6].

Case Report 2:

A 23 year old heroin addict man was certified dead six hours later when he was first seen in café. During examining externally a recent injection site was found in the right antecubital fossa. The important findings was clearly noticeable cyanosis of the lips and fingertips. During Internal examination it was revealed generalized all organs had widespread congestion. The heart was normal but showed few epicardial hemorrhages. Although the stomach was empty it had some atrophic gastritis. During toxicologically examining only samples of peripheral blood and hepatic blood contained xylometazoline. Urine testing revealed a trace quantity. None was found in the stomach contents, proving that the substance was probably injected [7].

Case Report 3:

Three 3 year old boys (triplets), were diagnosed by toxicological analysis for a xylometazoline intoxication. All 3 children's were not responsive till admitted to an emergency unit. One of them showed breathing rate of 15-20 breaths/min. which needed to carry oxygen (3L/min.) through face mask. And his ECG test showed sinus bradycardia of 64 beats/min. with supraventricular extra systoles. Two of them woke up after 11 hrs. of incident took place and were not still completely placed. The third boy woke up at 20 hrs. Following by nasal drops installation. The pharmacy's compounding error led to intoxication, with the concentration being 40 times higher than the adequate dosage for children [8].

Organ Systems Affected

The severity and frequency of adverse effects varies and depends on the dose, route of administration, the extent of exposure and individual factors. The specific organ systems affected by oxymetazoline toxicity, such as cardiovascular (hypertension, tachycardia, arrhythmia, palpitations) central nervous system, respiratory, ocular systems, and congestion of all organs The adverse effects are more likely to come to exist with higher doses or by injecting the component and also due to prolonged use. In children, small doses can be quickly harmful and toxic.

Factors Influencing Toxicity

1. **Dose and Concentration:** The quantity of oxymetazoline consumed or used has a big impact on how harmful it is. The risk of negative consequences might rise with higher dosages or concentrations [10].
2. **Administration Route:** Oxymetazoline is mostly used by applying or spraying in the nose. The absorption and systemic effects are negligible when taken as instructed by doctor. However, overuse or unintentional ingestion, such as ingesting nasal spray or drops, can result in greater toxicity [8].
3. **Age:** Compared to adults, children under the age of five are more prone to the harmful consequences of oxymetazoline poisoning. Even at little dosages, they have an increased chance of developing severe symptoms [10].
4. **Individual Sensitivity:** Each person's sensitivity to oxymetazoline may be different. While some people may be more susceptible to side effects even at lower levels, others may handle greater doses without having any noticeable symptoms.
5. **Duration of usage:** Oxymetazoline toxicity risk can be increased by prolonged or regular usage. Rebound congestion occurs when the nasal passages become much more clogged after the drug wears off, necessitating more doses to provide relief. This illness is caused by continuous usage for a longer time than the advised length [1, 11].
6. **Frequency of use:** Repeated or frequent use can raise the risk of oxymetazoline toxicity. Rebound congestion is when the nasal passages are considerably worse after the medication wears off, prompting extra doses to relieve the symptoms. Continuous use for a longer period of time than is suggested results in this sickness [1, 3].

Mechanisms of Toxicity

The pharmacological actions of oxymetazoline on numerous bodily systems and receptors make up the underlying mechanism of its toxicity. Despite the fact that the precise mechanism is not entirely understood, the research that is currently accessible sheds light on some of the potential harmful effects of oxymetazoline. Using the facts at hand, the some important points are, Alpha- Adrenergic Agonism, Cardiovascular Effects, Effects on Central Nervous System, Respiratory problems.

Regulatory Considerations

Approved Indications: In several nations, oxymetazoline can frequently be permitted for usage as a nasal decongestant. It is used to treat sinusitis, hay fever, allergic rhinitis, the common cold, and other respiratory disorders that cause nasal congestion. It reduces edema and congestion by tightening blood vessels in the nasal passages.

Label Warnings and Precautions: Depending on the country and the particular formulation of oxymetazoline, different warnings and precautions may be listed on the label. However, there are a number of typical dangers and recommendations related to using oxymetazoline, including

1. **Duration of Use:** To avoid the occurrence of rebound congestion, oxymetazoline nasal sprays shouldn't be used consistently for longer than a few days (often 3-5 days). When the medicine is withdrawn, continuous or excessive usage may cause congestion become severe.
2. **Nasal Irritation:** Oxymetazoline may irritate the nasal passages, resulting in blistering, itching discomfort or sneezing. It is advised to consult a doctor if these symptoms worsen or continue to persist.
3. **Contraindications:** Anybody who has a known allergy or hypersensitivity to the drug should avoid using this.

Consulting a medical expert or chemist from whom you can get precise information on its safety, possible warnings, application and precautions.

Future Directions

Despite the widespread usage of oxymetazoline as a nasal decongestant, there are still certain information gaps and areas that need for more research about its toxicity. Here are several crucial areas:

1. **Chronic Safety:** More long-term studies are required to assess the health risks of oxymetazoline when used for an extended period of time, particularly with regard to rebound congestion and possible side effects on the mucosa of the nose.
2. **Pediatrics Population:** Since most studies on oxymetazoline toxicity have been done in adults, further study is required to determine the drug's safety and effectiveness in children, as well as any possible impacts on their development, growth, and longevity.
3. **Drug Reactions:** Additional research is necessary to fully comprehend the effects of drugs with oxymetazoline. This involves researching the consequences of using one medicine while taking another, particularly those that may impact blood pressure or the workings of the central nervous system.

4. Mechanism of toxicity: The fundamental mechanisms of oxymetazoline toxic effects are understood, but more investigation is required to identify the precise paths and receptors involved as well as the precise dose-related interactions and possible genetic factors which may be responsible for individual response change.

5. Overview Studies: Studies comparing various oxymetazoline the composition and doses might assist ascertain the relative risk aspects and effectiveness of various medications on the market.

6. Real-world Safe Records: Oxymetazoline's safety profile can be better understood by maintaining tracking and analyzing post-marketing surveillance data and adverse event reports. This can help to spot uncommon or persistent side effects that may not have been noticed in clinical studies.

Filling up these knowledge gaps and performing further study in these areas can help us comprehend the safety and possible hazards of oxymetazoline, resulting in better recommendations, labelling information, and patient care techniques.

Conclusion

These case studies demonstrate the occurrence and effects of xylometazoline usage and intoxication in various situations. Xylometazoline and an unidentified metabolite were discovered in the postmortem findings in Case Report 1, indicating past usage. In Case Report 2, an injection of xylometazoline caused a heroin user to die from extensive organ congestion. A pharmacy error in Case Report 3 shows the serious consequences of xylometazoline overdose in young infants, leading to considerable physiological symptoms and a protracted recovery period.

Important efforts in reducing the probability of fatality related with this prescription include raising healthcare providers' knowledge of the issue, offering thorough patient education, and promoting proper use of oxymetazoline. In order to ensure the safe and efficient administration of oxymetazoline, patients and medical professionals must work together.

The risk of oxymetazoline toxicity could be reduced by employing these techniques and encouraging a cooperative attitude between medical staff and patients, enabling the safe and efficient administration of this medicine.

Determining the cause of death, evaluating drug-facilitated crimes, comprehending interactions between drugs, taking postmortem redistributing into account, and giving expert testimony all depend on knowing the oxymetazoline toxicity from a forensic perspective. Overall, oxymetazoline toxicity research is essential for ensuring the medicine is used safely and effectively, detecting possible dangers, informing regulatory choices, and enhancing patient care.

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