CASE REPORTS

Toxic psychosis with antihistamines reversed by physostigmine

P. J. COWEN
B.Sc., M.B.

Department of Psychological Medicine, King's College Hospital,
Denmark Hill, London SE5 9RS

Summary
A case of toxic psychosis due to antihistamine poisoning is described. The reversal of this state by physostigmine supports the contention that it is caused by an anticholinergic syndrome. The management of antihistamine poisoning is discussed.

Introduction
Toxic psychosis is a recognized complication of antihistamine poisoning (Goodman and Gilman, 1975). It has been suggested that this toxic state might be caused by anticholinergic mechanisms and that treatment with physostigmine could reverse it (Granacher and Baldessarini, 1975). Despite this, physostigmine is not usually recommended in the management of antihistamine poisoning. A case is now reported of antihistamine poisoning which was complicated by marked central symptoms. These symptoms were abolished by physostigmine salicylate.

Case report
A 40-year-old housewife was admitted to the medical ward having taken an unknown number of promethazine tablets. She was deeply unconscious and responded only in a sluggish and inco-ordinated manner to pain. Her pulse was 104 beats/min. Her pupils were dilated and did not react to light. The deep tendon reflexes were present and symmetrical but both plantar responses were extensor. Gastric lavage had been performed in Casualty and 100 mEq of sodium bicarbonate left in the stomach. Routine observations were made and nursing care given.

Six hours after admission her level of consciousness had improved so that she was rousable but increasingly restless and difficult to nurse. Her fluid intake was poor and she was aggressive when approached. This state continued for the next 24 hr during which she received 2 i.m. doses of chlorpromazine 100 mg and 2 i.m. doses of diazepam 10 mg without effect. Psychiatric assessment was requested. Examination showed a restless, agitated woman who was walking unsteadily around the ward pouring water from a jug over patients and furniture. She was confused, disorientated in time and place, and had visual hallucinations.

There was no previous history of psychiatric illness. A diagnosis of a drug-induced toxic confusional state with features of an anticholinergic syndrome was made. She was given i.m. physostigmine salicylate 0.5 mg, and within 15 min was calm and able to orientate herself spatially and temporally. There was no evidence of confusion or visual hallucinations. After 2 hr she again became drowsy, agitated, and confused but remained quiet and did not present a nursing problem. Three hours later she was given another night sedation of one g oral chlorpromazine and slept until the following morning. She was then lucid and orientated with little memory for the confusional episode. Her mental state remained stable and she was subsequently discharged to attend the psychiatric out-patient clinic.

Discussion
The central effects of antihistamines constitute their greatest danger in acute poisoning. The presentation may vary from confusion, hallucinations and convulsions to deepening coma and respiratory arrest. Peripheral effects of poisoning include fixed dilated pupils, tachycardia, flushed skin and pyrexia (Goodman and Gilman, 1975).

In addition to H1-receptor blocking properties, antihistamines also possess peripheral and central anticholinergic effects (Goodman and Gilman, 1975). It is becoming increasingly recognized that drugs whose properties include anticholinergic activity may, in acute poisoning, produce a picture typical of peripheral and central anticholinergic toxicity. Such drugs include the tricyclic antidepressants and phenothiazines as well as more obvious examples such as belladonna alkaloids and anti-Parkinson agents (Granacher and Baldessarini, 1975).

Toxic anticholinergic effects may be reversed by treatment with a suitable anticholinesterase. Physostigmine is most commonly used because in contrast
to neostigmine it passes the blood–brain barrier and
reverses both central and peripheral anticholinergic
blockade (Duvoisin and Katz, 1968). The value of
physostigmine in atropine poisoning is well known,
and more recent reports have described its role in
the treatment of tricyclic antidepressant (Janson,
Watt and Hermos, 1977) and phenothiazine poisoning
(Wang and Marlowe, 1977). It appears that anti-
histamines, too, may produce an anticholinergic
syndrome. Indeed, most if not all of the clinical
features of antihistamine poisoning are attributable
to anticholinergic toxicity. The reversal by physo-
tigmine of the delirium described in the case report
supports this contention. In addition, physostigmine
has been shown to reverse central excitement and
depression following antihistamine premedication
(Lee, Turnedorf and Poppers, 1975).

Antihistamine poisoning in adults is not usually
a life-threatening event, and simple supportive
measures are adequate (Goodman and Gilman,
1975). In children and more severely poisoned adults
central complications are frequent, and it is here that
physostigmine may play a useful role. Features of
the anticholinergic syndrome such as confusion,
coma and convulsions may be expected to respond
(Rumack, 1973) and, in addition, peripheral anti-
cholinergic blockade will be reversed. Because of
the short half-life of physostigmine, demonstrated
by the return of symptoms in the case report, re-
peated doses may be needed. Physostigmine should
be used with caution in patients who have an under-
lying condition such as heart block or asthma which
would contra-indicate excessive cholinergic stimu-
lation (Granacher and Baldessarini, 1975). In these
patients, central excitement is best controlled with
sedatives which lack anticholinergic effects, for
example chlormethiazole or diazepam. Chlorpro-
mazine does possess anticholinergic activity and
should be avoided.

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