Lesson of the Week

Atropine poisoning in early infancy due to Eumydrin drops

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Although atropine poisoning may lead to death a search of Index Medicus from 1960-79 showed only a single case report of atropine methonitrate (Eumydrin) overdose in early infancy.1 After an infant was admitted with severe atropine poisoning due to Eumydrin drops, a review was made of similar cases in infants treated at this hospital.

Patients

Eumydrin is a bottled solution of 0·6%, atropine methonitrate in 90% alcohol. A special glass dropper attached to a rubber teat is provided. Each drop of this solution contains 0·2 mg atropine methonitrate. The case records of the eight children admitted to this hospital with Eumydrin overdosage between 1969 and 1979 were examined.

Case 1—A 6-week-old boy was admitted to hospital having been given three half-full droppers of Eumydrin on two occasions in the preceding 24 hours instead of three drops three times a day. The mother had misread the instructions. The Eumydrin, together with Otrivine nose drops (0·5% w/v xylometazoline hydrochloride) and a preparation of ampicillin and cloxacillin, had been prescribed the previous day by the general practitioner for a cough and cold. On examination the infant appeared extremely ill and was irritable and febrile (rectal temperature 41°C). His skin was flushed, warm, and dry, but his hands and feet were severely cyanosed. His mouth was dry and contained thick, tenacious secretions causing a hoarse cry, inspiratory stridor, appreciable subcostal recession, and tachypnoea (40 per minute). The peripheral pulses were weak and the heart sounds were normal (apex rate greater than 200 per minute). His abdomen was distended but soft, and there were scanty bowel sounds. The corneas were dry and cloudy, and his pupils were widely dilated and unresponsive to light. He was generally hypertonic with normal plantar reflexes but the tendon reflexes were difficult to elicit. Direct laryngoscopy showed thick tenacious secretions down to the level of the vocal cords. Clearing the airway considerably improved his respiration. He was admitted to the intensive care ward and treated with intravenous fluids, oxygen, humidity, and intramuscular phenobarbitone. He made an uneventful recovery and was discharged three days after admission.

Case 2-8—Seven further infants with atropine intoxication due to atropine methonitrate drops presented at this hospital. In one (case 2) the drops were prescribed by a paediatrician and in the remaining six they were prescribed by the general practitioner. In these six cases the mothers had misread the instructions and gave a varying number of full droppers to their infants, four cases having received one dose whereas two cases had received a further dose after an interval. The error was realised immediately in one case and only after the development of signs in five cases.

In these eight infants, all of whom were less than 7 months of age, the reason for prescribing Eumydrin drops was intermittent non-projectile vomiting in four, a cough in two, and “colic” in two.

Depending on how hard and how many times the teat is squeezed, each full dropper contains 10 to 30 drops—that is, 2 to 6 mg atropine methonitrate. For the purpose of estimating the administered dose, a full dropper is considered as 20 drops here. The total dose of atropine methonitrate given varied between 0·8 mg and 16 mg (0·39 mg/kg and 3·55 mg/kg).

Three of the eight infants were admitted to the intensive care ward for observation, and two were severely ill. The major clinical findings are summarised in the table. The duration of stay in hospital was between one and 14 days.

Comment

“Hot as a hare, red as a beet, blind as a bat, dry as a bone, and mad as a wet hen” has been used to describe the appearance of the patient with atropine intoxication. Atropine is well absorbed from the gastrointestinal tract, has a prolonged duration of action, and is almost entirely excreted by the kidneys. It competitively inhibits acetylcholine at the neuroreceptor site, which initially results in stimulation and subsequently in depression of the central nervous system. Peripherally it is a competitive inhibitor of the muscarinic effects of acetylcholine.2 Manifestations of atropine intoxication may include fever, hot dry flushed skin, skin rashes, dilated pupils, blurred vision, increased intraocular pressure, tachycardia, tachypnoea, dry mouth, decreased gastrointestinal peristalsis, hyperactivity, hallucinations, muscular stiffness, convulsions, and coma.

Atropine methonitrate is said to have much less of an effect on the central nervous system than atropine sulphate, and therefore is safer than the latter.3 In this series, however, three infants were very irritable and hypertonic, and one was restless. Therefore atropine methonitrate does have an important effect on the central nervous system (see Addendum). Intoxication due to 0·5%4 and 0·1%5 atropine sulphate and 2% homatropine hydrobromide6 eye drops has been reported. Atropine sulphate intoxication leading to convulsions and coma has been reported.

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Atropine methonitrate is not indicated in whooping cough and has a doubtful place in the management of clinically confirmed congenital hypertrophic pyloric stenosis

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Addendum.

1 Atropine methonitrate has been contained to be ineffective in infantile colic.
2 Definitive reference to be supplied by author.
3 Definitive reference to be supplied by editor.
4 Definitive reference to be supplied by author.
5 Definitive reference to be supplied by editor.
6 Definitive reference to be supplied by editor.
on doses of approximately 0·09 mg/kg, and death has resulted from doses as low as 0·2 mg/kg. In this series the estimated total administered dosage of atropine methonitrate varied between 0·39 mg/kg and 3·55 mg/kg. These dosages are in the lethal range, though tolerance of atropine is variable.

Although three cases were admitted to the intensive care unit for observation, and two were seriously ill, no infant was treated with the specific antidote, physostigmine salicylate, which has been used successfully in the past. Physostigmine is a short-acting, tertiary amine anticholinesterase that readily crosses the blood-brain barrier, unlike the quaternary ammonium compounds such as neostigmine, pyridostigmine, and edrophonium chloride. Intravenous physostigmine (0·5 mg at five-minute intervals to a maximum of 2 mg) should be given slowly under electrocardiographic control. If bradycardia or excessive cholinergic activity results glycopyrrolate, a synthetic ionised quaternary ammonium compound that does not cross the blood-brain barrier, may be given slowly intravenously to block the peripheral muscarinic effects of acetylcholine. Activated charcoal delays the absorption of atropine from the gastrointestinal tract. Supportive treatment should include antipyretic measures and adequate hydration. Atropine is excreted into the urine and adequate bladder drainage of urine may require catheterisation. The control of fits may be achieved with paraldehyde. Other anticonvulsants such as diazepam and phenobarbitone may cause further depression of the central nervous system to compound that already caused by atropine in the severely intoxicated patient.

The treatment of choice for congenital hypertrophic pyloric stenosis is Ramstedt's pyloromyotomy. At this hospital there have been four deaths in 617 surgically treated cases (mortality 0·6%). All four deaths occurred in low birth-weight infants or in infants who were referred late. Suspected cases of pyloric stenosis should be referred to hospital early for definitive diagnosis and surgical treatment. In this series no attempt was made to palpate a pyloric tumour in any of the four cases treated for vomiting before prescribing the drops. No patient was shown subsequently to have pyloric stenosis.

Eumydrin drops are licensed and advertised for the treatment of whooping cough. Two patients in this series received Eumydrin drops for a cough, though neither had whooping cough. After this treatment the patient in case 1 was extremely ill with stridulous respirations owing to retained thick, tenacious pharyngolaryngeal secretions. This latter effect of atropine, resulting from drying of the respiratory tract secretions, suggests that Eumydrin is contraindicated in whooping cough.

The use of the Eumydrin dropper is clearly confusing to some mothers. Together with the indiscriminate prescription of Eumydrin, this has led to eight cases of atropine intoxication, two of whom were dangerously ill. The estimated total administered dosages were within the lethal range. Atropine methonitrate is contraindicated in whooping cough and has a doubtful place in the management of clinically confirmed congenital hypertrophic pyloric stenosis.

### References

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