HYPERGLYCAEMIA DURING XYLAZINE — KETAMINE ANAESTHESIA IN GOATS

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SUMMARY

Plasma glucose concentrations were determined in 12 healthy young goats before and after intramuscular administration of either xylazine, ketamine or xylazine-ketamine combination. Doses of 0.22mg xylazine and 11mg ketamine per kilogramme body weight were used. Xylazine-ketamine produced a deeper anaesthesia for a duration longer than that produced by either xylazine or ketamine when used alone. Plasma glucose levels increased significantly above baseline values 15 minutes after administration of either xylazine or xylazine-ketamine combination, with peak values occuring at 60 minutes. The level of increase and peak values in plasma glucose concentration for xylazine alone were lower than those observed for xylazine-ketamine combination, while no appriciable changes were observed for ketamine alone.

INTRODUCTION

Xylazine (2-(2,6-xylidino) 5, 6-dihydro-4H-1,3, thiazine hydrochloride) is a sedative, anaesthetic and muscle relaxant commonly used in large animal restraint. It is an alpha sympathomimetic agent and affects alpha adrenoreceptors which control central neuronal dopamine and norepinephrine storage and/or release (Hsu, 1981; Booth and McDonald, 1982).

Ketamine hydrochloride (2, (O-chlorophenyl) -2-(methyl amino-cyclohexane) is a dissociative anaesthetic agent noted for its analgesic properties and minimal cardiovascular depression (Muir *et al*, 1976). However, when used alone, ketamine gives poor muscle relaxation, muscular hypertonicity and violent recoverv (Waterman 1983).

Xylazine-Ketamine combination is commonly used to induce surgical anaesthesia in animals (Thurmon *et al.*, 1978; Keller and Bauman, 1978; Waterman 1983; Mgasa *et al.*, 1984). The combination has been found to produce better effects of anaesthesia and muscle relaxation than when the drugs are used in isolation. However, hyperglycaemia, hypoinsulinaemia, glycosuria and polyuria have been reported during xylazine-ketamine anaesthesia in cattle and horses (Symonds and Mallison, 1978; Eichner *et al.*, 1979; Tranquilli *et al.*, 1984). The effects of xylazine, ketamine or xylazine-ketamine combination on blood glucose levels in goats is reported here.

MATERIALS AND METHODS

Twelve healthy young local goats (Tanzanian Short horned goats) of mixed sexes (four males and 8 females) weighing an average of 15 kg. were used in this study. Goats were randomly divided into three equal groups. Group A was given xylazine, group B given ketamine and group C given xylazine-ketamine combination. The dosage used was 0.22mg/kg and 11mg/kg body weight of xylazine and ketamine, respectively, intramuscularly. Prior to administration of the drugs, all the goats were kept on full diet in pasture and not fasted.

Blood samples were collected from every goat via an eighteen gauge catheter placed percutaneously in the jugular vein and permenently maintained in place by suture. The catheters were initially flushed with heparin to prevent blood from clotting and clogging the catheter. A 10 ml blood sample for determination of baseline glucose concentration was withdrawn from each goat at 15 minutes before administration of the drugs. Eight other 10 ml samples were withdrawn from each goat at 5, 30, 45, 60, 75, 90, 105 and 120 minutes after administration of the drugs. All blood samples were collected on sodium fluoride and centrifuged for 20 minutes at 2,000 rounds per minute to obtain plasma. Plasma glucose was determined by the enzymatic Colorimetric method § and the data were analyzed using students t-test.

RESULTS

The onset and duration of anashesia following xylazine, ketamine and xylazine-ketamine combination is shown in Table 1. Goats treated with xylazine-ketamine combination (group C) were observed to have complete anaesthesia and muscle relaxation as evidenced by loss of pain reaction to pin

§ Sigma technical bulletin No 510(1983).

prick and absence of resistence to forced flexion and extension. Although goats in Group A were adequately tranquilized and recumbent, there was still some degree of voluntary movements of legs and head with incomplete muscle relaxation shown by some degree of muscular rigidity on flexion and extension. Goats in group B were recumbent with loss of sensation to pain but with no muscle relaxation as shown by persistent muscular rigidity. Tachycardia was also observed in group B and the goats were recumbent for a shorter time. On comparative basis, the degree of anaethesia and muscular relaxation produced by xylazine-ketamine combination was much more complete than that of either xylazine or ketamine alone.

The levels of plasma glucose at defferent time intervals are shown in Figure 1. Plasma glucose in ketamine treated goats (group B) did not change appriciably when compared to the baseline levels. Significant increases ($P < 0.05$) in plasma glucose, above baseline, were observed 15 minutes following administration of xylazine (group A) or xylazine-ketamine combination (group C). Plasma glucose level increased steadily in both groups and reached peak values at 60 minutes post injection time. Comparatively, xylazine-ketamine combination induced a higher increase in plasma glucose than that of xylazine treated goats throughout the sampling time and peak values for xylazine-ketamine combination was also higher than that of xylazine alone ($P < 0.05$).

DISCUSSION

The combination of xylazine-ketamine produced a more complete anaesthesia and muscle relaxation than that of xylazine or ketamine alone. This indicates that xylazine-ketamine combination is a much more potent combination than the individual drugs. These observations are in agreement with the results observed in goats by Keller and Bauman, 1978 and are also similar to results reported from cattle, horses, cats and pigs (Thurmon, 1976; Waterman, 1983; Tranquilli *et al.*, 1984; Trim and Gilroy, 1985).

A prolonged duration of sleep and anaesthesia was obtained with the combination. These prolonged effects have been attributed to the combined effects of the drugs. Waterman (1983) attributed these to be due to the effects of xylazine slowing down both the elimination of ketamine from blood and its metabolism in liver therefore maintaining high levels of ketamine in circulation for a longtime.

Hyperglycaemia following xylazine-ketamine anaesthesia has been observed in cattle and horses (Eichner, 1979; Symonds, 1978; Hsu, 1981; Thurmon *et al.* 1982; Tranquilli *et al.*, 1984). Similarly it has been shown in this study that goats developed hyperglycaemia following xylazine or xylazine-ketamine combination treatment. In horses and cattle a corresponding hypoinsulinaemia has been observed, which is believed to be the cause of hyperglycaemia induced by these drugs.

The sequence of events leading to the elevation of plasma glucose and hypoinsulinaemia have been explained in various ways. Considering that xylazine (an analoque of clonidine), is an alpha 2 and possibly a weak alpha 1 agonist (Hsu and Hummel, 1981). It is possible that the alpha 2 adrenoreceptors in beta cells of the pancreatic islets are blocked (McGrath, 1983) which inhibit insulin secretion (Kato and Nakaki 1983) and therefore causing an elevated blood glucose. It is also possible that xylazine could directly stimulate liver glycogenolysis through the sympathaominmetic action (Hsu and Hummel 1981).

Administration of ketamine alone was not followed by an increase in plasma glucose in all goats in this study. Similarly, Tranquilli et al., (1984) did not observe an enhancement of hyperglycaemia in horses given xylazine-ketamine combination beyond that which was induced by xylazine alone. These observations indicate that ketamine does not induce or enhence gyperglycaemia and that the effects observed are those of xylazine alone. Contrary to these observations, we observed an enhancement of hyperglycaemia in goats given xylazine-ketamine combination beyond that observed in goats given xylazine alone, indicating a possible involvement of ketamine in enhancement of hyperglycaemia.

The likely role played by ketamine in this respect is probably through the release of catecholamines which stimulate glycogenolysis, induce insulin resistance and inhibit insulin secretion (Tepperman, 1974; Wright, 1982; White, 1982). Explanations of ketamine induced increases in catecholamines are somewhat contraversial. It is also possible that, xylazine-ketamine may induce increased catecholamines through interference with enzymes catalysing metabolism of catecholamines, such as methylations of phenolic groups by catechol-o-methyl transferase or oxidation of amine side chains by mono amine oxidase. Alternatively, xylazine

ketamine products may competitively inhibit adrenaline metabolism serving as substrate for catechol-o-methyl transferase, as does pyrogallol, facilitating glycogenolysis through the effects of increased levels of epinephrine.

The results of the present study indicate that the alteration in plasma glucose concentrations induced by xylazine-ketamine combinations in goats may be enhanced by a mechanisms other than the direct or indirect effects of the individual drugs.

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