
Communication

Ocular Scopolamine-Induced Psychosis

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Anticholinergic agents such as atropine and scopolamine have long been known to produce central nervous system and systemic symptoms when administered in excessive doses. A psychotic-like reaction characterized by hallucinations, confusion, restlessness, and agitation may be seen. Other signs of anticholinergic toxicity, including tachycardia, flushing, hot dry skin, dry mucous membranes, urinary retention, and constipation, may also be present. While clinicians are generally aware of the dangers of oral anticholinergic agents, the potential toxicity of ophthalmic medications may be overlooked. The following case describes both the psychiatric and systemic manifestations of an overdose of scopolamine hydrobromide 1 percent ophthalmic solution.

Case Report

Mr. A., a 25-year-old married white man, presented to the emergency room with agitation and visual, auditory, and tactile hallucinations (seeing red and blue flashing lights and ghostly human-like images, hearing his name called, and feeling insects crawling on his skin). He made poor eye contact and appeared anxious. Upon questioning, he described feeling hot and flushed and having dry mouth and eyes. The day prior to the development of these symptoms, he had been involved in a fist fight and sustained a blow to his right eye, which produced pain, swelling, and a tear in the lacrimal duct. He was given prescriptions for scopolamine hydrobromide 1 percent ophthalmic solution (1 drop in the right eye four times a day), prednisolone

acetate 1 percent ophthalmic solution (1 drop in the right eye four times a day), erythromycin ophthalmic ointment, and an oral antibiotic. The patient believed that the scopolamine was simply an eye wash solution and placed 2 to 5 drops in both eyes eight to ten times over the next 12 hours "to get the red out." When the psychotic symptoms developed, he was brought to the emergency room by his family and was subsequently admitted to the Medicine Service.

Mr. A. denied recent use of alcohol, marijuana, cocaine, or other illicit drugs. Blood alcohol concentration on admission was 0 mg/dL; urine toxicology screen revealed only nicotine, its metabolites, and caffeine. The assay does not detect scopolamine. All other laboratory data were within normal limits. The only medications the patient was taking were those prescribed for his eye injury. Upon admission the scopolamine was discontinued; prednisolone was continued in the same dose. Haloperidol, 5 mg intramuscularly, was ordered on an as-needed basis; however, the patient did not receive any doses.

The Psychiatry Consultation-Liaison Service was asked to evaluate the psychotic presentation of the patient to rule out an underlying functional disorder. He was seen approximately 24 hours after the scopolamine was discontinued. Mental status examination revealed an alert, oriented, cooperative young man with appropriate mood and affect. His speech was clear, coherent, and relevant; his memory was intact. There was no evidence of an underlying thought disorder, and he was considered to have an organic hallucinosis secondary to scopolamine overdose. Prednisolone was ruled out as the etiological agent, since the psychotic symptoms abated while prednisolone was continued. The blow to his eye was consid-

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NITRO-BID® Ointment (nitroglycerin 2%) BRIEF SUMMARY

INDICATIONS: This drug product has been conditionally approved by the FDA for the prevention and treatment of angina pectoris due to coronary artery disease. The conditional approval reflects a determination that the drug may be marketed while further investigation of its effectiveness is undertaken. A final evaluation of the effectiveness of the product will be announced by the FDA.

CONTRAINDICATIONS: In patients known to be intolerant of the organic nitrate drugs.

WARNINGS: In acute myocardial infarction or congestive heart failure, nitroglycerin ointment should be used under careful clinical and/or hemodynamic monitoring.

PRECAUTIONS: Symptoms of hypotension, particularly when suddenly arising from the recumbent position, are signs of overdosage. When they occur, the dosage should be reduced.

ADVERSE REACTIONS: Transient headaches are the most common side effect, especially at higher dosages. Headaches should be treated with mild analgesics, and nitroglycerin ointment continued. Only with untreatable headaches should the dosage be reduced. Although uncommon, hypotension, an increase in heart rate, faintness, flushing, dizziness, and nausea may occur. These all are attributable to the pharmacologic effects of nitroglycerin on the cardiovascular system, but are symptoms of overdosage. When they occur and persist, the dosage should be reduced. Occasionally, contact dermatitis has been reported with continuous use of topical nitroglycerin. Such incidence may be reduced by changing the site of application or by using topical corticosteroids.

DOSAGE AND ADMINISTRATION: When applying the ointment, place the specially designed Dose Measuring Applicator supplied with the package printed side down and squeeze the necessary amount of ointment from the tube or pouch onto the applicator. Then place the applicator with the ointment side down onto the desired area of skin, usually the chest (although other areas can be used). Spread the ointment over a 6x6-inch (150x150-mm) area in a thin, uniform layer using the applicator. Cover the area with plastic wrap which can be held in place by adhesive tape. The applicator allows the patient to measure the necessary amount of ointment and to spread it without its being absorbed through the fingers while applying it to the skin surface.

The usual therapeutic dose is 2 inches (50 mm) applied every eight hours, although some patients may require as much as 4 to 5 inches (100 to 125 mm) and/or application every four hours.

TUBE: Start at ½ inch (12.5 mm) every eight hours and increase the dose by ½ inch (12.5 mm) with each successive application to achieve the desired clinical effects. The optimal dosage should be selected based upon the clinical response, side effects, and the effects of therapy upon blood pressure. The greatest attainable decrease in resting blood pressure which is not associated with clinical symptoms of hypotension, especially during orthostasis, indicates the optimal dosage. To decrease adverse reactions, the dose and frequency of application should be tailored to the individual patient's needs.

Keep the tube tightly closed and store at room temperature 59° to 86°F (15° to 30°C).


FOIL POUCH: The 1-gram foil pouch is approximately equivalent to one inch as squeezed from a tube and is designed to be used in increments of one inch. Apply the ointment by squeezing the contents of the pouch onto a specially designed Dose Measuring Applicator supplied with the package printed side down.

PATIENT INSTRUCTIONS FOR APPLICATION: Information furnished with Dose Measuring Applicators.

HOW SUPPLIED: NITRO-BID® Ointment is available in 20-gram and 60-gram UNI-Rx® Paks (six tubes per pack); in individual 20-gram, 60-gram, and 100-gram tubes; and in Unit Dose Identification Paks of 100 1-gram foil pouches.

Consult full product disclosure before prescribing.

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SCOPOLAMINE-INDUCED PSYCHOSIS

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ered insufficient to produce head trauma leading to central nervous system symptoms. He was discharged from the hospital after a stay of two and one-half days.

Comment

Few reports of toxic manifestations following ocular administration of scopolamine or atropine have appeared in the literature.¹⁻³ A small amount of the ophthalmic solution may be absorbed directly through the conjunctiva, but these solutions also drain through the tear ducts to the nasal mucosa and then to the gastrointestinal tract; systemic absorption may readily occur by means of this route.⁴ Since 1 drop of a 1 percent solution contains approximately 0.67 mg of active drug (assuming 15 drops per milliliter), this patient received between 10.72 and 33.5 mg of scopolamine over the 12-hour period. The toxic oral dose has been reported to be 5 to 10 mg.⁵ The recommended dose of scopolamine ophthalmic solution is 1 to 2 drops up to three times daily. Psychotic behavior has also resulted from use of the transdermal form of scopolamine, once thought to produce few systemic side effects.⁶ These case studies point out the need to be aware that extraorally administered anticholinergic medications have the same potential to produce serious adverse reactions as oral agents.

Differentiation must be made between an anticholinergic psychosis and a functional disorder such as schizophrenia or mania. In most cases, the acute onset of psychological symptoms, the accompanying physical signs, and the resolution of symptoms over 24 to 48 hours indicate an anticholinergic psychosis. When the diagnosis is in question, however, parenteral physostigmine salicylate can be used as a diagnostic test. Physostigmine, an acetylcholinesterase inhibitor, crosses the blood-brain barrier to counteract both central and peripheral effects of anticholinergic toxicity. The adult dose is 1 to 2 mg administered intramuscularly or by slow intravenous infusion. One half of this dose is used in children or the elderly. A positive response, consisting of slowing of the heart rate, decreased temperature, and improvement in men-

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tal status, indicates anticholinergic excess rather than a functional disorder. If a positive response does not occur within 15 to 20 minutes, the dosage regimen is repeated until a total of 4 mg (2 mg in children and the elderly) has been given, or symptoms of cholinergic toxicity appear. These include bradycardia, diaphoresis, rhinorrhea, salivation, and lacrimation.⁷ Since the effects of parenteral physostigmine last only one to two hours, the drug is more suitable as a diagnostic agent or emergency antidote than as a definitive treatment of an anticholinergic psychosis. The primary focus of treatment is close supervision of the patient, minimal sensory stimulation, and frequent reassurance and reorientation.

This case also illustrates the need for effective patient education for ophthalmic products. Many patients do not understand that prescription products differ from over-the-counter preparations de-

signed for symptomatic relief of red, tired eyes. Instruction provided by either the physician or the pharmacist, stressing the need to comply with the specified dose, may be helpful in preventing adverse reactions of the type described in this report.

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Before prescribing, please consult complete product information, a summary of which follows:

The effectiveness of Valium in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms similar to those with barbiturates and alcohol have been observed with abrupt discontinuation, usually limited to extended use and excessive doses. Infrequently, milder withdrawal symptoms have been reported following abrupt discontinuation of benzodiazepines after continuous use, generally at higher therapeutic levels, for at least several months. After extended therapy, gradually taper dosage. Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines,

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narcotics, barbiturates, MAO inhibitors and other anti-depressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation. The clearance of Valium and certain other benzodiazepines can be delayed in association with Tagamet (cimetidine) administration. The clinical significance of this is unclear.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neu-

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tropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

Dosage: Individualize for maximum beneficial effect.

Adults: Anxiety disorders, symptoms of anxiety, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. **Geriatric or debilitated patients:** 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) **Children:** 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

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