MJBU. vol 14, No. 1&2, 1996

EFFECT OF SOLUBLE INSULIN ADMINISTERED RECTALLY IN RABBITS

Sofik V. Vartan and Nabeel AJ. Ali

*Sofik V. Vartan MBChB, MSc Lecturer.
*Nabeel AJ. Ali MBChB, PhD Assist. Prof.

*Department of Pharmacology, College of Medicine, University of Basrah, Iraq.

ABSTRACT

Soluble insulin (10U/Kg) was given rectally to eight rabbits.Blood glucose level was found to be reduced one hour after insulin administration and the maximum reduction occurred after two hours. The blood glucose level started to recover to normal level after three hours.
It is recommended that the rectal route of insulin administration should be further evaluated for its potential use especially in diabetic ketoacidosis and in the maintenance therapy of insulin dependent diabetics.

INTRODUCTION

The current classification of diabetes mellitus identifies a group of patients who have virtually no insulin secretion and whose survival is dependent on administration of exogenous insulin, also called insulin-dependent diabetes mellitus [1]. Furthermore, the use of insulin is mandatory in diabetic ketoacidosis[2]. Insulin has several different effects on carbohydrate metabolism through its action on specific cell membrane receptors. It promotes glucose uptake and utilization in fat and muscle, increases hepatic glycogen formation and inhibits gluconeogenesis[3]. Subcutaneous and intravenous injections are generally regarded as means of controlling hyperglycemia and ketoacidosis respectively[4]. Other routes as intraperitoneal, eye drops[5] and intranasal were used[6]. As rectal route was not tried before up to our knowledge, and because glucagon rectally was

found to be able to significantly raise the blood glucose level in hypoglycemia[7], this encourages us to use such route in our study to see the effect of soluble insulin rectally on blood glucose level.

MATERIALS AND METHODS

Eight male locally bred rabbits, about 1 Kg in weight were used. All rabbits were fasted overnight before and during the experiment. Blood samples (0.1 ml) were taken from marginal ear vein before giving the drug. Soluble insulin (10 U/Kg, Actrapid MC, NOVO INDUSTRIA/S), was given rectally to all animals by injecting the drug through a 3cm tube connected to 1ml syringe introduced to the rectum. Blood samples (0.1 ml) were taken again from marginal ear vein 1h, 2h, 3h and 4h after the drug administration. Blood glucose level was estimated colorimeterically on the same day (8). The results were expressed as mean $\pm$ SEM. Statistical comparisons were made by paired t-test.

RESULTS

Blood glucose level at zero time (before taking the drug) was (95.4 $\pm$ 7 mg/100ml) and this value was considered as a control. The blood glucose level started to be decreased after 1h following insulin administration (61.2 $\pm$ 11) which is statistically significant ($p<0.05$) and maximum significant reduction was after 2h (50.8 $\pm$ 9.6) ($p<0.01$) when compared with control value. The blood glucose level started to recover after 3h (103 $\pm$ 8.4) and 4h (106 $\pm$ 15) following insulin administration (Table 1 and Figure 1).

Soluble insulin (5U/Kg) was injected intravenously to two fasting rabbits results in reduction of blood glucose level to dangerously low levels and death of the two animals.

Table 1. Effect of soluble insulin (10U/Kg) rectally on blood glucose level.

Rabbit No.	Time (hours) 0	1	2	3	4
1	130	125	34	103	106
2	107	61	50	103	106
3	88	62	16	112	80
4	95	12	50	128	80
5	75	66	53	84	151
6	80	66	48	106	106
7	91	64	76	72	90
8	95	95	76	114	133
mean ± SEM	95.4 ± 7.0	61.2 ± 11.0	50.8 ± 9.6	103 ± 8.4	106 ± 15.0

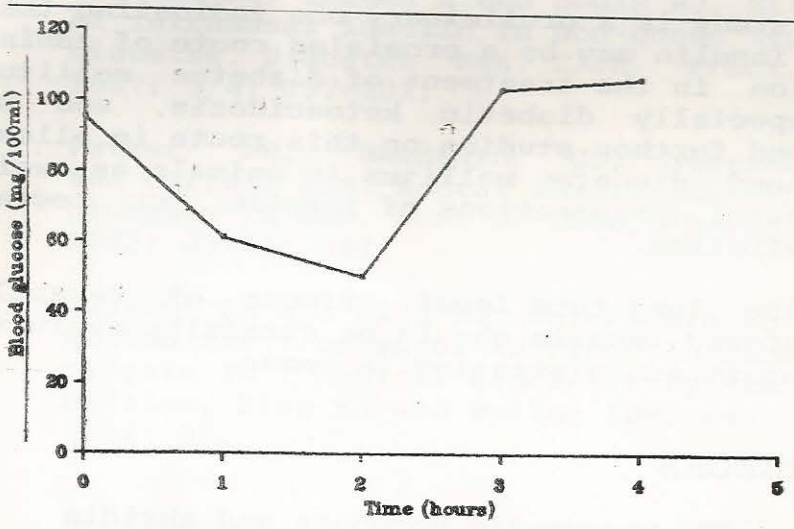

Fig 1. Effect of soluble insulin (10U/Kg) rectally on blood glucose level Data represent mean of 8 rabbits ± SEM.

DISCUSSION

Soluble insulin given rectally to rabbits caused significant and smooth decrease in blood glucose level as compared with i.v. route which we tried in two rabbits causing dramatic decrease in blood glucose beyond the normal level and death of the animals. Following s.c. administration to rabbits, insulin produces its peak effect at 3h after administration[5], while the rectal route in the present study produces the peak effect at 2h. So rectal route may be promising for maintenance treatment in children and in diabetic ketoacidosis as an alternative to i.v. route and as for other potentially useful routes like eye drops and intranasal drops or spray, the long term effects may be deleterious in these sensitive organs especially in the view of the long term effect of insulin on subcutaneous fatty tissue and skin as it causes lipodystrophy frequently[1].

So our study is a preliminary one indicating that rectal insulin may be a promising route of administration in the treatment of diabetes mellitus and especially diabetic ketoacidosis, and we recommend further studies on this route in alloxan-induced diabetes mellitus in animals as well as special preparations of insulin for rectal administration.

Also the long term local effects of rectally administered insulin should be carefully evaluated prior to administration to human.

REFERENCES

1. Karam JH. Pancreatic hormones and antidiabetic drugs. In: Katzung BG, eds. Basic and Clinical Pharmacology, third edition, 1987; 484-496.

2. Stenike J and Soeldner JS. Diabetes melli tus In:Thorn GW, Adams RD, Braunwald E, Isselbacher KJ, Petersdorf RG, eds. Harrison's principles of internal medi cine, eighth edition, 1974; 563-582.

3. Grahame-Smith DG and Aronson JK. Oxford Text book of Clinical Pharmacology and drug therapy, 1988; 440-457.

4. Felig P, Wahren J and Sherwin R. Insulin, glucagon and somatostatin in normal physi ology and diabetes mellitus. Diabetes 1976; 25: 1091-1099.

5. Al-Lami AHH. A comparative study of dif- ferent methods of insulin administration on blood glucose, serum phosphate and potassium in diabetic rabbits. J. Fac. Med. Baghdad, 1990; Vol. No.2: 131-137.

6. Frauman AG, Jerums G and Louis WJ. Effects of intranasal insulin in non-obese type II diabetes. Diabetes Res. Clin. Pract., 1987; 3/4: 197-202.

7. Parker DR, Basdevant GD, Newrick PG and Corrall RJM. Rectal absorption of glucagon in man. Eur. J. Clin. Invest., 1993; 23/S1: A42.

8. Asatoor AM and King EJ. Colorimeteric method for true sugar in blood in microa nalysis In : Medical Biochemistry, third edition, King EJ and Walton IDP, eds, 1954; 25.

تاثير اعطاء الإنسولين الصافي عن طريق الشرج في الارانب

م.م سوفيك وارجان فارتان و م.م نبيل عبد الجليل علي
كلية الطب - جامعة البصرة / فرع الانوية

تم اعطاء الإنسولين (١٠ وحدة / كغم) الى ثمانية أرانب عن طريق الشرج. لوحظ ان مستوى الكلوكوز في الدم قد انخفض بعد ساعة واحدة من اعطاء العقار وقد حدث اقصى انخفاض في مستوى الكلوكوز في الدم بعد مرور ساعتين من اعطاء العقار. بدأ مستوى الكلوكوز في الدم بالرجوع الى قيمته الطبيعية بعد ثلاث ساعات من اعطاء الإنسولين.

لذا يوصى بان استعمال عقار الإنسولين عن طريق الشرج يجب ان يقيم بصورة اوسع خاصة في حالات الحماض الكيتوني السكري ومرضى داء السكري المعتمد على الإنسولين.
