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DATA EVALUATION RECORD

TRICHLORFON

Acute and Subchronic Toxicity (and antidotal effects) in Calves

CITATION: Drumev DB, Georgiyev B. 1973. Some investigations relative to the toxicity of trichlorfon (Neguvon) and attempts to treat calves poisoned with it. Nauchn. Tr. Vissh. Vet. Inst. Sofia 23:391-401 [English translation].

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ACCESSION NUMBER: Not available.

MRID NUMBER: Not available.

LABORATORY: Not available.

TEST MATERIAL: Trichlorfon (purity not specified).

PROTOCOL:

1. Trichlorfon (Neguvon, purity not specified) manufactured by Farbenfabriken, Bayer, AG, was the test compound.

2. The experiment was performed on 16 calves of the Bulgarian brown strain which were 2-4 months old (weight not specified).

3. A 10 percent aqueous solution of trichlorfon was administered orally at dosages of 0.007-0.46 ml/kg [equivalent to 1.21 - 79.58 mg/kg]. The calves received single or multiple treatments (see Table 1). The antidotal effects of the following compounds were studied: 2.5 percent oil-lanolin emulsion with atropine sulfate (OLEAS), paverin-atropium (PA), diethazine hydrochloride (DC), benactizine (B), sodium bicarbonate ($NaHCO_3$), and tricalcium phosphate (TCP; see Table 2 for doses and routes of administration).

4. The activity of whole blood, plasma, and erythrocyte acetylcholinesterase and the following blood chemistry parameters were determined at various intervals during treatment: total protein, calcium, magnesium, phosphorus, glucose, SGOT, and SGPT.

RESULTS:

Table 1 presents the results obtained in calves treated with different amounts of trichlorfon following single or repeated administration

TABLE 1. Summary of Results with Trichlorfon Treated Calves

Animal No. and Dosage	Clinical Observations	Whole Blood Cholinesterase Inhibition[a] (percent)	Blood Sugar (percent increase)	Recovery/ Mortality
1–1.21 mg/kg	None	15 after 2 hrs 30 after 24 hrs	–	Recovery by day 5
4–3.46 mg/kg (day 1)	Epigastric distention (+30 min) tachycardia, dyspnea, 175 percent tachypnea, loss of appetite, disturbed coordination-- instability in hind quarters. (Urine positive for sugar).	60 after 1 hr PChE, 50 after 1 hr EChE, 20 after 1 hr	30	
13.84 mg/kg (day 2)	Epigastric distention, mild depression, decrease in appetite, etc. Normal on day 4.	70 after 1 hr 80 on day 3 22 on day 8 Normal on day 10	100 Normal on day 3	
5–55.36 mg/kg (day 1)	Anorexia, dyspnea, groaning, ataxia, etc.	70 after 1 hr PChE 90 after 1 hr EChE 80 after 1 hr 100 on day 4 PChE, EChE--95 on day 4	15 on day 1 90 on day 2 Normal on day 3	
6.92 mg/kg (day 4)	Intoxication	--	--	Death in 1 hr
6–69.2 mg/kg (day 1)	Toxicity signs more severe than animal 5.	PChE, EChE 80–90 on day 1, and 100 on day 2 and 3	200 on day 1	
6.92 mg/kg (day 2)	Intoxication	Normal on day 10	100 on day 2	

TABLE 1. Summary of Results with Trichlorfon Treated Calves (Cont'd.)

Animal No. and Dosage	Clinical Observations	Whole Blood Cholinesterase Inhibition[a] (percent)	Blood Sugar (percent increase)	Recovery/ Mortality
7, 10, 14-79.58 mg/kg (day 1)	Respiratory distress, asphyxia, tense extremities, muscle weakness, disturbed coordination			Death between 40 min--12 hrs
3-6.92 mg/kg/day (for 10 days)	Diarrhea, ataxia, bradycardia, bradypnea, decreased appetite, epigastric distention	PChE, EChE 35 after 1-3 hr; 50-80 on day 2; 100 on days 4-10; 75 after 17 days	20 after 1 hr Normal on day 18	Recovery by day 18

[a]PChE, plasma cholinesterase; EChE erythrocyte cholinesterase.

(10 days). Single treatment at 1.21 mg/kg produced no adverse clinical signs, and slight cholinesterase inhibition. The animal recovered by day 6.

Single dosages of 3.46, 55.36, and 69.2 mg/kg followed later by single doses of 13.84, 6.92, and 6.92 mg/kg, respectively, produced clinical signs of toxicity, severely depressed blood, plasma, and erythrocyte cholinesterase, elevated blood sugar, and miscellaneous other indications of systemic toxicity. Death resulted in only one of the 3 cases. Single dosages of 79.58 mg/kg resulted in death to all 3 calves within 40 minutes to 12 hours.

Daily administration of 6.92 mg/kg/day for 10 days resulted in clinical signs of toxicity, decreased cholinesterase levels, and increased blood sugar values, all returning to normal 8 days following the final administration.

Table 2 presents the results obtained in calves treated with 79.58 mg/kg trichlorfon along with various antidotal treatments. Only one of 7 animals died from treatment with this demonstrated lethal dosage.

CONCLUSIONS:

Trichlorfon at a dosage of 1.21 mg/kg produced no permanent toxic effect, while dosages of 3.46, 55.36, and 69.2 mg/kg produced evidence of systemic toxicity (clinical signs, cholinesterase inhibition, and elevated blood sugar) and a dosage of 79.58 mg/kg was lethal. Repeated administration of 6.92 mg/kg (10 days) produced evidence of systemic toxicity, which was reversed by 8 days after the administration of the last dose.

When antidotal treatment with atropine was administered along with a lethal dosage (79.58 mg/kg) of trichlorfon, the animals recovered.

An indication and characterization of the toxic effect produced by trichlorfon was demonstrated by this study. However, in the opinion of this reviewer, a larger number of animals per group and the use of control animals would be required for a more complete understanding of the compound's effect. With respect to cholinesterase and other biochemical parameters, individual data are essential to provide a clear understanding of the results.

CORE CLASSIFICATION: Supplementary data.

The number of animals used per dose level was small, and the purity of the test materials was not specified, limiting the usefulness of these data.

TABLE 2. Summary of Results with Trichlorfon and Antidote Treated Calves

Animal No. and Dosage	Clinical Observations	Whole blood Cholinesterase inhibition (percent)	Blood Sugar (percent increase)	Recovery/ Mortality
2–79.58 mg/kg (OLEAS–0.2 ml/kg + $NaHCO_3$–0.5 ml/kg + Ca_3PO_4–0.35 ml/kg)	Gastric distention, disturbed coordination, reduced respiratory rate, salivation, tachycardia	65 after 1 hr; PChE 30 after 1 hr; EChE 80 after 1 hr; 100 after 3 hr.	40 after 3 hr	
18– Same as above	Same as above with mild cyanosis	80 after 3 hr; PChE 100 after 3 hr; EChE 60 after 3 hr.	34 after 1 hr Normal after 3 hr	Death after 15 hr
9–79.58 mg/kg (OLEAS–0.3 ml/kg + $NaHCO_3$–0.5 ml/kg + Ca_3PO_4–0.35 ml/kg) (benactizene 200 µg/kg, after 3 hr)	Same as above	Same as No. 2		Normal on day 5
11, 12, 13, 16–79.58 mg/kg (OLEAS–0.3 ml/kg (papaverine–atropine 0.1 ml/kg)	Same as above	30–40 after 1 hr; 80–90 on day 2; Normal on day 14.		Normal on day 6–8