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Effects of natural honey intake on glycemic control and lipid profile in type 2 diabetes

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A B S T R A C T

Background: Natural honey is among products that are very rich in antioxidants. Several studies have demonstrated its advantages for human beings. However, diabetic patients are recommended not to consume a great amount because of its high content in sugar. The aim of the current study was to investigate the safety of natural honey in type 2 diabetes.

Methods: Thirty-three patients with type 2 diabetes were randomly recruited and ate 10g of natural honey with water per day during ten weeks. During the study period, they did not undergo any changes in their diet, drugs and lifestyle. Before the onset of the study and at the end, lipids, glycemic profile, and HbA1c were measured. The patients performed regularly capillary blood glucose monitoring too.

Results: We observed that HbA1c has significantly increased from 7.2% to 7.65% ($p<10\text{-}5$). Preprandial glycaemia has also increased, but not significantly. However, fasting and postprandial glycemias remained unchanged. Contrary to glycemic effects, honey improves lipid profile, but not significantly. Actually, total cholesterol, triglycerides and LDL cholesterol have decreased, and HDL cholesterol has increased.

Conclusion: Daily consumption of Natural honey can deteriorate glycemic control of diabetics. However, it is still much better than other sweeteners. So, diabetics should take precautions if they consume honey for its advantages, and they could use low doses of honey, less than 10 g per day. Nevertheless, more studies should be done to investigate if honey can be beneficial and to determine the mechanism by which it can be.

Introduction

Diabetes mellitus (DM) prevalence is increasing relentlessly all over the world, with an estimated number of 592 million by 2035 and a global prevalence of 10.1% [1]. The increasing prevalence is apparently due to life style modification, especially eating disorders and reduction in physical activity. DM is one of the major causes of mortality and morbidities worldwide. It is responsible for 3.96 million deaths per year [2]. This mortality is related to DM chronic complications, especially cardiovascular diseases and kidney failure. On another hand, numerous studies showed that diabetic patients have an increased risk for different kinds of cancer such as pancreatic, hepatic, colorectal, breast, urinary tract, and

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endometrial ones [3). DM is also incriminated in neurological diseases such as encephalopathy and Alzheimer disease responsible for cognitive and memory impairments [4). DM affects male fertility too by reducing sperm count [5,6). Apart from life style modification and diet, several pharmaceutical products are used in DM treatment; their response varies according to DM duration and complications, but also according to the patients' adherence or compliance with diet and medications.

All over the world and especially in developing countries, most people believe more in herbal medicine and natural products actions than in pharmaceutical drugs. Honey is one of these natural products, it is considered as a holy substance for most people. They do like using honey to sweeten several beverages, to heal wounds and to treat some diseases as in ancient times. Our aim was to analyze honey's impact on glycemic control and lipid profile in patients suffering from type 2 DM.

Methods

Before investigating honey effects on diabetic patients, we have calculated glycemic index of three types of honey which are well known in our area (Ghardaia, south of Algeria in 2015), and then we have chosen the one with the lowest glycaemic index, termed Euphorbe (Lebinat) = 61.1%, it contains 77% of carbohydrates of which 37% of fructose.

Thirty-three patients with type 2 DM were randomly recruited. Their median age was 55.15 years (34-77 years). Among this group, 16 were male and 17 were female. DM was diagnosed 1 to 13 years ago. No one was on insulin regimen, two were on diet alone, and thirty-one were on diet plus oral medication: 19 were taking one medication (Metformine 16 patients, Sulfonylurea 03 patients) and 12 were taking two medications (Metformine plus a sulfonylurea) (Table 1).

Patients had to eat 10g of natural honey per day dissolved in water (20-100 ml) before breakfast for 10 weeks. They did not undergo any changes in their diet, drugs, and lifestyle, especially physical activity. All of them were clinically examined and had biological assessments before honey intake, at the middle of the study and at the end. Glycemic and lipid profile were analyzed by usual methods. HbA1c was measured by high performance liquid chromatography (HPLC). Furthermore, we evaluated capillary blood glucose [fasting, pre-prandial and post-prandial] at the beginning, in the middle and at the end of the study.

Table 1. Demographic data of patients

Variable	Frequency
Number of patients	33
Gender (% females)	17 (51.5%)
Age in years (mean ± SD)	34- 77 (55.15±11.12)
Duration of diabetes (Mean± SD)	1- 13 (4.48± 3.68)
Treatment	
Diet alone	02
Metformin	16
Sulfonylurea	03
Metformin+ Sulfonylurea	12

For statistical analysis, we used the Z test on paired samples to compare mean values.

$Z = md/\sqrt{S_d^2/n}$.

md = mean value of the differences d for the paired sample data.

S_d^2 = variance of the differences d for the paired sample data.

n = number of paired sample data.

The difference was considered as significant if $p < 0.05$.

Results

We did not observe any adverse effect due to honey intake. HbA1c has increased significantly from 7.2±1.09% to 7.65±1.12% ($p<0.00001$) (Table 2). For individual results HbA1c increased in twenty volunteers (60.6%), remained unchanged in eleven (33.3%) and decreased in two (7.1%).

Pre-prandial mean glycaemia increased from 129±0.36 to 140±0.37 mg/dl, but the difference was not statistically significant. Mean postprandial glycaemia remained stable (Table 2).

Table 2. Glycemic control before and after honey intake

HbA1c (%)		Glycaemic cycle (g/l)							
		Fasting		Pre-prandial				Postprandial	
Before	After	Before	After	Before	After	Before	After	Before	After
7.20±1.09	7.65±1.12	128±0.32	128±0.30	127±0.33	129±0.36	136±0.34	140±0.37	174±0.47	177±0.44

Table 3. Lipid profile before and after honey intake

	Cholesterol(mmol/L)		TG		HDLc	
Time	Before	After	Before	After	Before	After
Values	1.79±0.37	1.71±0.32	1.12±0.47	1.01±0.48	0.46±0.13	0.49±0.06
P-value	0.08		0.11		0.027	

Table 4. Summaries of clinical studies

Reference of studies	Volunteers	Nb	Honey intake	Duration	Results							
					FG	Pre PG	Post PG	HbA1c	TC	TG	HDL	LDL
47	Non-obese healthy volunteers	36	21.6g	4 weeks	↗ *				↘	↘ *	↘	↘ *
41	overweight or obese	38	70 g	30 days	↘				↘ *	↘	↗ *	↘ *
43	Healthy	8	80g	2 weeks	↘ *				↘ *	↘ *	↗ *	↘ *
42	Healthy	24	GI= 60%	1 week	↘	-	↘					
44	Healthy	33	75g	acute			↘					
45	Healthy	12	20g	acute			↘					
46	Healthy	14	450 kcal	acute			↘					
48	Type 1DM	50		acute			↘					
45	Type 1DM	8	20 g	acute			↘					
49	Type 1DM	20	0.5ml/kg/d	12 weeks	↘		↘	↘ *	↘	↘		↘
54	Type 2DM	48	1-2.5 g/kg/d	8 weeks	↘ *			↗	↘	↘	↗	↘
43	Type 2DM	7	90g	acute			↗ *					
53	Type 2DM	12	53.5 g	40 days	*			*	↘		↗ *	↘
42	Type 2DM	16	GI= 60%	1 week	↘	-	↘					
45	Type 2DM	6	20g	acute			↘					
50	IGT/DM	30	-	acute			↘					
52	Type 2DM	12	33g	acute			↗			↘		
51	Type 2DM	21	20g	acute			↗ *					
This study	Type 2DM	33	10g	10 weeks	=	=	↗ *	↗	↘	↘	↗	↘
43	dyslipidemia	11	75g	2 weeks					↘			↘
55	High TC	60	75g	14 days					↘ *	↘*	↗ *	↘ *

[*] Non-significant effect, [=] no change, [IGT] impaired glucose tolerance, [FG] fasting glycaemia, [Pre PG] pre-prandial glycaemia, [Post PG] postprandial glycaemia, [Fruct] fructosamine, [TC] total cholesterol, [TG] triglycerides, [GI] glycemic index. For reference (54) they used 1 then 2.5 g/kg/d.

Honey improved lipid profile, but not significantly. Total cholesterol and triglycerides decreased respectively from 1.79±0.37 g/l to 1.71±0.32 g/l and from 1.12±0.47 g/l to 1.01±0.48 g/l. LDL cholesterol did not change (1.11±0.38 g/l to 1.02±0.28 g/l) and HDL cholesterol increased from 0.46±0.13 g/l to 0.49±0.06 g/l (Table 3).

Discussion

Natural honey contains at least 181 constituents including carbohydrates and bioactive substances such as phenolic acids, flavonoids, carotenoid derived compounds, nitric oxide (NO) metabolites, ascorbic acid, vitamins, enzymes, amino acids, …(7). Honey is used in medicine since ancient times till today, and several studies demonstrated an effective role of honey in different diseases leading to cardio protective [8-10], hypoglycemic [11], antioxidant [7,12,13], anti-inflammatory [14], and antitumor effects [13,15,16]. Antioxidant substances present in honey come from a variety of sources, and contain vitamin C, monophenolics, flavonoids, and polyphenolics [7, 17]. Through the synergistic action of these antioxidants, honey can reduce and remove the reactive oxygen species (ROS). Consequently, it may lower risks and effects of free radicals [18, 19].

Numerous studies showed a beneficial effect of honey in the development of various cancers by inducing cells' apoptosis [15]. On another hand, it is shown that moderate intake of antioxidants is beneficial in cancer treatment

[20].

Honey reduces the risk of cardiovascular diseases, it has beneficial effects in acute as well as in chronic administration [21,22]. Honey has protective effects against ischemia/reperfusion injuries in isolated rat heart [9], and it produces anti-arrhythmic effects during ischemia. Those effects seem to be more efficient with low concentrations of honey [22].

Experimental studies showed that honey induces lower glycemic response in both diabetic and non-diabetic rabbits [23-25]. However, according to Fasanmade *et al*., this effect is positive only in diabetic rats [26].

Honey supplementation reduces significantly blood glucose concentrations in alloxan-induced diabetic rats [24,26,27], but also in streptozotocin-induced diabetic rats [27]. Nevertheless, according to Sani *et al*., this reduction is not significant [28]. It seems that honey's hypoglycemic effect is positive even with low doses [25]. Some studies indicated that adding honey to glibenclamide or metformin in diabetic rats may improve glycemic control [23, 24]. On the other hand, honey produces a significant increase in insulin levels [23, 24] and has a cyto-protective effect against hyperglycemia on hamsters' beta cells [29].

In healthy sheep, honey improves lipid abnormalities, except for triglycerides (TG) [30] Whereas, in rats, HDL-cholesterol increases significantly in honey-fed rats compared with rats fed with sucrose or on sugar free diet, but no other differences in lipid profiles were found [31]. In streptozotocin-induced diabetic rats, honey supplementation increases significantly HDL cholesterol while it reduces TG and very low density lipoprotein (VLDL) cholesterol [24]. On the other hand administration of natural honey decreases significantly TG, VLDL and LDL cholesterol levels and increases the levels of HDL cholesterol in diabetic rats compared to diabetic control rats and diabetic rats treated with Metformin alone [23,27].

For honey long-term administration, data are scarce. Erejuwa indicates that administration of honey to streptozotocin-induced diabetic rats reduces significantly fructosamine serum concentrations [24], and the study done by Chepulis, in non-diabetic rats, shows that honey feeding for 52 weeks leads to a significant reduction in glycosylated hemoglobin (HbA1c) [31]. Furthermore, Erejuwa who worked on streptozotocin-induced diabetic rats suggested that honey can prevent diabetes mellitus late complications [32].

Glycemic index (GI) of natural honey varies from 32 to 85%, and it depends on its botanical sources. It is lower than many other carbohydrates contrary to what many people think [33,34], as the one which we have used in our study.

In literature, few studies have tested the safety of natural honey in diabetic patients despite encouraging results in animals. Table 4 summarizes studies that reported honey effects on healthy people and on patients with diabetes mellitus or dyslipidemia.

In healthy volunteers, honey reduces significantly fasting blood glycaemia [35,36], it attenuates postprandial glycaemia in acute administration after four weeks [36,37,38], and it increases plasma insulin and C-peptide levels too [36,39,40]. On another hand, several studies showed that natural honey decreases total cholesterol, triglycerides and LDL cholesterol, although the reduction was not constantly and statistically significant [35,39,40]. Regarding the HDL cholesterol, Derakhshandeh-Rishehri *et al* have demonstrated an unfavorable effect [40]. Therefore, further prospective investigations are necessary to clarify these findings.

In patients with type1 DM, honey decreases significantly fasting glycaemias, attenuates postprandial glycemias [41-43], and increases C peptide levels [42,43]. Furthermore, in long term administration, Abdulrhman demonstrated that honey can significantly reduce HbA1c levels 12 weeks after honey intake (0.5 ml/kg/day) [43]. Regarding HbA1c, our results are in total disagreement with Abdulrhman's. The difference can be explained by the chemical composition of honeys or by the mechanism of DM itself as type1 DM is different from type 2.

For lipids profile, we found only a single study done in type 1 DM that shows a significant decrease in total cholesterol, triglycerides and low-density lipoproteins (LDL) [43]. However, due to the small number of samples, further studies are expected to confirm honey benefic effect.

In patients with type 2 DM, several studies have shown that honey can significantly reduce postprandial glycemias or elicits much lower rise in plasma glucose than with other sugars or sweeteners [36,39,41,44,45]. Therefore, natural honey may be a precious sugar substitute for subjects with impaired glucose tolerance or mild diabetes [44]. Our results seem to confirm this action as our patients' postprandial glycemias do

not increase after honey intake. Al-Waili *et al* and Katsilambros *et al* have also tested the safety of honey in patients with type 2 DM. Those authors demonstrated that honey was safe as it improved glucose tolerance and reduced insulin resistance [36,46].

For chronic administration, Whitfield *et al* have compared twelve individuals with type 2 DM who received 53.5g of honey daily, with a control group who did not have honey. They found no difference in fasting glucose, HbA1c, and fasting insulin between the two groups [47]. However, Bahrami's study demonstrated that 8 weeks of honey consumption can provide a significant increase in HbA1c levels [48]. Our results are similar to Bahrami's as HbA1c increase in 60% of our population after 10 weeks of honey administration, contrary to fasting glycaemia and postprandial glycaemia which remained stable. HbA1c rise can be explained by the increase in pre-prandial glycemias.

Regarding lipid modifications, our results are in agreement with those of other authors who proved that honey has a beneficial effect on lipid profile as there were a significant reduction in total cholesterol, TG and LDL cholesterol, and an increase in HDL [47, 48]. The same findings were observed in patients with high cholesterol level before honey use, although the results were not statistically significant [49].

Conclusion

Chronic intake of natural honey increases glycaemia of diabetic patients, but it can improve their lipid profile. Thus, diabetics can consume small quantities of honey, less than 10 g per day, to take other advantages of honey which have been proven by several studies. Furthermore, knowing that all drugs existing today are of limited efficacy, diet remains the first line against diabetes. Nevertheless, more studies are expected to investigate whether honey can be beneficial to diabetics; if it can improve beta cell function, if it can attenuate insulin-resistance and if it protects diabetics against chronic complications.

Conflict of interest

The authors declared no potential conflicts of interest.

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