

Effect of Trauma on Serum Insulin Levels in Rabbits

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Received: April 8, 1971, accepted: July 26, 1971

Summary. Serum insulin levels were measured following the infusion of glucose orally, and intraduodenally after exposing the duodenum by surgery. Oral administration of glucose produced a marked rise in insulin levels whereas intraduodenal infusion of glucose in operated animals was not associated with any increase in serum insulin level. Reserpine treatment of animals prior to the operation and the intraduodenal administration of glucose, did not abolish this failure of insulin level to rise following the intraduodenal infusion of glucose. These findings suggest that the failure of serum insulin levels to increase following the intraduodenal infusion of glucose in operated animals was not due solely to enhanced release of catecholamines.

Effet du traumatisme sur les taux d'insuline sérique chez les lapins

Résumé. Les taux d'insuline sérique ont été mesurés après l'infusion de glucose par voie buccale, et intraduodénale après exposition du duodénum chirurgicalement. L'administration orale de glucose produit une augmentation marquée du taux de l'insuline, tandis que l'infusion intraduodénale de glucose chez les animaux opérés n'est associée à aucune élévation du taux de l'insuline sérique. Le traitement à la réserpine chez les animaux avant l'opération et l'administration intraduodénale de glucose n'ont pas aboli l'incapacité du taux de l'insuline à

augmenter après infusion intraduodénale du glucose. Ces résultats suggèrent que le fait que le taux d'insuline sérique n'augmente pas après infusion intraduodénale de glucose chez les animaux opérés n'est pas dû uniquement à une libération accrue de catécholamines.

Die Einwirkung eines Traumas auf den Seruminsulin-Gehalt beim Kaninchen

Zusammenfassung. Der Seruminsulinspiegel wurde im Anschluß an eine orale Glucoseinfusion und an eine intraduodenale Infusion nach chirurgischer Vorverlagerung des Duodenums gemessen. Orale Glucosegabe erzeugte einen deutlichen Anstieg des Insulinspiegels, während intraduodenale Glucoseinfusionen bei den operierten Tieren nicht von einem Anstieg des Seruminsulinspiegels gefolgt war. Reserpinbehandlung der Tiere vor der Operation und der intraduodenalen Glucosegabe verhinderte den mangelnden Anstieg des Insulinspiegels nach der intraduodenalen Glucoseinfusion nicht. Aus dem fehlenden Anstieg des Seruminsulinspiegels nach intraduodena-ler Glucoseinfusion bei den operierten Tieren ist nicht zu schließen, daß dies allein einer erhöhten Freisetzung von Katecholaminen zuzuschreiben ist.

Key-words: Serum insulin levels, oral and intraduodenal glucose, normal and operated animals, reserpine treatment.

It is well recognized that trauma impairs the metabolism of carbohydrates [2]. In several reports, this abnormality has been attributed to the release of epinephrine and ACTH during stress. Porté *et al.* [6] have shown that the intravenous infusion of epinephrine producing serum epinephrine levels equivalent to those noted during stress, inhibited the secretion of insulin. Allison *et al.* [1] have shown that the insulin response to an intravenous glucose load in humans was completely abolished during various stressful conditions. It has been further shown by Schalch [7] in humans that not only the serum insulin levels were maintained at the basal level during stress but serum growth hormone levels were much elevated. He proposed that stress may cause diabetes not only because of the release of epinephrine, which suppressed insulin secretion, but also due to the elevated levels of growth hormone. The exact mechanism of this process, however, remained to be established.

We report data suggesting that the inhibition of insulin secretion during stress is not due solely to the

release of epinephrine but probably a result of various factors.

Experimental Procedures

Healthy rabbits of mixed strain and of both sexes were used. The animals were anaesthetized with an intravenous injection of pentobarbital solution (30 mg/kg), and blood samples were obtained by cardiac punctures at 0, 15, 30, 60 and 120 min time intervals. The animals were treated as follows:

Group I: Physiological saline (0.85%) in volume equal to that of glucose solution, i.e. 3 ml/kg was administered through a stomach tube.

Group II: A 50% solution of glucose was administered by a stomach tube (1.5 g/kg).

Group III: The duodenum of an animal was exposed by a craniocaudal incision along the mid-ventral line. A predetermined dose of glucose (0.4 g/kg) which produced hyperglycaemia equivalent to that observed in group II, was injected into duodenum. The abdominal opening was closed immediately after the injection.

Group IV: Similar to group III but the animal received two intraperitoneal injections of reserpine prior to the experiment. The first injection (2 mg/kg) was given the day before, followed by another (0.2 mg/kg) on the day of the experiment approximately four hours before the onset of experiment.

Methods

Blood glucose concentration was estimated by the glucose oxidase method [4], and serum insulin was assayed by the immunoassay procedure of Soeldner and Slone [8]. The significance of differences between two groups of animals was computed by a Student's *t*-test designed for unpaired, unequal and a small number of observations.

Results

The results are shown in Fig. 1. The fasting level of blood glucose in rabbits was 94 ± 3 mg % (Mean \pm Standard Error of the Mean) and the serum insulin level varied from 4.0 to 25.0 μ Units/ml with a mean value of 11.8 ± 1.2 μ U/ml. In the control group I, there was no significant change in either the blood glucose or the serum insulin level from the basal level. The degree of hyperglycaemia produced in groups II, III and IV by the infusion of glucose was similar, except at 60 min time interval when blood glucose level in group IV was somewhat higher than that in the other groups. Serum insulin level in group II showed a marked increase over the basal level, whereas in group III, there was a slight decrease in serum insulin compared with the fasting level. Pretreatment of animals with reserpine, i.e. group IV, prior to the intraduodenal administration of glucose, did not modify this decrease in serum insulin levels observed in group III.

Discussion

The dose of glucose administered intraduodenally (group III) was adjusted such that it produced hyperglycaemia comparable with that noted following the oral infusion of glucose (group II). Despite the fact that blood glucose levels were similar in both groups II and III, serum insulin levels following oral glucose (group II) were much higher than those observed after the intraduodenal administration in operated animals (group III). These findings demonstrate that trauma abolished the increase in serum insulin level which normally followed glucose loading, and confirm the data of Allison *et al.* [1]. Our findings in terms of serum insulin levels might reflect the inhibition of insulin secretion. The dose of reserpine used in this study, i.e. 2 mg/kg, the day before and 0.2 mg/kg on the day of experiment, was believed adequate to deplete the rabbit tissues essentially of all the stored catecholamines. This inference was based upon the findings of other investigators where 0.1 mg/kg of reserpine given intra-

peritoneally was found to deplete the dog heart of noradrenaline within 12 to 24 h of the injection [9]. Holzbauer and Vogt [3] also showed that 0.4 mg/kg of intraperitoneal administration of reserpine was sufficient to exhaust the cat hypothalamus of noradrenaline. Therefore, the present findings that the inhibition of insulin secretion was similar in both the traumatized animals (group III) and the animals treated with reserpine before trauma (group IV) suggest that the release of epinephrine in stressful situations was not the only factor responsible for the inhibition of insulin secretion noted in the traumatized animals. It would

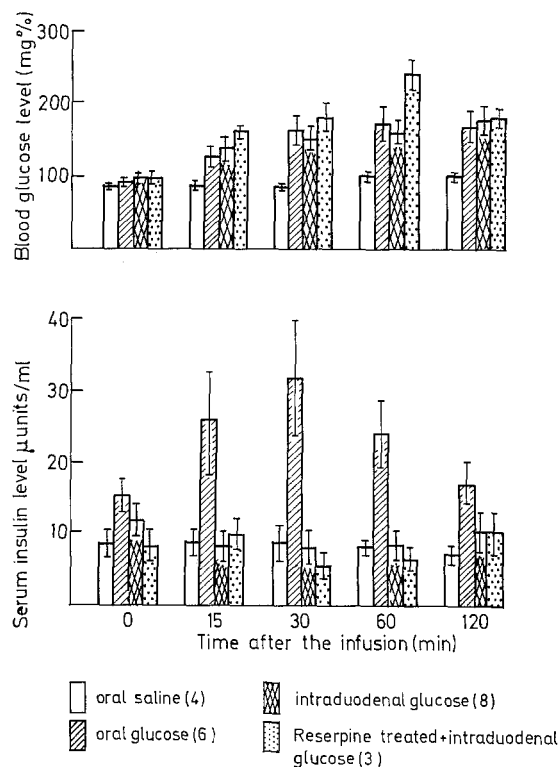


Fig. 1. Changes in blood glucose and serum insulin levels after oral and intraduodenal glucose, and after intraduodenal glucose in reserpine-treated animals. The intraduodenal glucose was given after exposure of the duodenum by surgery. The number in parentheses represents number of experiments. Both blood glucose and serum insulin levels are expressed as Mean \pm Standard Error of Mean

appear that the inhibition of insulin secretion in operated animals was a result of multiple factors. The possibility that epinephrine might still be a factor cannot be excluded completely in view of the findings of Kroeber and Schumann [5]. These authors have shown that although the adrenal medullae of rabbits treated with reserpine (4 mg/kg) were almost completely (depleted) of epinephrine 20 h after the injection, the secretion of epinephrine was reduced to only 50% of the control value. Therefore, the exact mechanism of inhibition of insulin secretion during operative stress remains to be elucidated.

Acknowledgement: The work reported in this communication was a part of a project supported by grants from the Medical Research Council of Canada and The W.A. Murphy Fund of the Winnipeg General Hospital. The authors thank Dr. M.C. Blanchaer for his criticism of the manuscript.

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