Screening of glucose/insulin metabolic alterations in men with multiple skin tags on the neck

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Summary

Multiple skin tags appear associated with abnormalities in glucose/insulin metabolism. Clinical and metabolic glucose/insulin characteristics of men with multiple (8 or more) skin tags on the neck were compared with a control group with few or none. Both groups were divided in two subgroups according to normal or abnormal laboratory findings. In the study subgroup with normal laboratory findings the number of skin tags varied from 8–33, whereas in those with abnormal laboratory findings the range was 9–65. Eight or more skin tags were related with statistically significant laboratory glucose/insulin abnormalities: basal hyperinsulinemia (p<0.002), postprandial hyperinsulinemia (p<0.003), and postprandial hyperglycemia (p< 0.01). In the multiple skin tag group 77 % had diverse laboratory abnormalities, including insulin resistance, basal hyperinsulinemia, postprandial hyperinsulinemia, glucose intolerance or type 2 diabetes, in contrast with the control group, where only 33 % showed laboratory abnormalities. One-third of the study group had acanthosis nigricans. Only 15 % of patients with metabolic abnormalities did not show any cutaneous expression of glucose/insulin alterations (9 or more skin tags on the neck, acanthosis nigricans, or waist circumference greater than 95 cm). Multiple skin tags were more sensitive than acanthosis nigricans in identifying those with alterations in the glucose/insulin metabolism (77 vs. 32 % respectively), although less specific (68 vs. 100 %). Multiple skin tags should raise suspicion of insulin resistance or hyperinsulinemia.

Introduction

The presence of skin tags on the neck is a common finding. While they may be a cosmetic concern and occasionally become irritated or necrotic and then painful, skin tags are generally ignored. In the last years the finding of multiple skin tags has been associated with abnormalities in the glucose metabolism, specifically type 2 diabetes and hyperinsulinemia. Our study hypothesis is that insulin is one of the mediators in the appearance of skin tags on the neck, since many times they are associated with acanthosis nigricans, which is a known cutaneous marker of insulin resistance. We compared the clinical and metabolic glucose/insulin characteristics of a group of male patients with multiple skin tags on the neck with another group with few or none.

Patients and Methods

Twenty-six men who complained of multiple skin tags on the neck were analyzed. A skin tag or acrochordon was defined as follows: a furrowed, pedunculated papule approximately 2 mm in wide and 3–6 mm in height, with a color ranging from skin color through various shades of brown. Although 46 % of the general population has skin tags, of these only 14.4% have 8 or more acrochordons all over the body [1]. We arbitrarily defined multiple skin tags as the presence of 8 or more acrochordons just on the neck. We examined only the neck because patients tend to report lesion in this site which is easily visible. Patients with known diabetes

mellitus and those taking any drug that could alter the glucose metabolism were excluded, in order to detect only new cases not previously diagnosed with any glucose/insulin alteration. Women were excluded since variations of insulin levels may occur depending on the stage of their menstrual cycle.

Another group of 21 men with 7 or less skin tags on the neck were selected as control group. All 47 patients were evaluated and compared with respect to their age, body mass index (BMI) (normal 18.85–24.9; overweight 25–26.9; obesity 27 or more) waist circumference (normal up to 95 cm), number of skin tags on the neck, and the presence of acanthosis nigricans (ranging from + to +++ depending on its severity).

Acanthosis nigricans was defined as symmetrical, pigmented, velvety plaques with verrucous excrescences confined to flexures. Skin tags as well as acanthosis nigricans in other locations (i.e. axillae, groins) were not considered.

Laboratory studies

Fasting glucose and insulin values (normal values less than 110 mg/dl and less than 20 U/ml respectively; glucose levels between 110 and 126 mg/dl were considered as glucose intolerance; glucose levels over 126 mg/dl were considered as diabetes mellitus), and the same values 2 hours post 75 g of oral glucose (normal values less than 140 mg/dl and less than 60 U/ml respectively; glucose levels between 140 and 200 mg/dl were consid-

ered as glucose intolerance; glucose levels over 200 mg/dl were considered as diabetes mellitus), and well as fasting glucose to insulin ratio (normal value more than 4.5) were determined in all patients. The results were analyzed through the Student T test for multiple independent variables, and the software GB-STAT V6.5 for MS WINDOWS was used.

Results

Clinical and metabolic findings of both study and control groups are summarized in Table 1 and 2. In the study subgroup with normal laboratory findings the number of skin tags varied from 8-33, whereas in the subgroup with abnormal laboratory findings they ranged from 9–65.

Table 1: Clinical and metabolic findings in study and control group.

Skin tags	Laboratory Findings	Age (years) X (r)	BMI X (r)	Waist (cm) X (r)	Skin tags Nº X (r)	Acanthosis Nigricans N° (r)	Fasting glycemia (mg/dl) X (r)	Fasting insulinemia (U/ml) X (r)	Postprandial glycemia (mg/dl) X (r)	Postprandial insulinemia (U/ml) X (r)	Fasting glycemia/ fasting insulinemia X (r)
Group A 8 or more N=26	Normal 6	49 (40–57)	29.3 (25.2–34)	101 (82–112)	15 (8–33)	0 (0)	92 (81–107)	10 (3–16)	92 (53–131)	28 (5–60)	12.6 (5.4–32.2)
	Abnormal 20	48 (34–66)	32.4 (24.2–42.6)	109 (84–126)	21 (9–65)	8/20 (o/++)	98 (62–138)	34 (15–68)	164 (97–440)	165 (34–352)	3.7 (0.9–7.7)
	X	48	31.7	105	20	8/26	97	28	147	133	5.7
Group B 7 or less N=21	Normal 13	40 (23–62)	24.7 (19.5–32)	87 (66–113)	1 (0–6)	0 (0)	84 (63–101)	11 (5–18)	91 (62–135)	39 (15–60)	8.6 (5.3–17.2)
	Abnormal 8	42 (20–58)	27.2 (20.4–33.4)	93 (75–107)	2 (0–4)	1/8 (o/+)	98 (76–116)	21 (7–34)	116 (70–234)	93 (19–280)	6.0 (3.1–10.7)
	X	41	25,6	89	1	1/21	89	14	101	59	7.6

X: average; r: range; BMI: body mass index.

Table 2: Clinical findings in study and control group.

		Study group 8 or more skin tags (26 patients)	Control group 7 or less skin tags (21 patients)
Weight (BMI)	Obesity	22 (84.6%)	8 (38%)
	Overweight	3 (11.5%)	4 (19%)
	Normal	1 (3.8%)	9 (42.8%)
Waist circumference	Normal	2 (7.6%)	14 (66.6%)
	Abnormal	24 (92.3%)	7 (33.3%)
Acanthosis nigricans	Present	8 (30.7%)	1 (4.7%)
	Absent	18 (69.2%)	20 (95.2%)

In the study group the great majority of patients was obese (84.6 %) and had an abnormal waist circumference (92.3 %). In contrast, in the control group only 38 % of patients were obese and one-third of them showed an abnormal waist circumference. 30.7 % of patients in the study group had acanthosis nigricans, in contrast with 4.7 % in the control group.

These three clinical differences were statistically significant between both groups. Metabolic abnormalities of study and control group are seen in Table 3. More than three-fourths of the study group showed a metabolic alteration: diabetes mellitus (3 cases), glucose intolerance (9 cases), and hyperinsulinemia and/or insulin resistance (8 cases); the control group showed only 1 case of diabetes mellitus, 2 cases with glucose intolerance, and 4 cases with hyperinsulinemia and/or insulin resistance.

Table 4 shows the glucose and insulin alterations in study and control group. In the study group the most frequent abnormality was in postprandial insulinemia, which was elevated in 19/20 patients (95 %), followed by fasting insulinemia which was elevated in 14/20 patients (70 %). These differences were statistically significant from the control group.

The results of statistical analysis comparing the study and control groups are shown in Table 5. There were significant statistical differences in weight, BMI, waist, number of skin tags, presence of acanthosis nigricans, fasting insulin, post prandial glucose and insulin. No significant statistical differences were found in the fasting glucose and in the glucose/ insulin ratio.

Eight of 9 patients with acanthosis nigricans had 8 or more skin tags on the neck.

Discussion

The presence of skin tags has been related with type 2 diabetes [2–5], glucose intolerance [3], fasting hyperinsulinemia [6], and obesity [7]. Margolis & Margolis [2] first stated that "one can almost predict that a male patient will have diabetes if the ... (skin tags)... are multiple, large, hyperpigmented and bilateral". They studied 47 male patients with skin tags and found that approximately 75 % of them had elevated fasting and postprandial glucose in the diabetic range [2]. Eleven years after this publication, Kahana studied 216

Table 3: Metabolic alterations in study and control group.

	Study group 8 or more skin tags (26 patients)	Control group 7 or less skin tags (21 patients)
Diabetes mellitus	3 (11.5%)	1 (4.7%)
Glucose intolerance	9 (34.6%)	2 (9.5%)
Hyperinsulinemia and/or insulin resistance	8 (30.7%)	4 (19%)
Total	20 (77%)	7 (33%)

Table 4: Glucose and insulin alterations in study and control group.

Study group 8 or more skin tags: 26 cases	Control group 7 or less skin tags: 21 cases
Normal exams : 6 cases	Normal exams: 13 cases
Abnormal exams: 20 cases (77%)	Abnormal exams: 8 cases (38%)
Fasting glucose	**Fasting glucose**
Glucose intolerance: 2	Glucose intolerance: 1
Diabetes mellitus: 2	Diabetes mellitus: 0
Postprandial glycemia	**Postprandial glycemia**
Diabetes mellitus: 3	Diabetes mellitus: 1
Fasting insulinemia	**Fasting insulinemia**
Hyperinsulinemia: 14	Hyperinsulinemia: 4
Postprandial insulinemia	**Postprandial insulinemia**
Hyperinsulinemia: 19	Hyperinsulinemia: 4

Table 5: Statistical differences among study and control group.

Groups	Weight X Kg	BMI X	Waist X cm	Skin Tags X N°	Acanthosis nigricans	Fasting glycemia X mg/dl	Fasting insulin X U/ml	Postprandial glycemia X mg/dl	Postprandial Insulin X U/ml	Fasting glycemia/ Insulinemia X
Skin tags 8 or more	91	31.7	105	20	8/26	97	28	147	133	5.7
Skin tags 7 or less	74	25.6	89	1	1/21	89	14	101	59	7.6
P value	<0.01	<0.01	<0.01	<0.01	<0.02	NS	<0.002	0.01	0.003	NS

NS: Not significant; X: average

patients with skin tags and found that overt diabetes mellitus was present in 26.3 % of patients and impaired glucose tolerance test was found only in 7,9 % of cases [3]. The prevalence of skin tags in the general population varies depending of the population studied, e.g. 46 % in Germany [1] or 0.7 % in India [4]. In this last study, 62.8 % of patients with skin tags had diabetes mellitus [4], comparable to the earlier report of Margolis & Margolis [2]. Norris [6] first mentioned that "skin tags are more closely related to fasting insulin than fasting glucose levels" and suggested that raised circulating insulin levels appeared to be associated with formation of skin tags, perhaps due to an insulin-mediated effect on epidermal proliferation. However, we believe that when hyperinsulinemia interacts with epidermal keratinocytes, the result is acanthosis nigricans. Skin tags must be the result of proliferation of dermal fibroblasts via activation of insulin-like growth factor 1 receptors acting in certain areas of skin folds (neck, axillae, groins, lids).

Acanthosis nigricans, a known marker of insulin resistance [8], was absent in 12 of 20 patients with multiple skin tags and metabolic abnormalities; therefore, in this group of patients, acanthosis nigricans was less sensitive than the presence of 8 or more acrochordons on the neck (range 9–65) of male patients to diagnose hyperinsulinemia, insulin resistance, glucose intolerance, and type 2 diabetes.

All 6 of the patients with 8 or more acrochordons and without laboratory abnormalities, were overweight or obese. Five of these patients had android (male-pattern or abdominal) obesity. This group of patients had an average of 15 skin tags on the neck, with a range between 8 and 33; none of them had acanthosis nigricans and their laboratory exams were normal. We speculate that these patients might have had in the past a transitory hyperinsulinemia, triggering their skin tags. Most patients stated that the skin tags had appeared as they gained weight. Perhaps they remained as a metabolic scar of past hyperinsulinemia. Most of them had subsequently reduced weight and this fact could perhaps explain the normal laboratory finding at this moment.

According to our data, a waist circumference of 95 cm or more has a sensitivity of 75 % and a specificity of 53 % to detect metabolic abnormalities of glucose and insulin metabolism. The presence of acanthosis nigricans showed a sensitivity of 32 % and a specificity of 100 % to detect glucose or insulin abnormalities. The finding of 8 or more skin tags on the neck of our male patients had a sensitivity of 77 % to detect metabolic abnormalities and a specificity of 68 %. We assume that insulin is not the only mediator for skin tags on the neck (as they also occur as a paraneoplastic marker, also associated with acanthosis nigricans), but it is probably the most frequent one. A possible mechanism is hyperinsulinemia acting on skin fibroblast receptors (classical insulin receptor and insulin growth factor receptor). Similarly, hyperinsulinemia interacts with skin keratinocyte receptors producing acanthosis nigricans [9].

The presence of 8 or more acrochordons on the neck in male patients is an important clinical finding because it is more sensitive but less specific than acanthosis nigricans in order to detect metabolic abnormalities like diabetes mellitus or hyperinsulinemia.

Of the laboratory exams, postprandial insulinemia was the most sensitive in detecting metabolic alterations (95 % of sensitivity versus 70 % for fasting insulin and 20 % for fasting glucose). We suggest that besides fasting glucose and insulin determinations, patients with multiple skin tags should also be evaluated with postprandial glucose and insulin analyses, especially if the patients have other cutaneous risk markers of hyperinsulinemia such as acanthosis nigricans or a waist circumference greater than 95 centimeters.

The finding of 8 or more multiple skin tags is a useful clue to suspect hyperinsulinemia, which can be considered a pre-diabetic state. Hyperinsulinemia is currently considered as the base of the metabolic syndrome [10–11], which includes type 2 diabetes, hypertension and dyslipidemia, all known predisposing factors for the development of coronary heart disease.

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