A Comparison of the effect of Xylazine on Plasma Glucose in Hereford and Friesian Steers

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Summary

Xylazine hydrochloride was administered intravenously to 17 Hereford and 17 Friesian steers on 84 occasions. In all animals plasma glucose concentration rose rapidly during the first half hour following injection. In the Friesian steers, it continued to rise steeply for a further one and a half hours, while in the Hereford steers only a small and statistically not significant further rise occurred during this time. At each sampling time from 1 to 6 hours following the xylazine injection, the glucose levels were found to be significantly different between the two breeds. It is postulated that the differing plasma glucose levels in response to xylazine between the breeds might be due to differences in the number and distribution of α_2-adrenoceptors in the α- and β- cells of the pancreatic islets and in the liver. Plasma insulin concentration was considerably reduced, but no changes in the concentration of blood free fatty acids were observed.

Xylazine hydrochloride (Rompun)** is widely used in domestic and wild animal species for its sedative, analgesic and muscle relaxing properties. It has been shown to produce a state of pronounced hyperglycaemia in cattle.[1-3] and Symods and Mallinson[2] found that the hyperglycaemia arose from a combination of increased hepatic glucose production and reduced plasma insulin concentration. More recently it has been found that the xylazine induced hyperglycaemia is mediated via α_2-adrenoceptors [4-7]. The intravenous dose of xylazine to induce recumbency has previously been shown to be significantly different in Hereford steers as compared with Friesian ones.[8] This paper reports the plasma glucose concentrations after intravenous xylazine administration in these two breeds of steer. In addition a few measurements were made on plasma insulin and free fatty acids (FFA).

Materials and Methods

A total of 34 steers, 17 Herefords and 17 Friesians, were used on 84 occasions for the purpose of obtaining perirenal and subcutaneous fat samples as reported elsewhere.[8] Each animal was used more than once but only after a minimum interval of three and a half months. They were 10 to 24 months of age and their body weight ranged from 209 to 563 kg (395±9.31 kg (mean ± SEM). Xylazine was injected intravenously, the mean dose rate for the Hereford steers being 0.23±0.01 mg/kg (mean ± SEM) and for the Friesian steers 0.27±0.07 mg/kg. The difference between these two means is statistically significant ($P<0.001$) as already reported.[8]

A blood sample was taken from the jugular vein prior to injection of xylazine and subsequently at 10 min, 30 min, 1 hr, 2 hrs, 3 hrs, 4 hrs, 5 hrs, 6 hrs and 24 hrs after the injection. Glucose determinations were made using the test kit by Boehringer (Mencheim) Glucose oxidase-peroxidase - ABTS. In 5 animals (4 Herefords and 1 Friesian) an insulin assay using a "solid-phase radioimmunoassay (Phadebas Test, Pharmacia)" was carried out on the pre-injection blood sample and the samples taken at 10, 30, 60 and 120 min. In addition, on blood samples taken from four animals (3 Herefords and 1 Friesian) before injection and at 10, 30 and 120 min after the xylazine, FFA values were estimated by a colorimetric method, using palmitic acid as standard.[9]

For statistical analysis the t-test for the difference between the means of two samples was used;[10] regression analyses of plasma glucose concentrations at each sampling time against the individual doses of xylazine were carried out for each breed.

Results

The results of plasma glucose determinations are shown in Fig. 1 and Table 1. It can be seen that up to about 30 minutes after the injection of zylazine, the rise of blood glucose was similar for each breed. Subsequently however, the path was quite different for each breed. In Herefords a small insignificant rise occurred from 30 minutes to 3 hours after the injection. In the Friesians on the other hand the glucose continued to rise significantly from 30 minutes

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to 2 hours. At each sampling time from 1 to 6 hours following the zylazine injection, the glucose levels were found to be significantly different betweens the two breeds.

Fig. 1 Plasma glucose concentrations after i.v. xylazine administration in Hereford and Friesian steers (mean ±SEM).
☆ = significant difference (P<0.05) between the glucose levels of the two breeds at the same sampling time (☆☆ = (P<0.001)
★ = significant difference (P<0.001) from the pre-injection value for the same breed.
_____ = Herefords ---- = Friesians

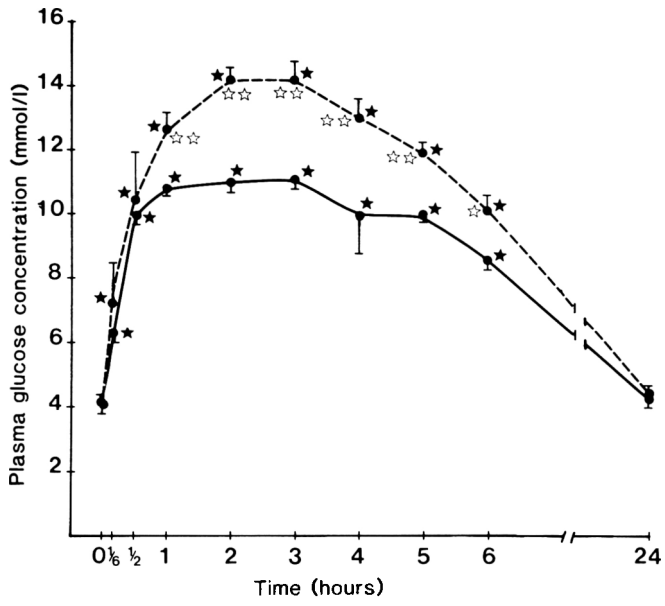


TABLE 1. Plasma glucose concentrations after i.v. xylazine administration in Steers (mmol/l).

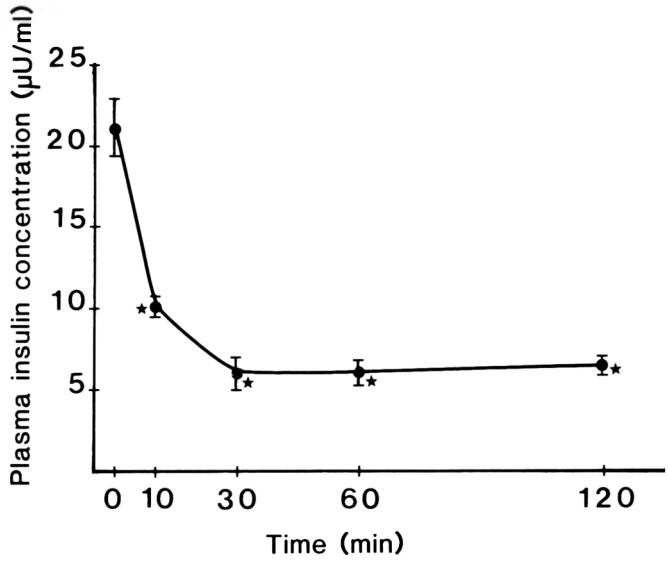
	Herefords		Friesians	
Sampling Time	Mean	SEM	Mean	SEM
0	4.2	0.13	4.1	0.22
10 min	6.3	0.22	7.2	1.27
30 min	10.0	0.25	10.4	1.51
1 hr	10.8	0.21	12.6	0.49
2 hrs	11.0	0.30	14.2	0.37
3 hrs	11.1	0.32	14.2	0.59
4 hrs	9.9	1.13	13.0	0.63
5 hrs	10.0	0.18	11.9	0.35
6 hrs	8.6	0.32	10.1	0.52
24 hrs	4.3	0.23	4.4	0.17

After the third hour, the plasma glucose concentrations began to fall comparably in both breeds, but six hours after xylazine administration they were significantly higher than the pre-injection levels (P<0.001). In both breeds, the levels were found to be normal at 24 hours.

From the results of the regression analysis it was shown that there was no significant relationship between the dose of xylazine and the plasma glucose concentration.

Plasma insulin concentrations were considerably reduced after the injection of xylazine (Fig. 2). From a pre-injection level of 21.2 ± 1.7 μU/ml (mean ± SEM), it was reduced to 10 ± 0.6 μU/ml 10 min after the injection. At the 30, 60 and 120 min sampling times it was 5.8 ± 0.9 μU/ml, 6.0 ± 0.7 μU/ml and 6.5 ± 0.3 μU/ml, respectively.

Fig. 2. Plasma insulin concentration after i.v. xylazine administration in 5 steers (mean ± SEM). Asterisk denotes significant difference from the pre-injection value (P<0.001).



The FFA plasma concentrations did not change following the injection of xylazine. The pre-injection value was 350.5 ± 31.7 μmol/l (mean ± SEM) and after the xylazine injection it was at 10 minutes 336.5 ± 26.8 μmol/l, at 30 minutes 308 ± 57.1 μmol/l and at 120 minutes 338.25 ± 53.73 μmol/l, there being no significant difference between these values.

Discussion

It is difficult to explain the greater rise in blood glucose concentration in the Friesian steers than in the Herefords other than the possibility that it might be related to the higher metabolic rate of Friesian steers compared to the Herefords.[11] In a previous study Friesian steers were fouind to be less sensitive to xylazine than Herefords[8] and so it was thought that the much higher dose of xylazine administered to the Friesians might be responsible for the greater rise of blood glucose in this breed. However, no relationship was found between the varying doses of xylazine and the corresponding glucose concentrations in both breeds.

The blood glucose levels began to fall 3 hours after administration of xylazine and this is consistent with the finding of Eichner et al in beef cattle.[3] In sheep, on the other hand, the blood glucose concentration was found

to start falling after reaching a maximum 30 minutes after the intravenous injection of xylazine.[12] Moreover in thoroughbred horses the hyperglycaemia and hypoinsulinaemia have been reported to be of short duration compared with cattle.[13,14] The rise in blood glucose following xylazine administration has been considered to be due to α_2-adrenoceptor stimulation. The effect of this on the β-cells of the pancreatic islets is to suppress insulin production and then, when this returns towards normal, the blood glucose concentration falls. In the horse the serum insulin was found to start rising between 30 and 60 minutes after injection of xylazine and showed a rebound effect, whereby it rose temporarily to a level significantly higher than normal at 120 minutes.[14] Similar changes in insulin levels have been reported in sheep.[6,12] In Friesian cows, however, Symonds & Mallinson[2] found that the plasma insulin concentration fell to a maximum between 30 and 120 minutes after xylazine administration rising after 4 hours to 2.6 to 4.6 times the pre-injection level. The findings of this study would seem to be in agreement with those of these workers in that insulin production was suppressed for at least 120 minutes.

In addition to the suppression of insulin production hyperglycaemia may be due to α_2-adrenoceptor stimulation of the α-cells of the pancreatic islets[12] releasing glucagon which is known to promote glycogenolysis and gluconeogenesis.[15] Furthermore there may be a direct effect on α_2-adrenoceptors in the liver.[6,16] However, while there was a rise in circulating glucagon after xylazine injection in sheep,[12] no such a rise was found in the cat.[17]

There are known differences in response to xylazine between species of animal possibly due to differences in the location and density of α_2-adrenoceptors as have been reported in vascular smooth muscle[18] and in the kidney.[19] With regard to the former, Angus et al[18] found that noradrenaline had no effect on coronary arteries previously constricted in response to a thromboxane mimetic preparation in cattle, but relaxed similarly constricted arteries in the pig and dog via endothelial α_2-adrenoceptors. The authors conclude that there may be, in addition, α_2-adrenoceptors located in the pancreatic islets and in the liver and that variations in their number and distribution could be responsible for the difference in plasma glucose levels found in this study between the two breeds of cattle.

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