THE EFFECT OF SOME DRUGS CONTAINING SULFONYLUREA GROUP ON BLOOD GLUCOSE LEVEL OF ANAESTHETISED DOGS

By

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Introduction

The hypoglycaemic activity of sulfonylurea drivatives has been attributed to the presence of sulfonylurea group in these compounds (Bander and Scholz, 1956; Colwell et al., 1956). It is, conceivable that drugs containing this group may have a glucose lowering effect. For this reason, the present study was conducted to find out if Bumetanide, Furosemide and Sulfamethoxydiazine which are commonly used drugs with sulfonylurea groups, have any effect on glucose levels in blood.

Materials and Methods

Drugs

1. Bumetanide (Burinex^{R}); leo Pharmaceutical Products, Denmark. (Ampoules containing 0.5 mg/2 ml).
2. Furosemide (Lasix^{R}); Farbwek, Hoechst, Germany. (Ampoules containing 20.0 mg/2 ml).
3. Sulfamethoxydiazine (Bayrena^{R}); Bayer Leverkusen, Germany. (Bottles containing 20.0 g/100 ml).

Animals

Twenty mongrel dogs of both sexes were used throughout the experiment. They were fed on an ordinary diet and were allowed water **ad libitum.** Their weight was 12.0 $\pm$ 1.4 kg (mean $\pm$ S.E.M.). They were divided into 4 groups of 5 dogs each and were anaesthetised with pentobarbitone sodium at a dose of 30.0 mg/kg body weight.

The first group was used to study the effect of intravenous pentobarbitone anaesthesia on blood glucose levels. The second, third and fourth groups were used for studying the effect of intravenous injection of bumetanide, furosemide and sulfamethoxydiazine on blood glucose level in therapeutic doses of 0.05, 1.0 and 30.0 mg/kg body weight, respectively.

Blood sampling

Blood samples from the femoral vein were taken before drug administration and at 15, 30, 60, 120, and 180 min. after drug administration.

Glucose level in blood was determined by the glucose oxidase method (GOD-Period) as adapted by Werner et al. (1970) using kits supplied by Boehringer Mannheim.

Statistical analysis of the results were evaluated by a student "t" test (Snedecor, 1969).

Results

The effects of the drugs under investigation on blood glucose level are shown in Table I.

Pentobarbitone anaesthesia in dogs resulted in a significant increase in blood glucose level after one hour of induction and continued till the end of the experiment which lasted for 3 hours.

Intravenous injection of bumetanide, furosemide and sulfamethoxydiazine in doses of 0.50, 1.0 and 30.0 mg/kg body weight in anaesthetised dogs respectively significantly decreased blood glucose level after 120, 60 and 15 minutes of drug administration respectively and was maintained up to the end of the experimental period. Sulfamethoxydiazine appeared to be the most potent of the three.

Discussion

In this investigation, pentobarbitone anaesthesia in dogs significantly increased blood glucose level after one hour and up to the end of the experiment.

Such an in crease could be attributed to the increase in the adrenergic tone induced by anaesthesia (Razzad et al., 1976). It is presumable that pentobarbitone-released epinephrine is expected to result in hyperglycemia by inhibiting insulin secretion (Porte et al., 1966; Malaisee et al., 1967) and by stimulating glycogenolysis (Goodman and Gilman, 1975).

Under our experimental conditions the intravenous injection of bumetanide, furosemide and sulfamethoxydiazine in doses of 0.05, 1.0 and 30.0

mg/kg body weight in anaesthetised dogs significantly decreased blood glucose level. Since these three drugs share in common a sulfonylurea group it is reasonable to assume that their hypoglycemic effects are similar to those of sulfonylurea drugs which is mediated by increased rate of secretion of insulin (Goodman and Gilman, 1975). For this reason the presence of responsive islets is considered essential for sulfonylurea drugs. this is supported by clinical studies which demonstrated that the sulfonylureas are ineffective in completely pancreatictomized patients and in juvenile-onset diabetic patients (Goodman and Gilman 1975). However, extrapancreatic effects of sulfonylureas could not be ignored, since a reduction in the hepatic uptake of endogenous insulin has been described (Marshall et al., 1970). Our report is in agreement with others who noted that a number of sulfonylurea compounds exert hypoglycemic activity (Goodman and Gilman, 1975). It is of interest to note that on the third hour, the blood glucose values in the drug-treated groups was higher than pretreatment values, but was significantly lower than the corresponding control value. This may indicate that the hypoglycemic effect exerted by these drugs overode the increased pentobarbitone-induced adrenergic tone.

It might be concluded that the hypoglycemic activity of bumetanide, furosemide and sulfamethoxydiazine is attributed to the presence of sulfonylurea groups and it would be advisable to pay particular attention to their hypoglycemic effect when these drugs are under clinical use.

Summary

The effect of bumetanide, furosemide and sulfamethoxydiazine on blood glucose level in pentobarbitone anaesthetised dogs was studied with time. Pentobarbitone anaesthesia resulted in a significant increase in blood glucose level started at one hour and continued till the end of the 3 hour experimental period.

Intravenous injection of bumetanide, furosemide and sulfamethoxydiazine in doses of 0.05, 1.0 and 30.0 mg/kg body weight in pentobarbitone anaesthetised dogs caused a significant decrease in blood glucose level after 120, 60 and 15 minutes after drug administration respectively. This effect was maintained till the end of the experiment.

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Table 1.

The effect of some drugs containing sulfonyurea group on blood glucose level (mg%) in anaesthetised dogs (5 dogs per group).

Drug	Dose (mg£kg b.wt.)	Before drug administration	Time after injection in minutes				
			15	30	60	120	180
Pentobarbitone sodium (Nembutal)	30.0	81.5 ± 12.4	123.8 ± 31.1	113.0 ± 20.6	207.0 ± 58.5	227.0 ± 64.0	204.0 ± 44.7
Bumetanide (Burinex^{R})	0.05	77.1 ± 10.7	146.2 ± 9.9	123.7 ± 19.9	120.0 ± 9.1	97.7 ± 15.4 *	95.6 ± 11.5 *
Furosemide (Lasix^{R})	1.0	63.6 ± 10.5	89.0 ± 14.8	39.8 ± 14.3	95.4 ± 11.2 *	100.9 ± 15.3 *	102.9 ± 17.7 *
Sulphamethoxydiazine (Bayrena^{R})	30.0	49.6 ± 14.5	51.6 ± 14.3 *	34.4 ± 2.7 ***	41.1 ± 8.4 **	41.1 ± 7.7 **	56.4 ± 10.4 **

Values are means ± S.E.M. and are compared with the corresponding values of the Pentobarbitone treated animals.

* ($P < 0.05$) ** ($P < 0.01$) *** ($P < 0.001$)