Treatment of Chronic Chlorpyrifos Poisoning in a Limousin Bull

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Introduction

A purebred three-year-old Limousin bull developed diarrhea, anorexia, and weight loss a few days following topical application of chlorpyrifos (Dursban 44) Dow Chemical Co., Midland, Michigan 48640.

Approximately one month following exposure, the bull was referred to the Oklahoma State University, College of Veterinary Medicine Teaching Hospital for evaluation and treatment. The clinical syndrome was very similar to chlorpyrifos poisoning previously described in dairy bulls.[1] Chlorpyrifos [0, 0-dimethyl-0-) 3, 5, 6-trichloro -2-pyridyl) phosphorothioate], (Dursban 44) insecticide is used for the control of lice and horn flies on beef-breed cattle by pouring on the skin at the withers as a one-time seasonal treatment.

History and Examination

The owner stated that the bull was exhibiting anorexia, weight loss, soreness and weakness in hind limbs, and had a chronic green diarrhea of two weeks duration. Physical examination indicated the bull to be in good nutritional condition with a normal rectal temperature and less than 5% dehydration. Heart and respiratory rates were within normal limits. The bull was depressed, lethargic, and had a green watery diarrhea. Rumen motility was very depressed and the rumen was slightly distended with fluid.

Because of the history of exposure to chlorpyrifos, a heparinized blood sample was submitted to the Oklahoma Animal Disease Diagnostic Laboratory for determination of blood cholinesterase activity, as measured by the ΔpH method.[2] The cholinesterase activity was severely depressed.

Treatment

Conventional treatment for organophosphate poisoning was administered on days 1, 2, and 3 following hospitalization *(Table 1)*. Evaluation of blood gas and chemistries

TABLE 1:

Conventional Therapy

Treatment: Day:	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
Protopam HCl (a) 10 mg/kg S.Q.	×	×	×		×	×	×	×		×			×		×	×				×				
Atropine 1 mg/kg S.Q.	×	×	×	×	×	×	×																	
ToxiBan (b) Granules 4# P.O.	×	×	×																					
Charcoal 2# P.O.					×	×	×	×	×	×			×			×				×	×		×	
Blood Transfusion				×																				

Additional Therapy—$Na\ HCO_3$), Alkaline Bath, Procaine Pen. G. I. M.,Phenobarbital, Oxytetracycline, and B-Vit.

(a) Protopam Hydrochloride (Praloidoxine Chlordine, Ayrest Lab., NYC, NY).

(b) ToxiBan Granules and Suspension (Activated Charcoal and Colloidal Kaolin, Vet A Mix: Shenandoah, Iowa).

indicated the bull was slightly alkalotic, hypocalcemic, hypochloremic, hypokalemic, with a slightly elevated SGOT *(Tables II, III, IV).* There was a slight reversal of lymphocyte-to-neutrophil ratio, probably due to stress. The bull gained some weight through water consumption, but there was no clinical improvement as measured by ΔpH, appetite, and fecal consistency *(Graph I).*

TABLE 2:

Blood Chemistry Values

		Pre-Transfusion		Post-Transfusion
	Day:	1	4	7
	Normal:			
Bun (mg/dl)	(3-31)	22	13	18
ca (mg/dl)	(8.6-10.8)	7.7	9.9	9
Cl (meq/l)	(95-106)	90	87	88
Glucose (mg/dl)	(43-81)	78		
Phosphorous (mg/dl)	(3.7-7.2)	7.2	5.5	6.3
Potassius (meg/l)	(3.5-5.3)	2.8	2.8	3.5
Sap (IU/l)	(34-113)	38	34	40
Sodium (meq/l)	(130-144)	148	145	142
SDH (IU/L)	(3.4-10.1)	8	8.1	10
SGOT (IU)	(34-80)	110	118	83
GGT (IU/l)	(20)	11	7	16

TABLE 3.

Blood Gas Analysis
(Venous Samples)

		Pre-Transfusion		Post-Transfusion
	Day:	3	4	7
	Normal:			
pH	(7.42)	7.52	7.44	7.39
PCO_2 mm HG	(39)	57	65	49
PO_2 mm HG	(91)	30	28	30
HCO_3 mmol/l	(25)	47	43	29

TABLE 4:

Blood Hematology Values

Day:	2
WBC (X100)	51
HGB (g/dl)	13.5
PCV	40
Neutrophils	2805
Lymphocytes	2091
Monocytes	153
Eosinophils	51
Total Protein (gm%)	65
Firinogen (mg%)	300

On the fourth day of hospitalization, the bull was treated with whole blood transfusions collected from a cross matched donor cow. Using the figure 64.3 ml of blood per kg of body weight, the bull's total blood volume was calculated to be approximately 45 L. The 450-kg Hereford donor cow was anesthetized with methoxyflurane; the carotid artery was cannulated, and blood collected. Sixteen liters of blood (ΔpH 0.70) were mixed with sodium EDTA, sodium penicillin, cross matched, and transfused by alternately removing 4 L and infusing 4 L intravenously over the next 30 minutes. The bull's pretransfusion was ΔpH was 0.006 pH units/hour. The post-transfusion ΔpH was 0.18 pH units/hour. Conventional treatment *(Table I)* was then continued.

On day 5, two days posttransfusion, appetite and feces began to return to normal. Clinical depression began to lessen *(Graph I).*

On day 7, the bull began to gain weight and appeared clinically normal. Conventional treatment was changed to every third day, and the atropine sulfate was discontinued. Blood values had returned to normal limits.

On the 14th day of hospitalization, although the bull was clinically normal, the ΔpH dropped to 0.13 pH units/hour. The protopam treatment was changed from I.M. to I.V. with no apparent benefit.

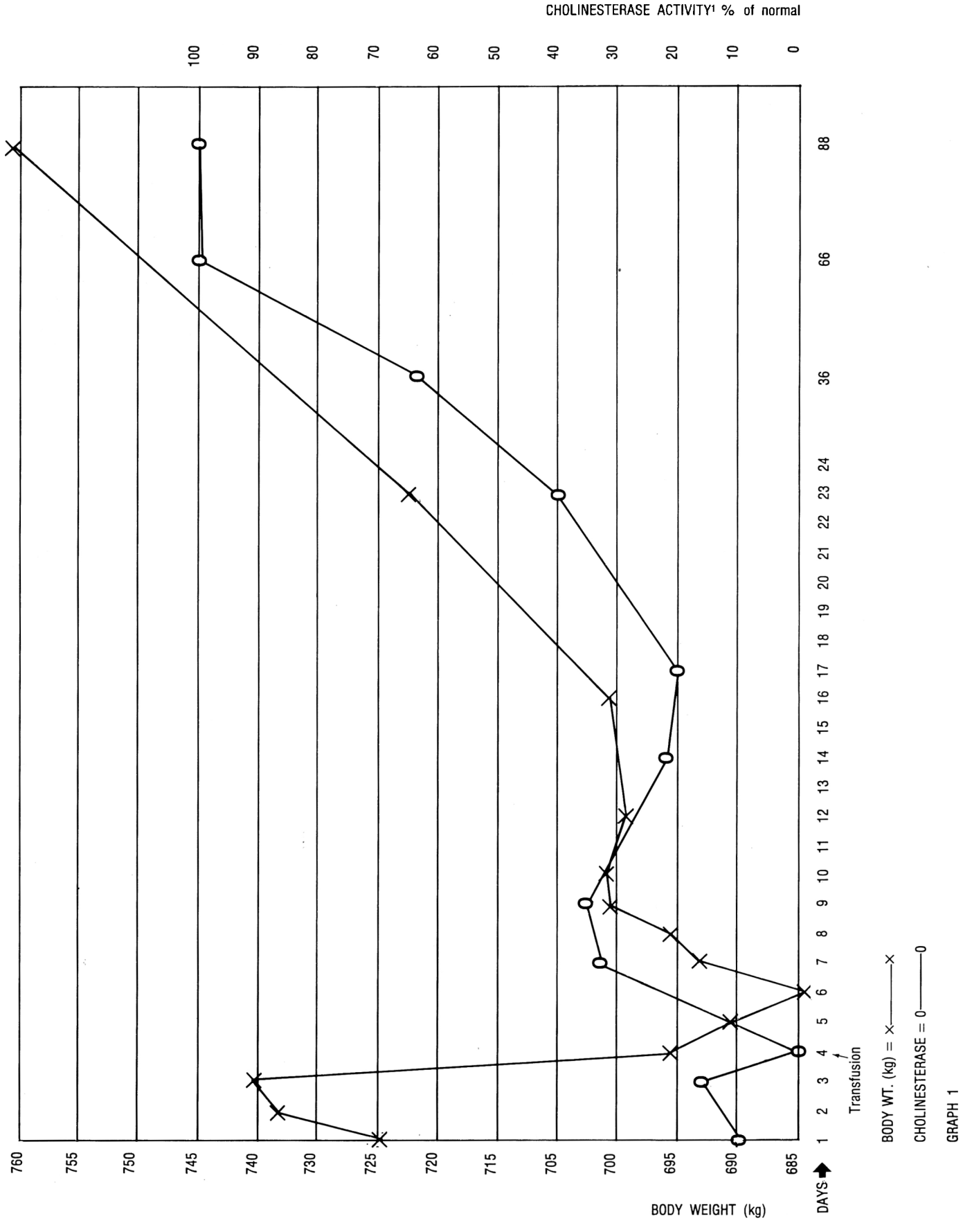
The bull was discharged after 23 days of hospitalization. He had gained 40.4 kg; his appetite and feces were still normal; and the pH was 0.24 units/hour. Blood ΔpH values were 0.38 and 0.65 at two and six weeks following discharge from the hospital.

At 12 weeks post-treatment, the ΔpH was 0.62, and the quality of semen graded as satisfactory using the Breed Soundness Standards of the Society of Theriogenology.

Discussion

While the mechanism of action of chronic chlorpyrifos toxicity has not been totally elucidated, it has been investigated. Chronic chlorpyrifos toxicity may involve metabolites such as the pyridinol and the oxygen analog (diethyl 3, 5, 6-trichloro-2-pyridyl-phosphate). The syndrome may also be related to high testosterone levels in the chlorpyrifos-treated animals.

In classical organophosphate poisoning, the protopam binds to the organophosphate-acetyl cholinesterase complex and cleaves off the organophosphate to form a protopam organophosphate complex which is excreted. After experiencing the lack of response to conventional therapy and following personal communication with other toxicologists who have investigated treatment by conventional methods, we chose to try a blood transfusion.[3,4] In chronic chlorpyrifos toxicity, it is postulated that the bond between the organophosphate metabolite and acetyl cholinesterase becomes "aged" and thus prevent protopam from cleaving off the organophosphate. The rationale for the blood transfusion was to remove the "aged" acetyl



GRAPH 1

cholinesterase-organophosphate complex and relace it with active acetyl cholinesterase that would bind with residual chlorpyrifos or its metabolites. It was postulated that the new blood would aid in the translocation of chlorpyrifos and its metabolites from tissue sites and that any new organophosphate blood acetyl cholinesterase complex would be more responsive to protopam.

Although unrepeated at this time, this case may be significant since it is the only reported recovery from chronic chlorpyrifos poisoning where initial treatment has been delayed.

References

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