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Abstract

A case of hypocholinesterasemia induced by ingestion of trichlorfon is presented. A female patient took 20 gm of this insecticide for the purpose of the suicide. She was brought to the hospital one hour later, and her life was saved by gastric lavage. Cyanosis on lips and nails, pupils with sluggish light reaction and fibrillary muscle twitch were observed upon arrival. Laboratory examination performed on the admission disclosed a serum cholinesterase activity of 0.3deltapH per hour. The enzyme activity was depressed to 0.05 deltapH per hour on the second day of hospitalization. The enzyme activity then increased gradually in the two subsequent weeks and the patient recovered.

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A CASE OF HYPOCHOLINESTERASEMIA INDUCED BY TRICHLORFON

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Abstract: A case of hypocholinesterasemia induced by ingestion of trichlorfon is presented. A female patient took 20 gm of this insecticide for the purpose of the suicide. She was brought to the hospital one hour later, and her life was saved by gastric lavage. Cyanosis on lips and nails, pupils with sluggish light reaction and fibrillary muscle twitch were observed upon arrival. Laboratory examination performed on the admission disclosed a serum cholinesterase activity of 0.3⊿pH per hour. The enzyme activity was depressed to 0.05 ⊿pH per hour on the second day of hospitalization. The enzyme activity then increased gradually in the two subsequent weeks and the patient recovered.

As an insecticide, o,o-dimethyl (2,2,2-trichloro-1-hydroxyethyl) phosphonate (trichlorfon) has attracted considerable interest for housefly control and for potential use as an insecticide in animals infected with endo- and ectoparasitic arthropods (1, 2, 3).

ARTHUR and CASIDA (4) suggested that trichlorfon is a direct inhibitor of acetylcholinesterase in the dog, while METCALF, *et al* (5) presented evidence that the compound *per se* is a poor inhibitor of flies. Dimethyl phosphonate is a major detoxication product in rat treated with trichlorfon, and glucuronide conjugate was found in urine (6). Three hours after oral administration of ^{32}P-labeled trichlorfon to cows, the concentration of blood radioactivity reached to maximum; at 24 hours the labeled trichorfon was not detected. The isotope was excreted in the urine and feces (7). LD_{50} was reported to be 630 mg/kg for oral administration to male white rats. The lethal dose was 200–500 mg/kg, and the maximum tolerated dose was 50–75 mg/kg in dogs (14). Human blood serum degraded this compound very rapidly *in vitro*, and such efficient enzymatic cleavage is considered to be the major factor for its low toxity to humans (4).

CASE HISTORY

On December 8, 1973, at 9 : 00 p.m., a 26-year-old housewife was brought to the emergency unit of Mitoyo General Hospital. On arrival, she looked deranged with tears, complained of chilliness, and vomited reddish gastric juice with alcoholic odor. The information was obtained from her husband. At approximately 8 : 00 p.m. on the same day, she took 20 gm of trichlorfon with 200 ml of red wine for the suicide. Within a few minutes, he found her lying on the floor, and brought her to their family physician. On the way, she vomited several times. At about 8 : 30 p.m., the physician found her lying on a passive supine with cyanosis on her lips. Blood pressure was below 80 mmHg. He brought her to the hospital by ambulance. Shortly after the arrival, gastric lavage was performed with 2,500 ml of saline. Physical examination revealed : body movement, voluntary ; blurred vision, positive ; the speech, slurred ; finger tremor, negative ; nutrition, good ; stature, normal ; cyanosis on the lips and nails, positive ; edema on the face or legs, negative ; pupils, small with sluggish light reaction ; ocular fundus, normal ; oral cavity, reddish in color ; thorax and lung, normal ; abdomen, normal ; knee and ankle jerks, normal ; fibrillary muscle twitch, positive on extremities. Laboratory examination performed on the admission disclosed : red cell count, 4,730,000 per cu mm ; hematocrit, 45 per cent ; hemoglobin, 14.0 gm per cent, white blood cell count, 11,000 per cu mm with normal differentiation ; reticulocyte, 0.9 per cent ; red cell sedimentation rate in the first one hour, 21 mm ; S-GOT, 9 Karmen unit ; S-GPT, 5 Karmen unit ; alkaline phosphatase, 2.8 Bodansky unit, cholinesterase, 0.3ΔpH per hour ; blood sugar, 140 mg per cent ; serum total cholesterol, 110 mg per cent ; blood urea nitrogen, 10 mg per cent ; serum electrolyte : K, 2.6 mEq/L, Na, 136 mEq/L, Ca, 4.4 mEq/L, Cl, 118 mEq/L and urinalysis, negative. Arterial gas analysis showed : pH, 7.35 ; PaO_2, 77.6 mm Hg, $PaCO_2$, 30 2 mm Hg ; HCO_3^-, 16.8 mEq/L ; base excess, −2.0 mEq/L ; $SaCO_2$, 93.8 per cent ; C. CO_2, 17.4 m mole/L. Chest roentgenogram and electrocardiogram were in normal range. Peripheral blood pressure, 130/80 mmHg with pulse rate of 84 beats per minute ; She was given intravenous fluid with 1,500 mg of PAM (2-pyridine aldoxime methiodide) and bicarbonate in the following 24 hours.

Laboratory examination performed on the second day of the admission revealed hemoglobin of 12.4 gm per cent ; hematocrit, 40 per cent ; white blood cell count, 10,300 per cu mm ; platelet count, 103,000 per cu mm ; S-GOT, 19 Karmen unit ; alkaline phosphatase, 2.8 Bodansky units ; cholinesterase, 0.05 ΔpH per hour ; lactic acid dehydrogenase, 285 units. The depressed serum cholinesterase (ChE) activity elevated gradually in the following two weeks. The data obtained were as follows : on December 10, 0.12ΔpH per hour ; on December 12, 0.27Δ pH per hour ; on December 14, 0.30Δ pH per hour ; on December 15, 0.35 ΔpH per hour ; on December 16, 0.36 ΔpH per hour ; on December 18, 0.37 ΔpH per hour and on December 21, 0.47 ΔpH per hour. On the second day of the admission, no toxic symptom could be found in spite of the low ChE activity. A slight microhematuria and proteinuria were observed on the third day of the admission. Finally, she became well and discharged on

December 21.

DISCUSSION

The patient took 20 gm of trichlorfon for the suicide, which was followed moderate toxic clinical symptoms. Serum cholinesterase dropped seriously to the value of 0.30 ⊿pH per hour (normal range: 0.8～1.1 ⊿pH per hour) one hour after the intake, and to 0.05 ⊿pH per hour about twelve hours after the intake, when no toxic clinical symptom could be found. The elevation of the serum ChE activity was found from the third day of the admission (8). The recovery was found of such a slow rate that it took more than thirteen days to return to normal range. Such a slow recovery of the serum ChE activity followed by intake of trichlorfon was reported by AAL, M.A.A., *et al* (9), in whose cases it took about four weeks after the cessation of administration of trichlorfon, for the serum cholinesterase activity to return to preadministration level. In the toxity of other organic phosphate insecticides such as Parathion, Ethion, and EPN, the serum cholinesterase activity was reported to normalize about three to four weeks after the intake (10, 11, 12, 13). After the inhalation of diisopropylfluorophosphate vapor (0.019 to 0.027 mg/L for 6.7 to 10.7 min), the serum cholinesterase activity was reported to return to about 30 per cent of the preinhalation value in four days, to about 50 per cent in eight days, and to about 70 per cent in fifteen days in the man (14).

There reported much toxicological variation among trichlorfon per se, its acetyl derivative and vinyl derivative, and in species susceptibility (4, 5, 6, 16, 17). The vinyl derivative is reported more toxic than the other two, and mammals are less injured than insects, possibly due to phosphonate hydrolysis by serum esterase and elimination of the trichloroportion of the molecule in the urine as trichloroethyl glucuronides. In the man, who can survive the acute phase, with normal function of the liver and kidney, the excretion of trichlorfon is supposed to end up within a few days after the intake. The slow rate of recovery of the serum cholinesterase activity is thought to be due to slow rate of regeneration of cholinesterase in the liver (8, 13, 14).

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