Acta Dermatovener (Stockholm) 53: 39–44, 1973

RESPONSE OF BLOOD INSULIN AND GROWTH HORMONE TO GLUCOSE INFUSION IN NORMAL, PSORIATIC AND DIABETIC PERSONS

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Abstract. The basal level of blood insulin and growth hormone and their response to intravenous glucose infusion was studied in 10 psoriatics, 3 maturity-onset diabetics and in 5 normal control persons. The controls as well as 8 of the psoriatics showed two different patterns of insulin response with either one initial peak or a double peak. The diabetics as well as two psoriatics of the older age group showed a slow insulin response. Two types of growth hormone response were observed, both in controls and in psoriatics: a slow rise or a rapid initial secretory peak. The diabetics showed typically a rapid and strong initial response. The results indicate that no characteristic psoriatic type of insulin or growth hormone response to glucose infusion supervenes. Psoriatics who show the diabetic type of response fall within the older age group suspectible to maturity-onset diabetes.

The increased level of carbohydrates in the normal skin of psoriatic patients as well as in the psoriatic lesions is well known (11, 23). Similarly, the activity of a number of enzymes active in the metabolism of carbohydrates in epidermis has been found to be increased in the psoriatic lesions (9, 12). The possible correlation between clinical diabetes and psoriasis has been the subject of several controversial studies (22). An increased incidence of diabetes in psoriatics has been reported by several workers (1, 20) while no such association has been found in other studies (3, 7, 16). In a Finnish material, diabetes was present in 2.6% of the psoriatic patients, which corresponds closely to the incidence of diabetes in the same age group of the normal non-psoriatic population (19). Fasting blood sugar levels were not more frequently elevated in psoriatics than in the other dermatologic patients. On the other hand, a pathologic prednisone-glucosuria test result was found considerably more often in psoriatics than in the control patients. This finding demonstrates that there is some kind of disturbance in the metabolism of carbohydrates in psoriatics.

The quality of the disturbance present in the carbohydrate metabolism of psoriatics is not known. Many factors can influence the blood glucose level, but the most important are the adequate secretory responses of insulin and growth hormone to the levels of glucose, amino acids and other metabolic agents. In psoriasis a disturbance may be based on changes in the level of these regulating factors or it may be due to an altered sensitivity of the target tissues to these hormones.

In order to delineate these possibilities we analysed (*a*) the fasting levels of insulin and growth hormone in a number of psoriatic patients, as well as (*b*) the secretory response of the same hormones to glucose infusion and compared the results with those obtained in diabetics and normal controls.

MATERIAL AND METHODS

The material consisted of 18 male patients, whose ages ranged from 25 to 68 years. Ten of the patients were otherwise healthy psoriatics (arthropathic changes were present in 2 patients), 3 maturity-onset diabetics, and 5 were normal control patients. Some data concerning the patients are given in Tables I and II. The mean weight in all patient groups lay between 70 and 87 kg. The mean length of the disease history in the psoriatic patients was 17.3 years while the patients suffering from diabetes had histories averaging 3.4 years. The patients were hospitalized in the Dermatologic Clinic and were all treated in the same way.

The fasting levels of glucose and growth hormone were analysed from serum samples taken 10 minutes before, and at the moment of starting the glucose infusion. Thirty

Table I. *Data on the test persons and their glucose, insulin and growth hormone responses to glucose infusion at 0, 30, 60 and 120 min after starting the infusion*

Patient				Glucose (mmol/l)				Insulin (ng/ml)				Growth hormone (ng/ml)			
Dg.	No.	Age (y.)	Weight (kg)	0	30	60	120	0	30	60	120	0	30	60	120
Control	1	25	72	3.9	10.1	7.7	3.9	0.5	1.7	1.7	0.5	2.9	1.2	3.5	3.8
	2	21	66	4.2	12.5	10.1	6.1	0.4	2.2	1.3	1.0	4.2	7.6	6.6	3.7
	3	39	90	4.0	12.2	8.5	5.5	1.1	2.4	2.4	1.7	2.7	3.4	2.8	2.4
	4	17	74	4.4	12.5	5.9	5.5	0.5	3.2	1.8	0.6	3.9	10.2	4.5	2.5
	5	55	84	4.0	14.5	9.9	5.6	1.4	3.0	8.6	4.3	5.6	3.0	3.3	3.6
Psoriasis	6	48	77	4.1	10.5	7.6	5.4	0.9	1.8	1.7	0.5	1.7	5.0	5.3	2.7
	7	59	112	4.6	10.1	8.2	6.2	0.9	2.0	1.6	1.5	1.9	1.7	3.7	2.6
	8	41	100	5.0	8.4	5.0	4.5	0.7	1.8	0.8	0.5	2.3	2.5	3.7	4.1
	9	25	95	5.2	10.4	7.5	4.7	1.1	4.0	2.2	0.8	1.8	2.8	3.0	2.5
	10	68	64	5.1	11.1	7.7	6.3	0.5	1.9	2.5	1.7	1.6	1.0	2.0	3.3
	11	41	83	4.7	12.4	8.3	4.6	0.9	0.8	1.4	0.6	2.6	2.6	1.3	1.5
	12	63	61	4.1	14.1	10.5	7.2	0.3	0.9	0.7	0.6	10.7	5.8	3.8	1.2
	13	35	88	4.5	11.6	9.3	5.0	0.5	0.8	1.0	0.7	2.5	17.3	24.0	9.2
	14	53	107	3.9	11.7	8.1	5.1	0.9	3.1	2.2	1.7	2.5	3.1	4.7	3.5
	15	65	86	5.2	12.8	8.3	5.3	1.0	2.4	4.1	1.0	3.5	2.6	5.8	4.6
Diabetes	16	78	72	5.8	17.0	11.5	9.4	0.3	0.9	1.2	1.7	1.7	2.5	3.4	6.6
	17	65	60	7.8	15.4	11.2	11.6	0.9	1.3	1.3	2.1	1.1	5.0	2.2	2.2
	18	31	80	11.4	17.0	20.0	15.3	1.1	3.3	2.3	1.2	2.6	12.0	4.7	4.6

grams of glucose was given by an intravenous infusion in 300 ml of 10% aqueous glucose solution during half an hour. Blood samples were subsequently drawn at 10, 20, 30, 40, 50, 60, 90, 120, 150, and 180 minutes. The blood samples were left to coagulate, and were centrifuged 2 hours later. The glucose and hormone determinations were carried out from the clear sera.

Determination of glucose was carried out by an auto-analyzer modification (15) of the *o*-toluidine method (13). Serum insulin and growth hormone were determined using the immunosorbent radio-immunoassay method according to Wide & Porath (24). The WHO human insulin (WHO International Laboratory for Biological Standards; National Institutes for Medical Research, Mill Hill, London N.W.7) was used as standard (1 ng = 25 mU). The insulin antiserum was obtained from Novo Co. For the growth hormone assay the human growth hormone standard from NIH (NIH-GH-HSL 394) was utilized. The growth hormone-antiserum was prepared in guinea pigs against a growth hormone preparation kindly provided by Dr Tryggstad, Oslo, Norway.

Table II. *Characteristics of the control, psoriatic and diabetic patients and their fasting levels of blood glucose, insulin and growth hormone (mean values)*

Characteristics	Control (5)[a]	Psoriasis (10)	Diabetes (3)
Age (y.)	31.4	49.8	58.0
Weight (kg)	77.2	87.2	70.6
Disease history (y.)	—	17.3	3.4
Blood glucose (mmol/l)	4.1	4.7	8.4
Blood insulin (ng/ml)	0.80	0.77	0.88
Growth hormone (ng/ml)	3.89	3.23	1.82

[a] Number of patients.

RESULTS

Fasting values

Data of the characteristics of the patients and of the fasting values recorded in the control, psoriatic and diabetic patients are given in Tables I and II. The blood glucose level was somewhat higher in the psoriatics than in the controls. In the diabetics, values about twice as high were recorded. The fasting insulin levels were about equal in all patient groups. The growth hormone level was about the same in the controls and psoriatics while considerably lower values were recorded in the diabetics.

Responses to glucose infusion

Blood glucose. The blood glucose responses obtained in the control and psoriatic patients during and after the glucose infusion were closely similar, as seen in Table I and in Fig. 1 *a, b*. The diabetic curves, on the other hand, showed higher starting values and the curves remained at a high level, as might be expected (Fig. 1 *c*).

Blood insulin. Two types of blood insulin response curves were recorded in the controls:

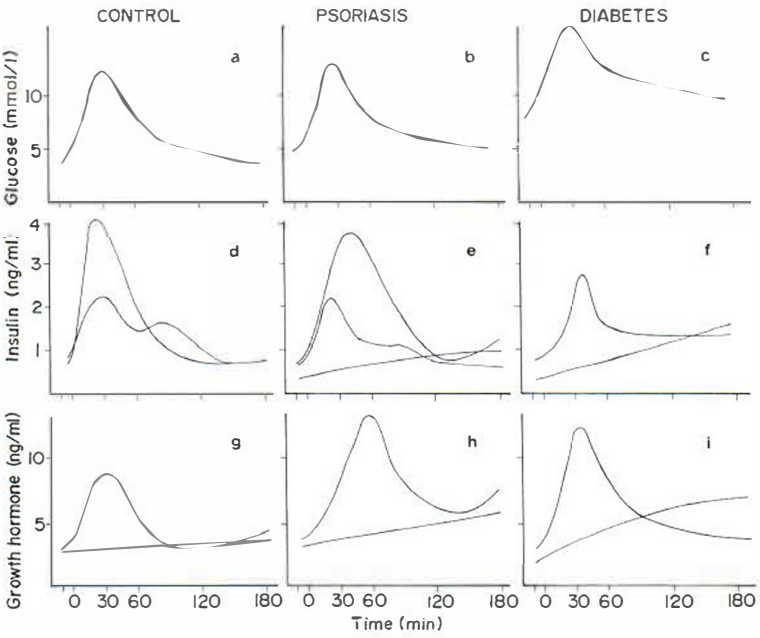

Fig. 1. Schematic presentation of the glucose, insulin and growth hormone responses to an intravenous glucose infusion.

one showed a high initial peak at 20–40 min followed by a steady decrease ("Early high" in Table III), while the other showed a smaller initial response followed by another maximum ("Biphasic") roughly 90 minutes after the beginning of the infusion (Fig. 1 *d*). Three basically different types of insulin response were recorded in the patients suffering from psoriasis (Fig. 1 *e*). In 7 patients the response curves resembled those recorded in the controls: in 3 patients there was a high initial increase ("Early high") followed by a steady decrease in the blood insulin level, while in 4 patients a low initial response peak was followed by another peak at 60–90 min, i.e. a biphasic response curve was obtained as in the controls (Fig. 1 *e*). In 1 patient the early response was delayed roughly half an hour in comparison with the controls. In 2 psoriatics with a diabetic family history no initial rapid insulin secretion peak supervened, but the curves showed a slow and steady rise during the whole experiment ("Slowly rising"). Thus the insulin response of these last 2 patients was roughly similar to those recorded in the diabetics, as will be described.

In the diabetic patients the response could be characterized as being somewhat delayed and lower than in the controls: in 2 of the patients a low initial response was clearly recorded about 20–30 min later ("Early low") than in controls while in 1 patient the insulin level was steadily

Table III. *Characteristics of the control, psoriatic and diabetic patients arranged according to the kind of insulin response to glucose infusion*

	Control		Psoriasis			Diabetes	
Insulin response ...	Early high (2)[a]	Biphasic (3)	Early high (3)	Biphasic (5)	Slowly rising (2)	Early low (2)	Slowly rising (1)
Characteristics							
Age (y.)	36.0	28.0	47.6	51.4	49.0	48.0	78.0
Weight (kg)	79.0	76.0	96.0	87.2	74.0	70.0	72.0
Disease history (y.)	—	—	27.3	8.7	23.5	2.5	5.0
Blood glucose (mmol/l)	4.2	4.0	4.7	4.7	4.3	7.8	5.8
Blood insulin (ng/ml)	1.17	0.69	1.01	0.79	0.38	1.02	0.30
Growth hormone (ng/ml)	4.75	3.33	2.96	2.04	6.60	1.85	1.75

[a] Number of patients.

Table IV. *Characteristics of the control, psoriatic and diabetic patients arranged in groups according to the kind of growth hormone response to glucose infusion*

	Control		Psoriasis		Diabetes	
Growth hormone response ...	Early high (2)[a]	Slowly rising (3)	Early high (3)	Slowly rising (6)	Early high (2)	Slowly rising (1)
Characteristics						
Age (y.)	19.9	39.6	49.3	47.8	48.0	78.0
Weight (kg)	70.0	82.0	83.6	93.5	70.0	72.0
Disease history (y.)	—	—	19.6	13.4	2.5	5.0
Blood glucose (mmol/l)	4.3	3.9	4.6	4.8	7.8	5.8
Blood insulin (ng/ml)	0.47	1.02	0.78	0.51	1.02	0.30
Growth hormone (ng/ml)	4.12	3.73	2.60	2.31	1.85	1.75

[a] Number of patients.

rising ("Slowly rising") during the experiment (Fig. 1 *f*). This latter type of response was shown by those psoriatic and diabetic patients who had the lowest fasting insulin levels (Fig. 1 *e, f*). The insulin levels at 3 hours were considerably higher in all diabetics than in the controls. The body weight as well as the blood insulin fasting levels of the psoriatic patients with a slow insulin response were lower than those of the controls (Table II). The other characteristics of the patients in the different response type groups did not differ significantly.

Growth hormone. Two types of growth hormone response were recorded in the control patients, as shown in Table IV and Fig. 1 *g*. One type showed a steady and continuous slow rise in the hormonal level during the observation period ("Slowly rising"), while the other type showed a clear initial response peak with a maximum at about 30 min after commencement of infusion ("Early high"), i.e. at the time when the blood glucose was at its maximum. As can be seen in Table IV, the control patients with a slow growth hormone response could be characterized as older and heavier with twice the initial fasting insulin value.

In principle, the psoriatic patients showed the same two types of response: 6 patients showed a slow response while in 3 patients a strong initial insulin peak could be recorded about 30–60 min after commencement of the infusion (Fig. 1 *h*). The psoriatics of both these response types were essentially similar in age, weight and history of the disease.

Two of the diabetic patients showed characteristically an early high growth hormone peak (Fig. 1 *i*). The highest response was recorded in the youngest patient. The lowest and slowest response with the maximum at 2 hours was recorded in the oldest patient (78 years of age).

A quite abnormal curve was found in one psoriatic patient with a high initial growth hormone level which steadily decreased during the experiment. The 2 psoriatic patients with arthropathia did not differ from the other psoriatics in the insulin and growth hormone response curves: in insulin response one belonged to the group "Early high" and the other to "Biphasic", and in the growth hormone response, to "Early high" and "Slowly rising", respectively.

DISCUSSION

The basal level of blood glucose in controls as well as in most of the psoriatics revealed normal values. A few of the psoriatics and all of the diabetics had blood glucose levels above the normal, suggesting the presence of an abnormality in the carbohydrate metabolism in these patients. The diabetics are to be considered as being of the so-called late-onset diabetes type.

The basal blood insulin levels recorded are of the same order as described by other investigators employing similar assay methods (5, 6). The fact that no differences were found in the basal insulin level in the control and diabetic patient groups is in accord with the fact that there is no fixed relationship between insulin and glucose in the fasting state (18). It would appear, however, that the psoriatic patients do not differ in their basal blood insulin level from the other patients.

The growth hormone level of our control and psoriatic patients is the same as found previously in normal persons by other investigators (27). Our finding of considerably lower values in the diabetics is somewhat surprising since few investigators have reported lower-than-control values in this disease (21), while some have reported no difference from the controls (8, 14, 17) and higher-than-control values have been found by some others (27).

According to the response to intravenous glucose infusion the psoriatic patients with a normal fasting blood glucose level, as also the control patients, can be divided into different populations: one group has a single initial insulin peak, while the other group is characterized by two peaks at about 60 min intervals. Both types of response can be considered as basically non-diabetic. A low insulin response in a non-diabetic has been considered as a prerequisite for the future development of diabetes mellitus (6). In 1 psoriatic patient the insulin response was delayed and in 2 it was very slow, corresponding to that found in the 3 maturity-onset diabetics. Thus it can be concluded that the insulin response in the psoriatic patients can be similar to the controls as well as identical to that of the diabetics. Therefore, no insulin response characteristic of psoriasis can be demonstrated. The older patients can be expected to acquire the diabetic type of insulin response more easily since the patients with this response type belonged to the older age group.

The growth hormone response to glucose infusion also showed two different patterns in the control patients and similar responses were also observed in the psoriatics. The early strong growth hormone response was characteristic of diabetes in the present study and is in keeping with earlier observations both in juvenile (26) and in maturity-onset diabetes (10, 27). It is therefore apparent that the growth hormone response to glucose infusion has no characteristic pattern in psoriasis, either, but together with the insulin response it may reveal patients among the psoriatics who have acquired a diabetic type of insulin and growth hormone response and may, in the future, disclose an overt type of maturity-onset diabetes.

Increased growth hormone secretion has been implicated in the pathogenesis of diabetes (25) and of diabetic capillary disease (2). Growth hormone may be responsible for the increased glucose levels in diabetes (26, 27). In most patients suffering from psoriasis the growth hormone levels were comparable to those in the control patients, and therefore the contribution of growth hormone to the pathogenesis of this disease appears questionable. Thus, neither insulin, nor growth hormone basal level, or the response to glucose infusion discloses any abnormalities which might be characteristic of psoriasis.

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Received April 28, 1972

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