Preliminary Communications

Insulin Secretion in Cardiogenic Shock

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Summary: A nearly complete suppression of insulin secretion was observed in four patients in circulatory shock following acute myocardial infarction. This may be due to intense sympathetic activity and raised catecholamine excretion associated with shock.

Introduction

Hyperglycaemia has been described as a frequent feature of the circulatory shock syndrome associated with myocardial infarction (MacKenzie *et al.*, 1964). The raised blood glucose concentration observed has in the past usually been attributed to the glycogenolytic effects of excessive catecholamine activity. Further studies now suggest that a different and possibly therapeutically important mechanism may also be involved. This preliminary report describes the nearly complete suppression of insulin secretion that was observed in patients in cardiogenic shock.

Methods

Patients.—Observations were made on four men aged 65, 62, 64, and 58 years who had suffered an acute myocardial infarction during the preceding 12 hours ; all had developed severe cardiogenic shock before admission to hospital. The systolic pressure in all four patients was below 100 mm. Hg and all presented evidence of severe vasoconstriction. Their skin was pale, cold, and clammy to the touch, and they were oliguric and showed signs of mental confusion. The patients were studied in the coronary care unit during routine resuscitative procedures.

Plan of Investigation.—Initial control venous samples for blood glucose and plasma insulin assay were taken immediately on arrival in the unit. This procedure was followed by the intravenous injection of 1 g. of tolbutamide, and further venous blood samples for glucose and insulin estimation were withdrawn through an indwelling cannula at 1, 2, 5, 10, 15, 30, and 60 minutes.

Laboratory Techniques.—The blood glucose concentration was estimated by an autoanalyser glucose oxidase technique (Morley *et al.*, 1968). At a blood glucose concentration of 106 mg./100 ml. our laboratory coefficient of variation is 4·6%. Immunoreactive insulin was estimated by a modification of the method of Hales and Randle (1963) with the reagents and Oxoid membrane filters supplied by the Radio Chemical Centre at Amersham. The standard deviation of the assay method calculated from the differences between 144 duplicate determinations was ±3·46 over a plasma insulin concentration range of 0 to 49 μU./ml.

Results

The injection of tolbutamide was not associated with the development of any symptoms or signs of hypoglycaemia. In the four patients studied the control blood glucose concentrations ranged from 98 to 138 mg./100 ml. The control plasma insulin concentrations were 12, 21, 18, and 9 μU./ml. The intravenous injection of 1 g. of tolbutamide produced little or no change in either the blood glucose or plasma insulin levels. The values of each are given in the Table.

Blood Glucose and Plasma Insulin Levels After Intravenous Tolbutamide

Case No.	Insulin μU./ml.; Glucose mg./100 ml.	Control	Minutes after Intravenous Tolbutamide						
			1	2	5	10	15	30	60
1	Insulin	12	13		13	25	33	23	29
	Glucose	127	135		118	115	113	102	103
2	Insulin	21	27	36	34	33	40	49	34
	Glucose	113	113	113	105	120	105	116	120
3	Insulin	18	18	20	73	45	40	36	33
	Glucose	138	134	140	133	128	128	123	118
4	Insulin	9	7	25	10	14	17	16	15
	Glucose	98	100	93	100	96	98	95	88

Discussion

These observations suggest that suppression of insulin secretion is an integral part of the shock syndrome occurring after myocardial infarction.

Intravenous tolbutamide is an extremely potent and rapid stimulator of the release of preformed insulin from the beta-cells of the pancreas (Seltzer, 1962). The degree of insulin suppression in the four shocked patients studied is emphasized by the complete or nearly complete absence of any insulin secretion after intravenous injection of the drug. A similar suppression of insulin release by tolbutamide has so far not been observed in patients with uncomplicated myocardial infarction. Allison *et al.* (1967) found a delayed rise in plasma insulin in two non-shocked patients after myocardial infarction, and the same authors found a failure of insulin response to glucose-load in shocked patients after burn injuries (Allison *et al.*, 1968).

The precise mechanisms responsible for this suppression are unknown, but the collated evidence is suggestive. MacKenzie *et al.* (1964) suggested that the intense sympathetic activity and excess catecholamine production associated with the shock syndrome were probably responsible for the hyperglycaemia they often observed in their deeply shocked patients. Increased catecholamine output in cardiogenic shock was subsequently shown (Valori *et al.*, 1967). Nevertheless, in addition to the direct effect of adrenaline in promoting liver glycogenolysis, a further possible mechanism to account for the hyperglycaemia so often observed is suggested by the finding that adrenaline is a potent suppressor of the normal insulin response to a glucose load (Porte *et al.*, 1966). Further investigation of the mechanisms by which insulin release is suppressed is in progress.

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