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OBSERVATION
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# NAPHAZOLINE NASAL DROPS INTOXICATION IN CHILDREN

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Naphazoline, a sympathomimetic and an imidazoline derivative, is used as 0.05–0.1% solution for local decongestion of the nasal and ocular mucosa. In excessive dosage, or if ingested by accident, may cause depression of the central nervous system (disturbances of consciousness progressing to coma), hypothermia, bradycardia and sweating. These naphazoline effects are particularly strongly pronounced in children. Anglo-Saxon pharmacotherapy excludes the application of naphazoline nasal drops in children younger than six years, whereas the Croatian pharmacotherapeutic literature (and practice) allows its use even in infancy. At the Kantrida Paediatric Clinic, Clinical Hospital Centre in Rijeka, 11 children with signs of intoxication with naphazoline nasal drops were hospitalized from 1990 to 1992. The symptoms pertaining to the central nervous system i.e. disturbances of consciousness in the form of somnolence were clearly marked in all children. Some children developed skin pallor, bradycardia, bradypnoea and hypothermia. Resolution occurred within 24 hours and the findings returned to normal values. Clinical picture followed by rapid resolution and normal findings, with a personal history of drug taking, is a safe indication for diagnosis. There are several reasons to account for intoxication (drops difficult to use with children, containers inadequate for proper dosage), but the major factor is the age of the patient – all hospitalized children were younger than six years. It is pointed out that administration of naphazoline drops at an early age is not advisable.

*Key terms*:
adverse effects, Croatian pharmacopoiea, sympathomimetic agent, toxic effects, young children

Naphazoline is a sympathomimetic agent, an imidazoline derivative. Although the mechanism of its action has not been completely explained, especially in the central nervous system, most pharmacologists believe that the drug directly stimulates alpha-adrenergic receptors (of the sympathetic nervous system) and exerts little or no effect on beta-adrenergic receptors (1–5). Naphazoline is used most frequently alone or in different combined preparations for relieving congestion of the ocular and nasal mucosa in acute and chronic inflammations. When applied

topically in recommended dosages as a 0.05–0.1% solution, the incidence of serious adverse effects is low. Its prolonged use (for more than 4–5 days) may bring about irritation of the mucosa and result in its ulceration, nasal cilia paralysis and anosmia (4, 5). Like other sympathomimetics, naphazoline may cause, after discontinuation of treatment, adverse reactions associated with »rebound phenomenon« (vasodilation, congestion, rhinorrhea, etc.). Although naphazoline absorption through the lipid matrix of biological barriers is good, local application on the ocular and nasal mucosa rarely causes general sympathomimetic effects. An overdosage of the drug, or its accidental oral consumption, may cause a very severe intoxication with the central nervous system depression, hypothermia, bradycardia, sweating, disturbances of consciousness and even coma (6–8). Toxic effects of naphazoline are very frequent and serious in children younger than six years. This is the reason why the Anglo-Saxon pharmacotherapeutic literature excludes the application of naphazoline drops in younger children (4, 6, 7). It is to be regretted that the Croatian literature mentions (and practice confirms) the possibility of its use even in infancy (9, 10). Being aware of this and also of the fact that physicians are not sufficiently informed of the problem and that literature data in this field are scarce, we considered it worthwhile to present own experiences in naphazoline intoxication in children and to offer several recommendations.

## PATIENTS AND METHODS

The patients in the investigation were hospitalized at the Kantrida Paediatric Clinic, Clinical Hospital Centre in Rijeka, from 1990 to 1992, with signs of intoxication by naphazoline nasal drops. After a personal history and the clinical status were taken, routine laboratory tests were made (complete blood test, acidobasic status, electrolytic status, blood sugar, urine analysis). An examination of the eye fundus, otorhinolaryngologic examinations and electroencephalography were made. Some patients, where it was diagnostically justified, were tested by other diagnostic methods (lumbar puncture and ultrasound of the head).

## RESULTS

Eleven patients were hospitalized in the Kantrida Paediatric Clinic from 1990 to 1992. The examinations confirmed suspected naphazoline nasal drops intoxication (clinical picture and personal history with other normal findings). Among the patients there were seven girls and four boys. Most patients were in the 2–3-year age group (three aged one year, six aged 2–3 years and two aged 4–6 years). The youngest patient was two months old, and the oldest five years and eight

months. In eight cases the drops were administered by parents (mother), in two cases the content of the bottle was swallowed accidentally, and one child took the drug by himself. In all cases the naphazoline solution concentration was 0.05%. Age distribution, sex, drops application and symptoms (somnolence in all 11 patients – the most pronounced symptom bringing all the patients to the physician) are shown in the Table.

It should be pointed out that in children to whom the drops were administered by parents (Table) the dosage (according to personal history) was in allegedly therapeutic limits. Therapeutic dosage (1–2 drops) was certainly exceeded in three cases (Table – two by swallowing, one self-administered). The recovery in all the patients was very fast, within 24 hours, and without consequences.

## DISCUSSION AND CONCLUSIONS

According to data from literature (4, 6–9), naphazoline effects are known as depression of the central nervous system.

They appeared in all 11 patients (in eight cases the drops were administered by parents – obviously overdosage of the drug). Dominant clinical symptoms are characterized as mild disturbances of consciousness (somnolence) and in some cases, pallor, hypothermia, bradycardia, bradypnoea and sweating (Table). This clinical picture and personal history of naphazoline nasal drops administration, with other normal findings, are an indication for diagnosing naphazoline intoxication. We may also say that the results in cases of milder disturbances of consciousness will also be favourable and that there will be no need for additional

Table *Distribution of the children intoxicated with naphazoline nasal drops by age, sex, mode of administration and symptoms of intoxication*

| Age | Sex | Drops application | Symptoms |
|---|---|---|---|
| 2 months | F | by parent | somnolence, pallor, bradycardia |
| 4 months | F | by parent | somnolence, pallor, bradycardia, bradypnoea |
| 5 months | F | by parent | somnolence, pallor, hypothermia |
| 1 year | M | by parent | somnolence, pallor |
| 1.2 years | M | by parent | somnolence |
| 1.8 years | F | by parent | somnolence, hypothermia, sweating |
| 2.5 years | F | swallowed | somnolence |
| 2.5 years | F | by parent | somnolence, bradycardia, sweating |
| 2.8 years | M | swallowed | somnolence, pallor, hypothermia |
| 4.5 years | F | by parent | somnolence |
| 5.8 years | M | self-applied | somnolence, pallor, hypothermia, bradycardia |

symptomatic treatment or other supportive measures (control is sufficient). The following may be suggested as causing naphazoline nasal drops intoxication:

- It is extremely difficult to administer drops to children (children resist administration of drops; they do not follow definite rules; so, the effects are rather poor).
- Packing inadequate for proper dosage - administration of a proper dose is much easier if a bottle with a dropper is used. A bottle equipped with a plastic extension (widely used in recent years) is not suitable for administration to children and proper dosage is very difficult. Nasal sprays may be preferable to drops because of the lesser risk of swallowing the drug and resultant systemic absorption.
- Age is the most important factor in naphazoline drops intoxication. All the children were younger than six years of age (Table).

We may conclude that naphazoline drops should not be administered to children younger than six years. This should find mention in the pharmacotherapeutic literature (9, 10) and application in medical practice. The pharmaceutical industry should also take account of this recommendation and accordingly supplement the directions for using the drug. Certain characteristics of a child's age should be taken into account too. This age requires a specific design of drug containers for proper therapeutic dosage.

## REFERENCES

1. *Grana E, Barbieri A, Zonta F.* Effects of cromakalin (BRL 34915) on mechanical responses of rat vas deferens to noradrenaline and naphazoline. Eur J Pharmacol 1991;192:79-84.
2. *Diaz-Toledo A, Marti MC.* Relationship between alpha adrenoceptor occupancy and contractile response in rat vas deferens. Experimental and theoretical analysis. Eur J Pharmacol 1988;156:315-24.
3. *Hiramoto T, Kushida H, Endoh M.* Further characterization of the myocardial alpha adrenoceptor mediating positive inotropic effect in the rabbit myocardium. Eur J Pharmacol 1988;152: 301-10.
4. *Wade A, ed.* Martindale the Extra Pharmacopoiea. 29th edition. London: The Pharmaceutical Press, 1989: 1453-70.
5. *Granata AR, Reis DJ.* Hypotension and bradycardia elicted by histamine into the C1 area of the rostral ventrolateral medulla. Eur J Pharmacol 1987;136:157-62.
6. *McEvoy GK, ed.* AHFS Drug Information 92. Bethesda: American Hospital Formulary Service, 1992:1682-4.
7. AMA Division of Drugs. Drug Evaluation. 6th edition. Philadelphia: WB Saunders Co, 1986:369-91.
8. *Van Montfrans GA, Van Steenwijk RP, Vyth A, et al.* Intravenous naphazoline intoxication. Acta Med Scand 1981;209:429-30.
9. *Varagić V, Vrhovac B, eds.* Farmakoterapijski priručnik. 2nd edition. Zagreb: Centar za organizaciju i ekonomiku zdravstva, 1985:580-1.

10. *Kovačić K, ed.* Registar osnovnih podataka farmakoinformatike. 36th edition. Zagreb: Udruženje organizacija zdravstva Hrvatske – Sekcija za ljekarne, 1992:118–9.

*Sažetak*

## INTOKSIKACIJA NAFAZOLIN KAPIMA ZA NOS U DJECE

Nafazolin je simpatomimetik, derivat imidazolina, a primjenjuje se kao 0,05–0,1% otopina za lokalnu dekongestiju sluznice oka i nosa. Predoziran ili slučajno uzet peroralno može uzrokovati depresiju središnjeg živčanog sustava (poremećaje svijesti sve do kome) te hipotermiju, bradikardiju i znojenje. Navedeni učinci nafazolina napose su izraženi u djece. Anglosaksonska farmakoterapija isključuje primjenu nafazolina u djece do šest godina starosti dočim naša farmakoterapijska literatura (a i praksa) dopušta njegovu uporabu već od dojenačke dobi. Na Klinici za dječje bolesti Kantrida Kliničkog bolničkog centra u Rijeci, u razdoblju od 1990. do 1992. godine hospitalizirano je 11-ero djece sa znacima trovanja nafazolin kapima za nos. U sve djece bili su izraženi simptomi poremećaja središnjeg živčanog sustava i to poremećaji svijesti u vidu somnolencije. U neke djece pridruženo je bilo i bljedilo kože, bradikardija, bradipneja i hipotermija. Oporavak je u sve djece uslijedio unutar 24 sata, a učinjenom obradom dobiveni su uredni nalazi. Klinička slika s brzim oporavkom i urednim nalazima uz anamnestički podatak o uzimanju lijeka siguran je putokaz k dijagnozi. Razloga koji su doveli do otrovanja ima više (otežano ukapavanje djeci, neadekvatna ambalaža za ispravno doziranje) no svakako je najistaknutiji faktor uzrast. Sva hospitalizirana djeca bila su naime mlađa od šest godina. Zaključuje se da u ovoj starosnoj skupini nije uputno primjenjivati nafazolin kapi. Farmaceutsku industriju valja upozoriti na neke osobitosti dječje dobi koja postavlja specifične zahtjeve za oblikom i ambalažom ljekovitog pripravka, a domaću farmakoterapijsku literaturu obogatiti ovim spoznajama.

*Ključne riječi:*
djeca, hrvatska farmakopeja, simpatomimetici, štetni učinci, toksični učinci

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