A case of naphazoline intoxication after the ingestion of a topical antiseptic solution

服食外用消毒藥液後的一個萘甲唑啉中毒個案

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Senepul™ solution is frequently used as a topical antiseptic solution in Korea in cases with abrasion, laceration and impetigo. 100 ml of this solution contains a mixture of 100 mg naphazoline hydrochloride, 100 mg dibucaine hydrochloride, 200 mg chlorpheniramine maleate, and 100 mg benzethonium chloride. Naphazoline is an alpha sympathomimetic and an imidazoline derivative. In excessive dosage or ingested by accident, naphazoline may cause not only local but also systemic side effects like hypertension, bradycardia with arrhythmia, hypotension, respiratory depression, excitation or severe central nervous system depression. We report a case of a patient with prolonged bradycardia, hypotension, central nervous system depression that occurred after ingestion of a small amount of this topical antiseptic solution. (Hong Kong j.emerg.med. 2010;17:364-366)

Senepul™藥液在韓國是常用於擦傷，裂傷及膿瘍病個案的外用消毒藥液。100毫升溶液載有100毫克萘甲唑啉、鹽酸鹽・100毫克地布卡因鹽酸鹽・200毫克氯苯苄胺馬來酸鹽及100毫克苯甲氯胺的混合物。萘甲唑啉是α類交感神經剝及咪唑的衍生物。過量或意外服食時，萘甲唑啉不單只可引致局部的副作用，亦可引致全身性的副作用，如高血壓、心搏徐緩伴以心律不齊、低血壓、抑壓呼吸、激動或嚴重的中樞神經系統衰弱。本文報告一名病人服用小量這外用消毒藥液後，出現長時間心搏徐緩、低血壓及中樞神經系統衰弱的個案。

Keywords: Bradycardia, local anti-infective agents, naphazoline, solutions

關鍵詞：心搏徐緩、局部消毒劑、萘甲唑啉、溶液

Introduction

Senepul™ solution is frequently used as a topical antiseptic solution in Korea in cases with abrasion, laceration and impetigo. Each 100 ml of this clear and transparent solution contains a mixture of 100 mg naphazoline hydrochloride (sympathomimetic agent with marked alpha-adrenergic activity), 100 mg dibucaine hydrochloride (local anaesthetic), 200 mg chlorpheniramine maleate (antihistamine), and 100 mg benzethonium chloride (antiseptic and germicide). Naphazoline is an alpha-sympathomimetic and an imidazoline derivative. In excessive dosage, or when ingested by accident, naphazoline may cause not only local but also systemic side effects like hypertension, bradycardia with dysrhythmia, hypotension, respiratory depression, excitation or severe central nervous system (CNS) depression.

Case

A 14-year-old female accidentally ingested 15 ml of Senepul™ solution in August 2009 and was sent to our emergency department 10 hours after the
ingestion. The patient was not on any medication and had no known diseases. She complained of sleepiness, general weakness, sweating, lips and oral cavity swelling, and epigastric abdominal pain. These symptoms developed five minutes after the ingestion. She had alert mental status and normal findings on neurologic examination. Her vital signs showed a blood pressure of 70/50 mmHg, pulse rate 40 beat/min, respiratory rate 20 breath/min, and body temperature 36.8°C. The physical examination revealed mild lips and oral mucosal swelling, slow heart beats without murmur, and mild abdominal tenderness in the epigastric area. Otherwise, it was unremarkable. The initial electrocardiogram finding was sinus bradycardia (Figure 1). Laboratory data, including haemoglobin, platelet count, white blood cell, blood chemistry, and cardiac markers were all normal. Urinalysis was normal and urine human chorionic gonadotrophin test was negative. The chest radiograph showed normal findings. To evaluate the cardiac condition, an echocardiogram was performed and revealed normal findings. The provisional diagnosis was intoxication by the antiseptic solution containing naphazoline. She was admitted for observation and supportive treatment. After admission, she had hypotension and bradycardia despite dopamine infusion for three days (Figure 2). She was finally discharged on the 5th day without complication.

![Figure 1](image1.png)

**Figure 1.** Electrocardiogram showing sinus bradycardia at 40 beats per minute.

![Figure 2](image2.png)

**Figure 2.** Schematic course of the patient’s circulatory data after admission.
Discussion

Naphazoline is an imidazoline derivative and \( \alpha_2 \)-adrenergic agonist. Imidazoline derivatives such as naphazoline are frequently used as local vasoconstrictive and decongestant drugs. Due to its \( \alpha \)-sympathomimetic effect, this agent has topical and systemic side effects. Reactive hyperaemia and atrophic rhinitis sicca are well-known local side effects. Inappropriate use or unintentional ingestion of naphazoline can quickly cause severe CNS depression and cardiovascular adverse effects.\(^1\) Systemic vasoconstriction through peripheral \( \alpha \)-adrenoceptors leads to arterial hypertension with reflex bradycardia and possible ischaemia of vital organs. Stimulation of central alpha-adrenoceptors leads to CNS depression, ranging from drowsiness to coma, persisting cardiovascular hypotension, reduced respiratory rate leading to Cheyne-Stokes breathing and possibly pulmonary oedema. Other side effects include hypothermia, mydriasis, hyperhidrosis, and transient excitation hyperreflexia.\(^2\)

Mahieu et al reviewed 261 calls on imidazoline exposure, and 19 cases of involuntary paediatric patients with naphthylimidazoline exposure had sufficient data for a more detailed study.\(^3\) Intoxication may occur at a dose of 0.05 mg/kg body weight after nasal application, 0.1 mg/kg after oral ingestion in babies and 0.3 mg/kg after oral ingestion in children older than 2 years.\(^4\) This agent is absorbed rapidly, so symptoms develop within one hour, peak after 8 hours, and disappear in 24 hours. All had complete recovery in 24 hours with supportive treatment.\(^5\)

No specific antidote is available and there is controversy about the general treatment. In our case, the 14-year-old female was admitted to the emergency department 10 hours after ingestion of naphazoline, a dose of 0.24 mg/kg. Although we gave her hydration fluids and dopamine infusion, the vital signs remained unstable for three days. Most cases reported symptom resolution within 24 hours.\(^5\) Up till now, information on the distribution and the elimination of this drug in humans is not available. However, we know the symptoms may prolong for a few days.

Naphazoline-containing Senepul™ solution is an over-the-counter solution frequently used as a topical antiseptic for cases of abrasion, laceration and impetigo in Korea. Only topical toxicity like rash, hyperaemia and itching sensation but not systemic toxicity of naphazoline is mentioned in the instruction. Some reports of naphazoline intoxication pointed out that the manufacturer did not indicate systemic side effects of naphazoline.\(^1\) Naphazoline has a narrow therapeutic-to-toxic window.\(^6\) In our case, the patient ingested only 15 ml of solution, producing a dose of 0.24 mg/kg of naphazoline.

Conclusion

In general, physicians and pharmacists and the public should be educated about the toxicity of over-the-counter preparations, especially those with a narrow therapeutic-to-toxic window like naphazoline.

References