4th Sci. Cong. Proc., April 3-6, 1996
Vet.Med.J.,Giza. Vol.44, No.2.(1996): 507-513.

EFFECT OF XYLAZINE ON SOME ENDOCRINOLOGICAL AND HAEMATOLOGICAL PARAMETERS IN HEIFERS UNDER THERMONEUTRAL OR HEAT STRESS CONDITIONS

ABDALLA, E. B.* and FAYED, A. H.**

* Fac. of Agric., Ain Shams Univ., Shobra El-Kheima, Egypt.
** Fac. of Vet. Med., Alex. Univ., Edfina, Egypt.

SUMMARY

A study was performed to assess the effect of xylazine HCl (0.1 mg/kg of body weight, IV) in heifers maintained at thermoneutral (TN; 18°C, 42% RH) or heat stress (HS;33°C, 63% RH) conditions. Xylazine injection resulted in a sharp increase ($P<0.05$) in serum cortisol levels after 15 minutes in both groups. However, cortisol levels gradually declined and reached basal levels after 45 minutes and 3 hours in heifers maintained under TN and HS conditions, respectively. Xylazine administration increased ($P<0.05$) serum T_3 concentrations after 15 and 30 minutes in the thermoneutral and heat-stressed animals, respectively. Serum T3, however, gradually decreased and reached basal values after 3 hours in both groups. The xylazine-treated heifers had lower ($P<0.05$) red blood cells, haemoglobin and packed cell volume under TN conditions, while higher ($P<0.05$) values were observed under HS conditions.

All the above parameters were greater ($P< 0.05$) in the thermoneutral animals than in the heat-stressed ones either before or after xylazine administration. It is possible that an undesirable interaction occurred between xylazine and the hot environment, thus it is suggested that xylazine should be used cautiously in hyperthermic animals.

INTRODUCTION

Xylazine Hydrochloride is widely used in veterinary practice either alone or in combination with other agents for its potent sedative and analgesic effects (Moye et al., 1973; Yates, 1973). Xylazine produced hypoinsulinemia and hyperglycemia in cattle (Symonds and Mallinson, 1978; Eichner et al., 1979; Hsu and Hummel, 1981). Moreover, xylazine administration increased cortisol level in white-tailed deer, but did not affect T_3, T_4, parathormone and calcitonin levels (Chao et al., 1984). Transient haematological changes following xylazine administration have been reported in beef cattle (Eichner et al., 1979) and buffaloes (Nouh et al., 1990). Raised environmental temperatures are known to depress the secretion of cortisol and T_3 (Prapa et al., 1987; Katti et al., 1991) and produce changes in some blood parameters (Mehrotra et al., 1954).

However, the effects of xylazine in animals exposed to high environmental temperatures have not been studied. Therefore, the present study was designed to investigate the effect of xylazine on serum cortisol and T_3 levels in heifers maintained under heat stress condition and comparison with those in a normal environment. The effect of xylazine administration on some haematological parameters was also investigated.

MATERIALS AND METHODS

Animals:

Twelve healthy Holstein heifers weighing 350 to 400 kg were used in this study. The animals were divided into 2 groups of 6. The first group was maintained in a temperature-and humidity-controlled environmental chamber under a thermoneutral condition (TN group; 18°C, 42 % RH), while heifers in the second group were maintained under a heat stress environment (HS group; 33°C, 63%RH). Water and food were provided ad libitum. After 5 days of exposure to the environmental conditions, all heifers were fasted overnight before xylazine injection.

Drug anad Blood Sampling:

On the day of the study, 3 basal blood samples were collected by jugular venepuncture at - 30, - 15, and 0 minutes (0 minute = time of xylazine administration, i. e., sampling is immediately followed by xylazine administration). Xylazine (Rompun, Miles Laboratories Inc., Shawnee, KN) at a dose of 0.1 mg/kg of body weight (Takase et al., 1986) was administered intravenously (IV), and subsequent blood samples were obtained at 15, 30, 45 and 60 minutes and then at 2, 3, 4, 5, 6, 12 and 24 hours after xylazine administration. Blood samples were allowed to clot, and serum was separated and stored at - 20°C for subsequent cortisol and T_3 determinations by a solid-phase radioimmunoassay kits (Diagnostic Products, Los Angeles, California). All samples were analyzed in duplicates. Additional blood samples were collected into EDTA tubes for immediate determination of red blood cell (RBC) count, haemoglobin (Hb) and packed cell volume (PCV) using a coulter counter. Data were statistically analyzed by unpaired Student "t" test to compare between means of the two groups and paired "t" test to compare among means of the same group (Snedecor and Cochran, 1980).

RESULTS

Mean serum cortisol and T_3 concentrations before and after xylazine administration in the TN and HS heifers are shown in Tables 1 and 2. A sharp increase ($P< 0.05$) in serum cortisol levels was detected in both groups 15 minutes after IV xylazine injection. However, cortisol level increased 3-5 fold as compared with the pre-injection level in the HS group. The cortisol level gradually declined and reached the basal concentration after 45 minutes and 3 hours in the TN and HS heifers, respectively.

Serum T_3 increased ($P< 0.05$) in heifers under TN environment and HS condition following IV xylazine administration. The serum T_3 concentration peaked at 45 minutes post-injection (1.62 ng/ml and 1.30 ng/ml in the TN and HS groups, respectively)followed by a gradual decrease until it reached the basal concentration after 3 hours. Generally, the magnitude of hypersecretion of T_3 in response to xylazine injection was higher in the HS group (123%; $P< 0.05$) than in the TN group (110%; $P< 0.05$) as compared with the corresponding basal level in each group. The hyperthermic heifers had lower ($P< 0.05$) cortisol and T_3 concentrations than the TN ones either pre-or post-injection of xylazine. Moreover, xylazine administration appeared to induce a transient decrease ($P< 0.05$) in RBC, Hb and PCV (an hour after administration) in the heifers under TN environment, while an increase in these parameters (6 hours following administration) was observed in the heifers under HS condition (Fig. 1).

Table (1): *Mean values (± SEM) of serum cortisol concentration (ng/ml) before and after xylazine administration to heifers under the thermoneutral (TN) or heat stress (HS) conditions.*

Time	Condition	
	TN (n = 6)	HS (n = 6)
-30 min	17.79±3.17	3.65±0.64+
-15 min	25.75±5.98	4.42±0.93+
0	28.68±4.44	5.02±1.14+
15 min	42.62±4.82*	23.74±4.60*,+
30 min	32.99±5.48*	25.77±4.52*
45 min	27.06±5.07	20.15±3.91*
60 min	21.28±2.86	15.87±3.17*
2 hr	19.51±7.41	12.35±3.47*
3 hr	11.69±2.05	8.42±2.87
4 hr	17.31±4.43	6.10±1.17
5 hr	21.22±4.29	5.59±0.74+
6 hr	24.57±8.09	4.70±0.38+
12 hr	20.91±3.83	6.49±1.60+
24 hr	19.35±4.89	3.56±0.69+

* Siginificant at $P < 0.05$ compared with the basal concentrations mean within the same condition.

\+ Significant at $P < 0.05$ compared with the TN mean at the same time .

O time = time of xylazine administration .

n = numbers of animals.

Table (2): *Mean values (± SEM) of serum triiodothyronine (T_3) concentration (ng/ml) before and after xylazine administration to heifers under the thermoneutral (TN) or heat stress (HS) conditions.*

Time	Condition	
	TN (n = 6)	HS (n = 6)
-30 min	1.42±0.07	1.05±0.10+
-15 min	1.40±0.07	1.01±0.10+
0	1.44±0.08	1.04±0.11+
15 min	1.54±0.09*	1.14±0.10+
30 min	1.60±0.11*	1.24±0.11*,+
45 min	1.62±0.12*	1.30±0.14*,+
60 min	1.55±0.08*	1.23±0.10*,+
2 hr	1.53±0.09*	1.15±0.10+
3 hr	1.41±0.07	1.01±0.19+
4 hr	1.42±0.06	1.04±0.08+
5 hr	1.53±0.07*	0.95±0.18+
6 hr	1.49±0.08	1.07±0.10+
12 hr	1.37±0.06	1.08±0.11
24 hr	1.27±0.09	1.01±0.09

* *Siginificant at $P < 0.05$ compared with the basal concentrations mean within the same condition.*

\+ *Significant at $P < 0.05$ compared with the TN mean at the same time .*

O time = time of xylazine administration .

n = numbers of animals.

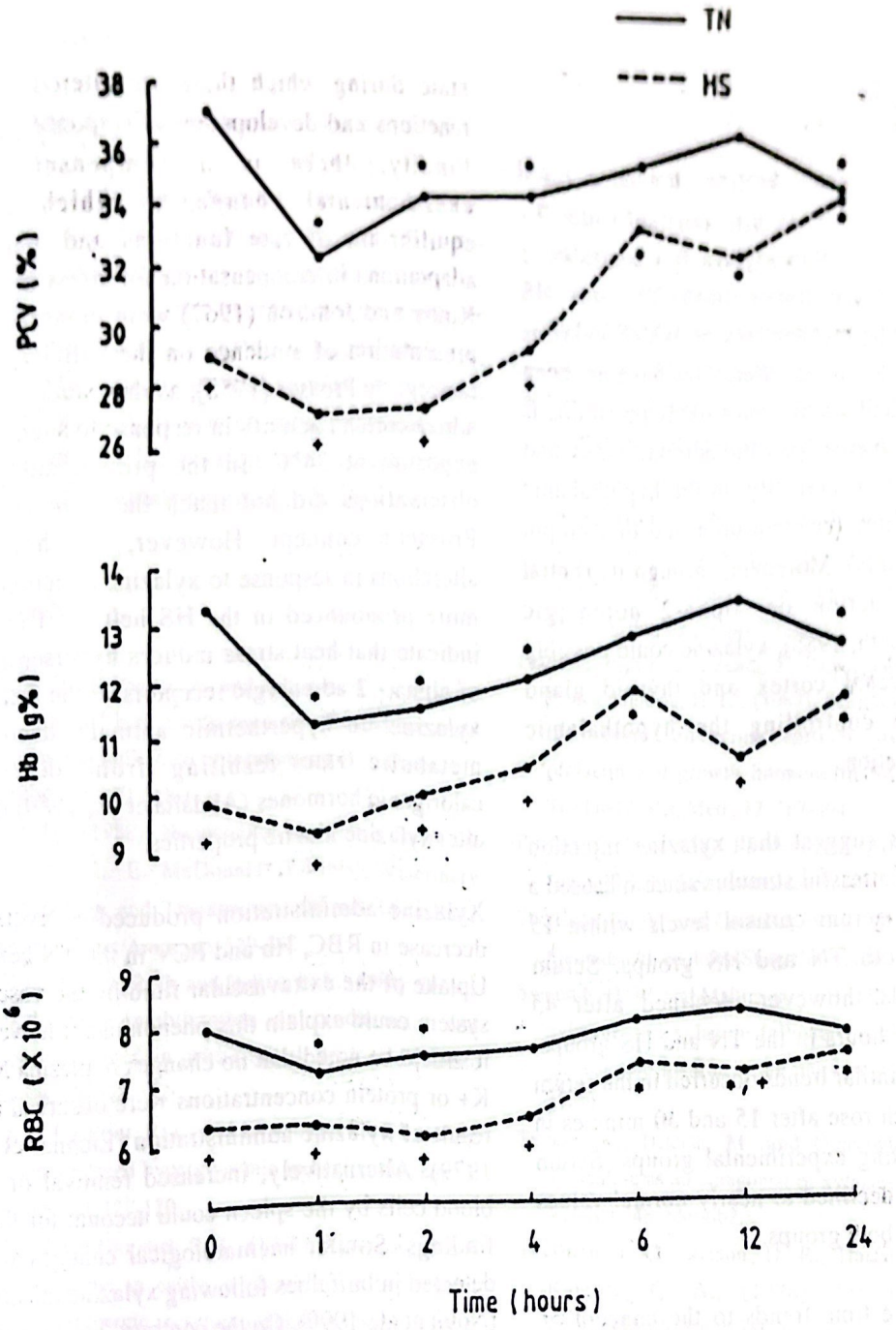

Fig. 1- Mean values for red blood cell (RBC ; $X 10^6$), hemoglobin (Hb ; g %) and packed cell volume (PCV ; %) after xylazine injection in the thermoneutral (TN) and heat-stressed (HS) heifers.

0 time = time of xylazine injection

* $P < 0.05$ from values at 0 time within the same group

+ $P < 0.05$ between the two groups at the same time.

DISCUSSION

The xylazine-treated heifers showed a rapid hypersecretion of serum cortisol and T_3 concentrations, followed in a few hours by a gradual decrease under both TN and HS conditions. The mechanisms by which xylazine induces such hormonal alterations have not been fully established, but the most likely possibility is that it acts directly upon the adrenal cortex and thyroid gland or indirectly on the hypothalamic releasing factors (corticotropin and thyrotropin releasing factors). Moreover, through its central stimulatory action on alpha-2 adrenergic receptors (Booth, 1988), xylazine could possibly regulate adrenal cortex and thyroid gland function by controlling the hypothalamic hormone secretion.

These results suggest that xylazine injection could act as a stressful stimulus since it caused a sharp rise in serum cortisol levels within 15 minutes in both TN and HS groups. Serum cortisol levels, however, declined after 45 minutes and 3 hours in the TN and HS groups, respectively. Similar trends occurred in the serum T_3 levels which rose after 15 and 30 minutes in the corresponding experimental groups. Serum T_3 levels then declined to nearly normal values after 3 hours in both groups.

In relating these time trends to the concept of Prosser (1958) concerning the "nature of physiologic adaptation", the results from this study seem to be in agreement. According to Prosser's concept a sequence of adaptive changes could be an initial shock reaction and overshoot of metabolic rates as a result of sense organ stimulation (such as the neuroendocrine chain reaction in the case of mild heat stress). This immediate response is followed by a stabilized state during which there are altered rates of reactions and development of response patterns. Finally, there is a compensation for environmental change, in which a new equilibrium of rate functions and metabolic adaptations in compensation for stress develops. Kotby and Johnson (1967) were pioneers in the presentation of evidence on the validity of that concept by Prosser (1958), as they studied the rat adrenocortical activity in response to sudden heat exposure at 34°C. In the present study, the observations did not reach the third stage of Prosser's concept. However, the hormonal alterations in response to xylazine injection were more pronounced in the HS heifers. This may indicate that heat stress induces hypersensitivity of alpha - 2 adrenergic receptors to the action of xylazine. In hyperthermic animals, decreased metabolic rate resulting from decreased calorigenic hormones (Abdalla et al., 1989) might alter xylazine kinetic properties.

Xylazine administration produced a reversible decrease in RBC, Hb and PCV in the TN heifers. Uptake of the extravascular fluid by the vascular system could explain this phenomenon; however, it should be noted that no changes in plasma Na+, K+ or protein concentrations were observed as a result of xylazine administration (Eichner et al., 1979). Alternatively, increased removal of red blood cells by the spleen could account for these findings. Similar haematological changes were detected in buffaloes following xylazine injection (Nouh et al., 1990). On the contrary, heifers in the HS group had higher RBC, Hb and PCV following xylazine injection. These observations could be explained by haemoconcentration which migh occur either as a result of shifting body water to interstitial and / or intracellular fluid spaces on the expense of intravascular fluid to help animals to cope with continuous hyperthermia (Kamal et al., 1972) or as a result of greatly increased urinary output (Thurmon et al., 1978).

CONCLUSION

In conclusion, xylazine should not be used in animals when studying the hypothalamic-pituitary-adrenal or - thyroidal axis. Moreover, the present findings indicate that the effect of xylazine is exaggerated in the hyperthermic animals. Therefore, the dose of xylazine should be monitored under such hot climate with continuous and careful observation of treated animals. However, more information is needed to establish the safety and the side effects of xylazine in animals exposed to heat stress.

REFERENCES

Abdalla, E. B., Kotby, E. A. and Johnson, H. D., (1989): Environmental heat effects on metabolic and hormonal functions and milk yield of lactating ewes. J. Dairy Sci., 72 (Suppl. 1): 471 (Abstr.).

Booth, N. H., (1988): Nonnarcotic analgesics. In: N. H. Booth and L. E. McDonald (Editors), Veterinary Pharmacology and Therapeutics, 6th ed, Iowa State University Press/Ames, pp. 329-362.

Chao, C. C., Brown, R. D. and Deftos, L. J., (1984): Effects of xylazine immobilization on biochemical and endocrine values in white-tailed deer. J. Wildlife Diseases, 20: 328-332.

Eichner, R. D., Prior, R. L. and Kvasnicka, W. G., (1979): Xylazine-induced hyperglycemia in beef cattle. Am. J. Vet. Res., 40: 127-129.

Hsu, W. H. and Hummel, S. K., (1981): Xylazine-induced hyperglycemia in cattle: a possible involvement of alpha-2 adrenergic receptors regulating insulin release. Endocrinology, 109: 825-829.

Kamal, T. H., Shehata, O. and Elbanna, I. M., (1972): Effect of heat and water restriction on water metabolism and body fluid compartments in farm animals. Isotope Studies on the Physiology of Domestic Animals. Int. Atomic Energy Agency, Vienna.

Katti, P., Johnson, H. D. and Niwano, Y., (1991): Hormonal profiles of African Pygmy goats exposed to heat environment. Jpn. J. Zootech. Sci., 62: 12-17.

Kotby, S. and Johnson, H. D., (1967): Rat adrenal cortical activity during exposure to a high (34°C) ambient temperature. Life Sci., 6: 1121-1132.

Mehrotra, P. N., Mullick, D. N. and Kehar, N. D., (1954): Seasonal variation in the blood composition of sheep. J. Anim. Sci., 13: 1026 (Abstr.).

Moye, R. J., Pailet, A. and Smith, M. W. Jr., (1973): Clinical use of xylazine in dogs and cats. Vet. Med. Small Anim. Clin., 68: 236-241.

Nouh, S. R., Kassem, M. M., Kenawy, A. A. and Fayed, A. H., (1990): Clinical use of tolazoline as xylazine antagonist in buffaloes. Proc. 4th Sci. Congr. Fac. Vet. Med., Assiut, Egypt, pp. 277-281.

Prapa, L. N., Chanpongsang, S., Pichaichahanag, A., Katti, P. and Johnson, H. D., (1987): Effects of high ambient temperature on serum cortisol, triiodothyronine, prolactin and growth hormone in Swamp buffaloes. Thailand J. Vet. Med., 17: 287-304.

Prosser, C. L., (1958): Physiological Adaptation Symp., Amer. Physiol. Soc., Washington, D. C.

Snedecor, G. W. and Cochran, W. G., (1980): Statistical Methods. 7th ed, Iowa State University Press, Ames, IA.

Symonds, H. W. and Mallinson, C. B., (1978): The effect of xylazine and xylazine followed by insulin on blood glucose and insulin in the dairy cow. Vet. Res., 102: 27-29.

Takase, K., Hikasa, M. and Ogasawara, S., (1986): Tolazoline as an antagonist of xylazine in cattle. Jpn. J. Vet. Sci., 48: 859-862.

Thurmon, J. C., Nelson, D. R., Hartsfield, S. M. and Rumore, C. A., (1978): Effects of xylazine hydrochloride on urine in cattle. Aust. Vet. J., 54: 178-180.

Yates, W. D., (1973): Clinical use of xylazine, a new drug of old problems. Vet. Med. Small Anim. Clin., 68: 483-486.