

AN ASSOCIATION BETWEEN KHAT AND DIABETES

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Hypothesis: Chronic chewing of Khat sprayed with pesticides might be an important factor in the development of non-insulin dependent diabetes mellitus in chronic Khat chewers. Design: Prospective controlled study conducted between January 1998 and July 1999 and involved 240 subjects who were divided into two groups. The Khat chewer group (= 127 subjects) and the controls (= 113 subjects). Results: In the Khat chewing group; 41 subjects (32%) have non-insulin dependent diabetes mellitus. In the controls; 11 subjects (9%) have diabetes. $P < 0.05$. Conclusions: The study showed an association between the habit of Khat chewing and the development of non-insulin dependent diabetes mellitus and suggests that this might be attributed to the adverse health effects of pesticides residues on the Khat chewers.

Key words: Khat, Diabetes, Non-insulin pesticides, Khat chewers.

INTRODUCTION

Khat is grown in Yemen and some parts of East Africa, especially Ethiopia, Kenya. The plant belongs to the family Celastraceae. Khat is consumed mainly for its stimulating effects. These effects are caused by the psychotropic components in Khat (Khatamines). Cathinone is the main central nervous system stimulant in Khat (1,2,3). The Khat user, chews the young leaves and the twigs of the plant, the residue is stored in the cheek. The saliva is swallowed or spitted out. The chewing sessions usually lasts for 2 to 4 hours. In a study conducted by Manciola and Parinello (4) on 27410 Yemeni subjects, they found that 60% of males and 35% of females were chronic daily Khat chewers and that 30% of males and 24% of females chew Khat in weekends and special occasions.

It is estimated that 70% of pesticides imported or smuggled to Yemen Republic are used on Khat (5). Diabetes is one of the most serious challenges to health care worldwide. The world prevalence of diabetes is expected to more than double between 1994 and 2010 to 239 million people. This global increase is reported in developed and developing countries (6). In Yemeni population diabetes mellitus has become very important cause of morbidity and mortality. In this preliminary study an attempt is made to

find, if chewing Khat treated with pesticides, has a role in the development of non-insulin dependent diabetes mellitus in Khat chewing subjects.

METHODS AND SUBJECTS

This prospective controlled study involving 340 Yemeni subjects (136 males and 104 females) with ages ranging from 15 to 80 years. Subjects were divided into two groups. The first "exposed" group comprised 127 chronic Khat chewers; and the controls: 113 non-Khat chewers. Some subjects were recruited in the country by visits to Khat farmers. Other subjects were recruited in the Yemen Specialized Hospital between January 1998 and July 1999. The study included medical history, clinical examination, and the estimation of Haemoglobin, total white cell count and fasting blood sugars. Blood glucose was estimated after an overnight fasting. Venous blood was collected and the sample was left for 15 minutes to clot and serum was separated. The glucose was determined by enzymatic colorimetric test method without deproteinisation. The reagent glucose liquicolor from Human Gesellschaft for biochemical and diagnostic mbH. The glucose level is measured by RA-50 clinical chemistry Analyzer from Tecknicon-Ames. The investigators neither know the group of the each individual in the study, nor his or her results.

A questionnaire was conducted on Khat farmers concerning the use of pesticides on the Khat trees.

RESULTS AND STATISTICAL ANALYSIS

The mean age was tested for mean age difference in the Khat chewing group respectively, without significant difference.

In the Khat chewers group diabetes mellitus was found in 41 subjects (32%). In the control group diabetes mellitus was found in 11 subjects (9%). This is statistically significant ($P < 0.05$). In summary, to test for group difference, the statistical analysis (General linear model approach) yielded highly significant results. To test for age difference between subjects effects, where serum is the dependent variable, the results were found to be significant as well. The analysis results can be summarized in the ANOVA (Table 1).

Table (1): ANOVA table for dependent variable serum

Source	Mean Square	F-ratio	P-value
Group	8581.296	3.929	0.000
Ages	3674.231	2.133	0.000

The characteristics of the study groups are summarized in (Table 2).

Table (2): Characteristics of the study groups

	Khat chewers	Controls
No	127	113
Sex		
Males	91	45
Females	36	68
Ages (years)	19-70	15-18
Diabetics	41 (32.3%)	11 (9.7%)

Almost 100% of these cases were non-insulin dependent diabetes mellitus. 95% of Khat farmers reported that they apply one or mixtures of pesticides on the Khat trees and the remaining 5% use sand (Table 3).

Table (3): Pesticides used in mixtures on Khat, *Catha edulis* trees in Sana'a Governorate

Common Names	Trade Name	Type of Action
Dimethoate +	Prefekthion +	Insecticide
Trichlorfon +	Dipterex +	Insecticide
Penconazole	Topas	Fungicide
Methidathion +	Suprcide	Insecticide
Fenarimol +	Rubigan	Fungicide
D.D.T. or Lindane	D.D.T. or Lindane	Insecticide
Methidathion	Supracid	Insecticide
Penconazole	Topas	Fungicide

Common Names	Trade Name	Type of Action
Fenarimol	Rubigan	Fungicide
Dust	Dust	Fungicide
Iron Fertilizer	Iron fertilizer	Fungicide
Dimethoate	Prefekthion	Insecticide
D.D.T.	D.D.T.	Insecticide
Trichlorfon	Dipterex	Insecticide
Penconazole	Topaz	Fungicide

Total white cell counts and Haemoglobin values were similar in the two groups. The results of this study has shown for the first time, that there is an association between the habit of chronic Khat chewing and the development of non-insulin diabetes mellitus, and suggests that the abuse in pesticides application on the Khat trees might be the most important risk factor in the development of diabetes.

DISCUSSION

This study demonstrated that the frequent statement "Khat chewing is beneficial to diabetic patient" is not true and on the contrary, this paper suggests that chronic Khat chewing can be a major risk factor in the development of non-insulin dependent diabetes mellitus. Almost 100% of the reported cases in this study have non-insulin dependent diabetes. The relative frequencies of major types of diabetes in Yemeni diabetics were 11.5% for insulin dependent diabetes mellitus, and 84.8% for non-insulin dependent diabetes mellitus⁽⁷⁾. The diagnosis was made on finding, one fasting venous blood glucose level ≥ 7.8 mmol/l (140 mg/dl)⁽⁸⁾. In 5 out of 36 patients who had uncertain range (5.5-7.7mmol), the test was repeated or oral glucose tolerance test was done. Non-insulin dependent diabetes mellitus has been connected with both genetic and environmental factors⁽⁹⁾.

Non-insulin dependent diabetes is associated with increase in mortality and reduction in life expectancy⁽¹⁰⁾. The treatment of diabetes and its complications is expensive and beyond the limited resources of several developing countries. Hence the importance of performing several studies to identify the causes of this epidemic disease.

Khat protection from different pests is widely practiced to maintain fresh clean foliage. Ninety five percent of Khat farmers use pesticides on the Khat trees. There is no official recommendation for a relatively safe pesticides on the edible Khat, therefore the Khat farmers are taking the risk of using any available pesticides regardless of their hazards to the consumers.

Most of the chemicals used on Khat trees are not highly selective and generally toxic to many non-target species, including humans and some of the globally banned compounds even in Yemen were reported and documented to be used such as DDT and Lindane. (Table 3).

Some protein kinases are known to play role in the regulation of normal cell metabolism such as glycogen synthesis while a number of protein kinase activities were shown to be associated with growth factor receptors ⁽¹¹⁾. Others ⁽¹²⁾ reported that decreasing the activity of tyrosine kinase of insulin receptors is the cause of various types of diabetes.

In an experimental study ⁽¹³⁾, showed that several chlorinated hydrocarbon compounds; DDT, endrin, dieldrin, aldrin and deltamethrin, showed inhibitory effects on the activity of calcium-phospholipid-dependent protein kinase (PKC) and polypeptide-dependent protein kinase (PKP). In a study ⁽¹⁴⁾ conducted on rabbits to show the toxic effects of 3 pesticides (parathion, tamaron, confidor) on serum non-protein nitrogen constituents. It showed that glucose content in treated rabbits began to increase gradually by daily oral administration of pesticides and this effect was prominent after the tenth day ⁽¹⁴⁾. Some pesticides affect lipoprotein lipases, glucose transporter proteins, carbohydrate metabolism and insulin secretion ⁽¹⁵⁾. Carbaryl was reported to significantly elevated blood sugar levels in treated rats ⁽¹⁶⁾. Several studies demonstrated that DDT influences carbohydrate metabolism ^(17,18,19,20). The exact mechanism by which DDT induce hyperglycaemia is not clear, however, the following mechanisms are suggested:

DDT inhibit pancreatic secretory activity by increasing the activity of gluconeogenic enzymes ⁽²¹⁾.

Promoting hepatic glycogenolysis by activating glycogen phosphorylase ⁽¹⁷⁾.

DDT reduce calcium permeability and hence insulin secretion. ^(22,23).

In conclusion, the results of this study showed that there is an association between chronic Khat chewing and the development of non-insulin dependent diabetes mellitus. This association might be attributed to the long-term effects of pesticides residues on chronic Khat chewers.

Also this paper showed that diabetes has become a serious health problem in the Yemeni Society. Further studies are needed.

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