A CASE OF ACUTE IRON POISONING TREATED WITH DESFERRIOXAMINE B

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Iron, usually in the form of ferrous sulphate tablets, is a very common cause of accidental poisoning in the young child.[1] That this is so, is not surprising. It is frequently prescribed,[9] especially in pregnancy, and often the expectant mother already has a toddler just at the age when sugar-coated tablets are a temptation. Like aspirin it is freely obtainable and there is no law which compels the dispenser to issue any warning. The public and even a large section of the medical profession are apparently unaware of its dangers. In this regard it is significant that

the present case report concerns a doctor's daughter.

A great deal can be done to prevent such accidents through publicity, suitable labels warning the user (as has been done by some manufacturers in the United Kingdom), and possibly by the use of plain preparations without a sugar coating. As little as 3 G of ferrous sulphate can be fatal[2] and the mortality can be as high as 50% in treated cases.[1]

This case is published primarily as a reminder of the danger of iron poisoning in children and also to record the life-saving effect of 'desferrioxamine B' in its treatment. A similar case of acute ferrous gluconate poisoning, successfully treated with desferrioxamine B, has been reported by Henderson *et al.*[10]

Desferrioxamine B

Desferrioxamine B, a specific and powerful iron-binding substance, was developed by CIBA Laboratories in their search for a new antibiotic. It is derived from *Streptomyces pilosus*.

It has been used with much success as a chelating agent mainly in primary and secondary haemochromatosis, but, on the basis of their experimental work with guinea-pigs, Moeschlin and Schnider[3] suggested its possible use in acute iron poisoning.

In acute iron poisoning, the drug should be given orally as well as parenterally. Since it is not absorbed after oral administration, chelation of the iron in the gastro-intestinal tract is rapid, and further absorption and intoxication is reduced or prevented. Given parenterally, it combines with trivalent iron to form ferrioxamine B, a red-coloured compound soluble in water and easily excreted in the urine. Normally, urinary excretion of iron is negligible (0·5 mg. daily) whereas Moeschlin and Schnider found that in haemochromatosis treated with desferrioxamine B an excretion as high as 50 mg. daily could be obtained. Other chelating agents, including calcium disodium versenate (EDTA)[4, 5] and diethylene triamine penta-acetate (DPTA, an analogue of EDTA) have been used, but desferrioxamine B has the advantage of being more specific in its affinity for iron.

CASE REPORT

European female aged 2½ years. The mother was pregnant and had been given ferrous sulphate tablets. On 30 January 1964 at 9 p.m. the child was found asleep with the empty medicine bottle next to her. The bottle had contained 50 tablets (of gr. 3 each).

After being wakened by her alarmed parents, she started vomiting, mainly food and a few remnants of the hard white coating of the tablets, but there were no intact pills. Her condition deteriorated during the next hour and she was brought to hospital. On arrival she was shocked, with cold extremities, dehydrated and semi-comatose, responding poorly to stimulation. Breathing was Kussmaul in type. BP 80/30 mm.Hg. Pulse 140/min.

The stomach was washed out with copious sodium bicarbonate solution. Intravenous rehydration was immediately commenced with half-strength Darrow's solution and 2½% dextrose. Within 20 minutes desferrioxamine therapy was started. This was given as follows: (1) 10 G desferrioxamine by intragastric tube. This immediately altered the stomach contents to an orange-coloured fluid which had the distinct smell of iron rust. (2) 1 G of desferrioxamine was added to a vacolitre of 150 ml. of 5% dextrose in water, and this was given intravenously over 1 hour.

The patient responded rapidly and within an hour she was sitting up and asking for water. Her BP rose to 110/70 mm.Hg and her pulse slowed to 108/min. The other features of her illness are given in diary form and the biochemical details are tabulated.

30 January 1964 (On admission). Clinical examination of systems essentially normal. Hb 15 G/100 ml. blood, WBC 21,600 with a normal smear. Urine examination normal. Electrolytes: Serum Cl 102 mEq./l.; Na 126 mEq./l.; K 4·5 mEq./l.; CO_2 combining power 16·7 m/Eq./l. and blood urea 29 mg./100 ml.

31 January 1964. In the early hours of the morning she passed a loose rusty-coloured stool. She vomited occasionally and small flecks of blood were noticed in the vomitus. Small quantities of milk were given orally. Intravenous fluids were continued as half-strength Darrow's and 2½% of dextrose solution. The urine passed was of an orange-red colour and did not contain haemoglobin, methaemoglobin or red blood cells. When equal quantities of aqueous ammonium sulphide and the patient's urine (not centrifuged) were mixed there was a heavy precipitate of black granules of ferric sulphide.[11] X-ray of the chest was normal, and straight X-ray of the abdomen showed no opaque material in the stomach or bowel. BP maintained at 100/70 mm.Hg, Hb 14G/100 ml. Achromycin 62·5 mg. *b.i.d.* was commenced. Desferrioxamine B given intravenously as in Table I. Later in day, patient was sufficiently alert to pass urine into an iron-free container. Urinary output is recorded in Table II.

TABLE I. ADMINISTRATION OF DESFERRIOXAMINE B

Serum iron	*Normal*	*Admission*	*1st day*	*2nd day*	*3rd day*	*4th day*	*5th day*	*6th day*
Total Fe (μg./100 ml.	60—160		276·0	52·6	16·8	15·7	40·0	53·0
To tal Fe binding capacity (μg./100 ml.	204—429		345·0	313·6	538·0	365·0	389·0	255·0
Saturation %	14—51%		80·0%	16·7%	4·7%	4·3%	10·3%	21·0%
Desferrioxamine B given:							*Total*	
Intragastric—G		10·0					10·0G	
Intravenous—G		1·0	2·0	0·96	0·5		4·46G	

TABLE II. IRON EXCRETION IN URINARY OUTPUT

	1st day	*2nd day*	*3rd day*	*4th day*	*5th day*	*6th day*
Volume urine ml./24 hours. (owing to difficulty in urine collection, this specimen was incomplete)	600	600	600	400	460	300
Fe concentration μg./100 ml.	150·3	180·7	228·6	249·7	172·0	118·4
Fe excretion mg./24 hours ..	9·02	1·0	1·37	1·0	0·95	0·36

1 February 1964. Pyrexial for first time (up to 100·4°F). Patient had productive cough, and crepitations were heard at both lung bases. BP remained at 100/70 mm.Hg. Vomiting was still troublesome, but this difficulty was overcome by giving the patient egg albumin in small doses over an hour. Subsequently oral fluids were well tolerated. Repeat electrocytes showed: Serum Cl 102·0 mEq./l.; Na 129·5 mEq./l.; K 4·3 mEq./l.; CO_2 combining power 17·8 mEq./l. and urea 7·2 mg./100 ml.

2 February 1964. Patient well clinically. Crepitations still present at lung bases. BP 110/70 mm.Hg.

3 February 1964. Once again apyrexial. Minimal crepitations at lung bases. Intravenous fluids were discontinued. Light diet was commenced; mostly fluids. Colour of urine returned to normal.

4 February 1964. Chest clear. Liver function tests were done: Bilirubin—normal; thymol turbidity 2·0 units; thymol flocculation—nil; zinc turbidity 4·1 units; SGOT 20·0 units; alkaline phosphatase 7·2 KA units; inorganic phosphate 7·4 mg./100 ml. blood; cholesterol 165 mg./100 ml. blood; serum proteins: albumin 3·42 G/100 ml.; globulin 1·84 G/100 ml. and blood urea 11·0 mg./100 ml.

Achromycin was stopped on 8 February 1964, and the patient was discharged on this date. Physical examination now was completely normal.

She returned on 23 March 1964 (7 weeks after the ingestion of iron) for a barium meal examination which was reported as completely normal.

COMMENT

In the treatment of acute iron poisoning it is worth while re-emphasizing the value of emergency measures and rehydration.

Serum-iron estimations were not done until 16 hours after therapy was begun, when presumably a large quantity of iron had already been excreted. (The crude side-room test of the urine done with ammonium sulphide, would indicate this.) These figures are thus not a true reflection of the amount of iron absorbed but the initial high figure does show that iron was being mobilized from the tissues and the subsequent fall in serum iron indicates its rapid excretion. This is well supported by the high urinary excretion of iron from 31 January 1964 to 1 February 1964 (9·02 mg. in 24 hours). Much of the ingested iron was also chelated in the gastro-intestinal tract and consequently not absorbed.

There are 3 danger periods following the ingestion of iron. The first follows soon after the pleasure of consuming the sugar-coated tablets, often within 30 minutes. There is excessive vomiting, resulting in dehydration, shock and acidosis,[10] coma and sometimes death. Rarely, haematemesis, melaena, and perforation may occur. Apart from the corrosive action of the drug on the gastro-intestinal tract (one of the old names for ferrous sulphate is 'green vitriol'), the normal blocking mechanism for restricting absorption of iron is not operative. The result is that there is excess circulating iron and this can disrupt cellular metabolism and inactivate enzyme activity.[8]

If the patient survives the initial insult there is usually a period where, except for vomiting, the child appears to be out of danger. This is fallacious. Sudden deterioration with recurrence of circulatory collapse, coma and perhaps death, may occur 20 - 72 hours after the ingestion of a toxic dose. It is for this reason that desferrioxamine B was continued here until the fourth day. This phase of relapse is not well understood. There is probably a release of excess ferritin into the circulation from the reticulo-endothelial system as well as serious liver damage.[4, 5]

Finally, as a result of corrosive action on the gastro-intestinal tract, there may be late effects of fibrosis and scarring and stricture formation[6, 7] resulting in pyloric or oesophageal stenosis. This may occur in 3 - 6 weeks.

SUMMARY

The danger of iron poisoning is referred to and a new iron chelating agent is briefly described. The effect of this drug in the treatment of a child, who had swallowed ferrous sulphate gr. 150, is detailed and the conclusion drawn that it is indeed a valuable addition to the therapy of accidental iron poisoning.

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