Bull. Environ. Contam. Toxicol. (1989) 43:776–778

Bulletin of Environmental Contamination and Toxicology

Effect on *Bubalus bubalis* Thermoregulation by Monocrotophos and Antidotal Therapy

Harpal S. Sandhu and Jitendra K. Malik[1]

Dept. of Pharmacology and Toxicology, College of Veterinary Science, Punjab Agricultural University, Ludhiana 141004, India

Thermoregulation is one of the essential mechanisms of biological survival. Control of body temperature depends on the co-ordinated activities of many organs of the body but overall control of thermoregulation is dependent on the integrity of hypothalamus and functions of certain biogenic amines (Ling et al. 1975). Anticholinesterase agents have shown variable effects on body temperature in different species with human beings showing hypothermia (Willems et al. 1971), mice, guinea pigs and rabbits no hypothermic effects (Meeter and Wolthuis 1968) and rats hyper or hypothermia in different conditions (Meeter 1973). The purpose of the present study was to demonstrate the thermoregulatory effect of monocrotophos [O,O-dimethyl-O-(2-N-methyl carbamoyl-1-methyl vinyl) phosphate] a direct acting organophosphorus insecticide in buffalo calves and to examine the possible effects of some commonly used therapeutic agents on it.

MATERIAL AND METHODS

Eighteen nondescript male buffalo calves (70-130 kg) maintained on standard conditions were divided into Group I and II having 12 and 6 animals, respectively. Group I was subdivided into 3 having 4 animals each which received monocrotophos (Nuvacron^{R} 36% w/w, Hindustan Ciba-Geigy Ltd., Bombay) in single oral doses of 10, 20 and 40 mg/kg body weight, respectively. Group II, subdivided into 2 having 3 animals each, received monocrotophos in single oral dose of 40 mg/kg and subsequently treated by diacetyl monoxime and atropine sulfate, respectively. Diacetyl monoxime was administered at the dose rate of 30 mg/kg by i.v. route as 6% solution in sterile isotonic saline. Atropine sulfate (0.15% in isotonic saline) was given at the dose rate of 0.5 mg/kg by 1/4th i.v. and 3/4th by i.m. routes followed by 0.5 mg/kg by intramuscular route on the reappearance of toxic symptoms. Antidotal therapy was instituted at the onset of Ist toxic symptoms i.e. salivation and lacrimation. Rectal temperature was recorded at predetermined times before and after administration of insecticide and institution of antidotal therapy.The experiment was carried out at an ambient temperature of 25-28^{o}C. Data was analysed statistically by using students t-test and significance assessed at 0.01 and 0.05 levels.

Send reprint requests to Dr. Harpal S. Sandhu at above address.

RESULTS AND DISCUSSION

Monocrotophos administered in single oral doses of 10 mg/kg body weight was not lethal whereas 20 and 40 mg/kg dose levels produced 50 and 100 per cent lethality in buffalo calves, respectively (Sandhu and Malik 1988). All the doses of monocrotophos produced significant ($P \leq 0.01$) fall in body temperature. Hypothermia produced by insecticide intoxication was found to be dose and time dependent. Lomax (1970) and Meeter (1973) suggested that excitation of cholinergic synapses in the pre-optic area of the hypothalamus due to release of acetylcholine from the brain causes hypothermia due to lowering of the set point of the hypothalamic thermostat. Meeter and Wolthuis (1968) found that anticholinesterase agents capable of penetrating into the CNS produced marked fall in the body temperature and also caused collapse of thermoregulatory mechanisms.

In group II, antidotal therapy was instituted to the buffalo calves acutely intoxicated with 100 per cent lethal dose (40 mg/kg) of monocrotophos. Administration of diacetyl monoxime (DAM) and atropine sulfate completely antagonized the hypothermia produced by monocrotophos. However, diacetyl monoxime and atropine failed to protect the animals from the lethality of insecticide intoxication. Table 2 indicates that diacetyl monoxime, a centrally acting cholinesterase enzyme reactivator oxime and atropine sulfate an antimuscarinic agent when given to monocrotophos intoxicated animals even caused rise in body temperature. The reversal of monocrotophos induced hypothermia by diacetyl monoxime and atropine clearly indicates that former is central in origin and acetylcholine has an excitatory role in the warm sensor to heat loss effector pathway. Likewise some cholinomimetic and anticholinesterase agents are reported to cause profound fall in body temperature in the mouse that could be antagonized by administration of atropine (Brimblecombe 1973, Lomax 1970).

Table 1. Effect of single oral administration of monocrotophos on body temperature in buffalo calves

Dose (mg/kg)	Time after administration (h)					
	0	2	4	12	24	168
	Body temperature (^{o}C)					
10	38.3 ±0.2	38.0 ±0.3	37.6 ±0.2	36.9** ±0.2	37.5* ±0.4	38.1 ±0.1
20	37.9 ±0.0	36.6** ±0.2	36.3** ±0.3	35.9** ±0.2	36.4** ±0.3	37.7[a] ±0.0
40	37.7 ±0.1	35.7** ±0.2	35.2** ±0.3	34.1** ±0.4	33.6[b]	

Values given are mean ± SE of the results from 4 animals unless otherwise stated.
a - Value is mean of 2 animals.
b - Value of 1 animal.
* $P \leq 0.05$ ** $P \leq 0.01$

Table 2. Effect of different therapeutic treatments on body temperature of buffalo calves intoxicated with monocrotophos (40 mg/kg, po)

Drug	Time after monocrotophos administration (h)	Time after antidotal therapy (h)				
	0	0	2	4	12	48
	Body temperature (^{o}C)					
DAM[c]	37.8 ±0.1	36.9**e ±0.1	38.4* ±0.1	39.4[a] ±0.0		
Atropine[d]	38.0 ±0.3	37.5[f] ±0.3	38.8 ±0.1	39.0* ±0.1	38.3 ±0.1	38.1[b] ±0.1

Values given are mean ± SE of the results from 3 animals unless otherwise stated.

a - Value is mean of 2 animals.

b - Value of 1 animal.

c - 30 mg/kg by i.v. route.

d - 0.5 mg/kg 1/4th by i.v. and 3/4th by i.m. route and repeated by i.m. route in the dose rate of 0.5 mg/kg at 6-8, 16-18, 24-26 and 32-36 h.

e - 90-100 min after monocrotophos administration.

f - 30-40 min after monocrotophos administration.

* P $\leq$ 0.05 ** P $\leq$ 0.01

REFERENCES

Brimblecombe RW (1973) Effects of cholinomimetic and cholinolytic drugs on body temperature In : Schonbaum E, Lomax P (eds) The pharmacology of thermoregulation. Karger, Basel pp. 182-193.

Ling GM, Hrdina PD, Singhal RL (1975) Chlorinated hydrocarbons as pharmacological tools in studies on thermoregulation In : Lomax P, Schonbaum E, Jacob J (eds) Temperature regulation and drug action. Karger, Basel pp. 257-265.

Lomax P (1970) Drugs and body temperature. Int Rev Neurobiol 12 : 1-43

Meeter E (1973) Cholinergic factors in central thermoregulation In : Schonbaum E, Lomax P (eds) The pharmacology of thermoregulation. Karger, Basel pp. 490-492.

Meeter E, Wolthuis OL (1968) The effect of cholinesterase inhibitors on the body temperature of the rat.European J. Pharmac 4: 18-24

Sandhu HS, Malik JK (1988) Biochemical alterations after single oral dose of monocrotophos in Bubalus bubalis. Bull Environ Contam Toxicol 41 : 337-343

Willems J, Vermeire P, Rolly G (1971) Some observations on severe human poisoning with organophosphate pesticides. Arch Toxikol 28 : 182-191.

Received December 20, 1988; accepted April 22, 1989.