

DATA EVALUATION RECORD

(1) CHEMICAL: Trichlorfon

(2) TYPE OF FORMULATION: Unspecified

(3) CITATION: Totiva, N.N., and Badiugin, I.S. 1970. [Acute chlorofos poisoning.] Kazanskii Med. Zh. 1:37-40 (Translated from Russian)

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(6) TOPIC: Case History

(7) MATERIALS AND METHODS:Patient 1:

- (a) Poisoning Victim: The patient was a man 25 years old.
- (b) Poisoning Incident: He rubbed a concentrated chlorofos solution into the skin of the forearms and trunk five times over a period of 3 days to avoid scabies.
- (c) Amount of Exposure: Unknown
- (d) Route of Exposure: Through the skin
- (e) Symptoms: On the 3rd day of exposure, the patient felt weak. On the 4th day, he was hospitalized in a pre-comatose state. He had attacks of dyspnea, vomiting, diarrhea, elevated blood pressure, bradycardia, and dilation of the pupils. On the 6th day, he was responding; he was conscious and entered into conversation. The pupils were normal. The face and upper portion of the body were hyperemic. Muscles of the upper abdomen were fibrillating. He was asthmatic. Pulse was 48 and blood pressure was 220/110. His liver bulged from beneath the right lower rib by 2 cm and was painful upon palpation.
- (f) Emergency Treatment: Atropine was administered for 3 days (0.1% solution, 1 ml twice a day) plus cardiovascular substance (unspecified) and oxygen inhalation.
- (g) Continued Treatment: The recommended therapy was atropine each half hour, 1-2 ml of 0.1% solution, pachy-carpine, 5.0 units 3% solution until nicotinic symptoms

disappeared, 10% dipyrroxime (TMB-4) solution, 5.0 ml intravenously twice a day, and oxygen therapy.

(h) Result: Treatment proved ineffective. The patient died on the 7th day.

Patient 2:

- (a) Poisoning Victim: The patient was 30 years old.
- (b) Poisoning Incident: Unspecified
- (c) Amount of Exposure: Unknown quantity of chlorofos
- (d) Route of Exposure: Oral (ingestion)
- (e) Symptoms: Bronchospastic dyspnea attack, severe headache, dizziness, speech disorders, disorientation, tremor, convulsions, and coma
- (f) Treatment: The symptoms continued after 3 ml of 0.1% atropine. The resident physician considered these phenomena to be signs of atropine overdose. Actually, these were central nervous system effects of chlorofos appearing after blockage of the M-cholinoreactive system.
- (g) Result: Outcome not given

Other Patients:

- (a) Poisoning Victims: A total of 42 patients (19 males and 23 females ranging in age from 14 to 66 years) who had been poisoned were observed by the authors.
- (b) Poisoning Incidents: Three patients had attempted to treat rashes by rubbing chlorofos on the skin; two of them died. Four patients were poisoned as a result

of inhalation of chlorofos during insect control operations in hot, unventilated rooms.

One patient consumed food products stored in a cabinet that had just been treated with chlorofos. Three more drank accidentally from unmarked containers containing chlorofos. Twenty patients drank chlorofos while extremely drunk. Eleven patients were suicide attempts.

(c) Amount of Exposure: The authors thought that mild or moderate poisoning developed after ingestion of a dose of 40 mg/kg and severe poisoning from a dose of 80-700 mg/kg or higher.

(d) Route of Exposure: The majority of the cases (35) of poisoning were oral with 3 dermal and 4 inhalation cases.

(e) Symptoms: The severity of the poisoning was determined not only by the dose of chlorofos, but also by the time before medical assistance arrived. Poisoning was mild in 14 patients, moderately severe in 10, and severe in 18, of whom 5 died.

For mild poisoning, digestive tract disorders of cholinergic type, psychomotor excitation, muscular fibrillation, and elevated blood pressure were typical. Myosis was reported in "a number" (unspecified) of patients.

In moderate poisoning, the symptoms listed above were present, plus respiratory dyspnea. Convulsions, with subsequent immobility and onset of a comatose state,

with clear myosis and moderate hypertension were typical for severe poisoning. The comatose state may develop without convulsions.

The clinical picture was one of excitation of all segments of the cholinergic system, characterizing chlorofos as an anticholinesterase poison. However, a number of symptoms were noted that do not fit cholinergic disorders: fever (28 patients), accelerated erythrocytic sedimentation rates (20), leukocytosis (21), and neutrophilic leukocytosis (26). These noncholinergic phenomena were considered by the authors to be a manifestation of acute dystrophic changes in the parenchymatous organs.

During the initial stage of poisoning, differences that related to the route of exposure were noted in the clinical picture. After oral exposure, gastrointestinal disorders predominated; whereas after inhalation poisoning, ocular symptoms and psychomotor excitation were common.

Among 14 cases of mild poisoning, psychotic disorders were observed in five patients who required psychoneurologic consultations and two patients required transfer to a specialized ward. Difficulties arose in differentiating the causes of psychotic disorders, since patients received large doses of cholinolytics, and poisoning with chlorofos was frequently accompanied by alcohol intoxication. Incorrect recognition of the causes of central nervous system disorders may result in errors in therapeutic tactics.

Arachnoiditis with epileptiform seizures was observed in one patient poisoned by chlorofos.

Toxic hepatitis and enlarged livers were observed in five patients. Of the five patients who died, one had clinical pulmonary edema, which was confirmed by autopsy.

(g) Treatment: The authors formulated the following principles of combined therapy:

1. Remove the chlorofos before it is absorbed.
2. Eliminate it from the body.
3. Neutralize chlorofos that has been absorbed.
4. Reactivate cholinesterase.
5. Eliminate afferent impulsation from cholin-sensitive and pain receptor zones in the internal organs.
6. Treat oxygen starvation.
7. Protect the liver.

Various methods of cleansing the gastrointestinal tract and dialysis should be continued for several days, since chlorofos remains in the circulating blood for up to 5 days and is excreted from the body for 10-15 days. Blood replacement two or three times and forced diuresis should be utilized. Since chlorofos is converted to an even more toxic compound (dimethyl-2,2-dichlorovinylphosphate), in an alkaline or neutral medium, acidifying substances such as an acidified solution of potassium permanganate should be used to treat contaminated skin areas, for gastric lavage, etc. The first gastric lavage should be performed

before atropine-like substances are administered. The use of alkaline solutions may worsen the poisoning.

In order to neutralize the chlorofos and reactivate phosphorylated cholinesterase, intravenous solutions of TMB-4 and purified cholinesterase are recommended.

Elimination of excessive afferent impulsion from the cholin-sensitive and pain receptor zones represents an important link in the chain of combined therapy. The muscarinic syndrome is important in the clinical manifestation of this intoxication. Therefore, atropine should be given every 20-30 minutes until signs of over-atropinization appear (manifest by tachycardia and mydriosis, dryness of the mucosa, etc.). Signs of excitation of peripheral H-sensitive cholinoreceptors can serve as a basis for administration of pachycarpine, hexonium, and other gangliolytics. The use of cholinolytic myorelaxants (tubocurarine, diplacine, and paramion) is permissible only in combination with artificial respiration. Psychomotor excitation is reduced by the usual neuroplegic mixtures; however, effective prevention and elimination of convulsive syndrome is achieved by timely administration of central cholinolytics: spasmolitin, amicil, tropacin, arpenal, etc. It is desirable to administer 1-2 ml of 1% amicil and 20% spasmolitin per injection.

Since pain from spasm of the intestines, bronchi, and coronary arteries plays a definite role in the pathogenesis of poisoning, a novocaine block may be indicated.

The use of magnesium sulfate (25% solution intramuscularly) may be successful in controlling convulsions.

In order to eliminate oxygen starvation following chlorofos poisoning, cholinolytic substances with various action spectra can be used. In severe cases, even when spontaneous respiration is present, long-term artificial respiration (50% oxygen-air mixture) is indicated.

The complex of vitamins K, PP, C, B₁, B₆, and B₁₂, in combination with such lipotropic factors as lipocaine and methionine and a protein-carbohydrate diet will facilitate detoxification of the liver.

(h) Clinical Laboratory Tests: Blood analyses revealed accelerated erythrocytic sedimentation rates (in 20 patients), leukocytosis (21), and neutrophilic leukocytosis (26). Eight patients had a positive Weltmann reaction; five, a decrease in prothrombin; three, an increase in bilirubin in the blood; and seventeen, protein in the urine. Six patients had an increase in the number of erythrocytes and hemoglobin, which are considered results of fluid loss caused by diarrhea and vomiting.

Butyryl cholinesterase activity of 1 ml of blood serum (from a victim of chlorofos poisoning who died) dropped to 0.10 to 0.15 N moles acetylcholine per minute, 1/30 to 1/50 normal.

CORE CLASSIFICATION: Not applicable

MRID:

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- (8) REPORTED RESULTS: A total of 42 patients of chlorofos poisoning were observed by the authors. Poisoning was mild in 14 patients, moderately severe in 10, and severe in 18 of whom 5 died. The symptoms and rationale for treatment were presented.
- (9) TECHNICAL REVIEW TIME: 6.5 hours