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Plasma glucose level decreases as collateral effect of fermented papaya preparation use

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Riassunto

Premesse. Il perparato di papaia fermentata (FPP) è considerato un farmaco sano e naturale di largo uso in Giappone e nelle isole Filippine. Questo integratore alimentare svolge azione antiossidante, inibisce gli effetti dannosi provocati dall'ossidazione sia a carico del DNA che dei tessuti, essendo un potente "spazzino" di OH. Il largo consumo di preparati a base di FPP, specialmente da parte degli anziani, ci ha fatto notare un effetto collaterale misconosciuto, almeno fino ad ora. Abbiamo notato infatti, che in alcuni casi, l'uso di FPP, si accompagna ad una diminuzione del tasso glicemico, specialmente durante le ore pomeridiane.

Scopo del presente lavoro è stato quello di verificare, in maniera scientifica, la possibilità che le persone che assumono l'FPP possano avere una diminuzione dei livelli plasmatici di glucosio.

Materiali e Metodi. A questo scopo sono stati reclutati 50 soggetti divisi in due gruppi. Il primo gruppo è costituito da 25 pazienti (13 di sesso femminile e 12 di sesso maschile), affetti da diabete mellito tipo 2 in trattamento con antidiabetici orali (glibencamide). Il secondo gruppo (controllo) è costituito da 25 soggetti sani, comparabile, per sesso ed età, al primo. A tutti i soggetti sono stati somministrati 3 grammi di FPP al dì, durante il pranzo per due mesi.

Risultati. I risultati ottenuti confermano quello che si era notato in maniera empirica e che cioè, l'uso dell'FPP può indurre una significativa diminuzione dei livelli plasmatici di glucosio sia nei soggetti diabetici che in quelli sani di controllo. L'effetto ipoglicemizzante è stato tale da indurre, in alcuni casi di pazienti diabetici, la riduzione della posologia della glibencamide (un paziente ha addirittura sospeso l'antidiabetico orale).

Conclusioni. I risultati ottenuti suggeriscono che l'uso di FPP può essere un utile ausilio terapeutico nella terapia ipoglicemizzante orale.

Parole chiave: *diabete mellito tipo 2, ipoglicemia, papaia fermentata*

Abstract

Aim. Fermented Papaya Preparation (FPP) is a natural healthy drug that has been commercially sold in Japan and Philippines. This nutricetive, bio-normalizer product has antioxidant action, inhibitory effect on oxidative DNA damage and tissue injury, being a potent OH scavanger. The wide use of FPP, expecially by elderly people, made us note an unknown collateral effect, i.e., blood sugar level dropping signs especially in the afternoon. The aim of the present work was to scientifically verify the possibility that individuals, who are taking the nutriceutical FPP, might have a decrease of plasma sugar levels.

Materials and Methods. For this purpose, 50 subjects, divided in two groups, were enrolled. The first group was made of 25 patients: 13 females and 12 males affected by type-2 diabetes mellitus under treatment with the oral antidiabetic drug, glybenclamide. The control group included 25 clinically-healthy subjects: 16 females and 9 males, matching in age. All subjects were given 3 grams of FPP daily, during lunch, for two months.

Results. The results of this study confirmed the empirical experience that FPP use can induce a significant decrease in plasma sugar levels in both healthy subjects and type 2 diabetic patients. This hypoglycaemic effect, associated with clinical signs, induced the diabetic patients to reduce the dosage of their antidiabetic oral therapy (in one patient the therapy was really suspended).

Conclusions. In accordance with these results, the FPP administration is suggested as an adjuvant drug to join the oral antidiabetic therapy in type 2 diabetes meltus.

Key words: *diabetes mellitus type 2, fermented papaya preparation, hypoglycemia*

Introduction

Fermented Papaya Preparation (FPP), is a natural health drug commercially sold in Japan and Philippines, that is made by yeast fermentation of the tropical fruit Carica Papaya Linn.

This nutricetive, bio-normalizer food is regarded as a drug in that it has an antioxidant action. FPP (50 mg/ml) scavanges 80% of hydroxyl radicals and it may be a prophylactic dietary supplement against the age-related and neurological diseases associated with free radicals (1).

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Some authors were able to show that FPP, as a strong OH scavanger, significantly inhibits thiobarbituric acid reactive substances formation in iron-induced seizure focus of rats (2). Additionally, it has been observed that FPP promote a decrease in monoamine metabolites released in iron-induced epileptogenic focus in the rats, while iron-induced lipid peroxidation relates to the turnover rate of monoamines and seizures (3). In 2001, a significant improvement in the scopolamine-induced impairment of short and long-term memory in mice by FPP oral administration was demonstrated (4).

The oral administration of the FPP for 4 weeks was seen to decrease lipid peroxide levels in the ipsilateral 30 min after injection of iron solution by iron into the left cortex of rats (5). An inhibitory effect of FPP on oxidative DNA damage and tissue injury in the brain caused by iron-induced epileptogenesis in rats was shown (6, 7).

A recent study in patients with Parkinson's disease presents, in turns, some evidence convincing for a neuroprotective effects of FPP, although its action on dopamine levels needs further investigation (8). FPP can also modulate immunological responses. As a matter of fact, there is a study showing that FPP exerts both immunomodulatory and antioxidant activity on the macrophage cell line RAW 264 (7), since in these cellular lines induces an increase in nitric oxide synthesis and TNF-α secretion (9).

Many other properties of FPP, as its antibacterial activity (10), or its role as potential chemopreventive agent in HP-eradicated atrophic gastritis patients (11) were shown.

Anecdotically speaking, in June 2002 Nobel Prize Luc Montagnier met the Pope Jean Paul II and prescribed him an experimental concoction of fermented Asian papayas, which he claimed could stimulate the immune system and mop up free radicals. Montagnier believes that free radicals play a role in many chronic diseases and could be used to treat conditions such as Parkinson's disease (12). Observers have remarked on a spectacular improvement in the Pope's health, especially his speech, during his trips to Canada and Poland (12). Newspapers emphasized this event and from that point in time many people have started taking drugs which contained fermented papayas.

The wide use of FPP, especially by elderly people, made us empirically note an unknown collateral effect of FPP. Some people, in fact, presented signs of blood sugar level dropping, especially in the afternoon. The aim of the present work is, thus, to verify scientifically the possibility that people who are taking the nutriceutical drug FPP have dropping levels of sugar in the plasma.

Materials and Methods

The present investigation was performed on 50 subjects, divided in two groups (25 subjects each). The first group was made of 25 subjects, 13 females and 12 males (mean age= 72.88 ± 4.39 years), affected by type-2 diabetes mellitus and treated with the oral anti-diabetic drug (OAD), glybenclamide. The control group included 25 clinically-healthy peoples, 16 females and 9 males (mean age = 75.08 ± 3.64 years), whose personal and family history was not indicative for cases affected by diabetes mellitus. All the enrolled subjects signed consent forms.

According to the protocol, each subject received 3 grams of FPP, daily, at lunch time, for two consecutive months. In diabetic people a mean of baseline fasting glucose levels and postprandial glucose levels taken two hours after lunch in one month, were considered. In healthy subjects a single determination of sugar plasma levels at fasting and two hours after lunch was considered. During FPP administration, sugar plasma determination at fasting and two hours after lunch were repeated every week in all subjects for two months.

The sugar plasma levels obtained before and after assumption of FPP were expressed as mean ± standard deviation. The t-Student test was used to compare the eventual difference in sugar plasma levels before and after FPP consumption. A p value ≤ 0.05 was considered as statistically significant.

Results

Clinically-healthy subjects

As shown in Figure 1, fasting sugar plasma levels (the two bars on left) were equal to 92.36 ± 6.4 mg/dl before FPP use, and to 88.64 ± 7.42 mg/dl after FPP use. Such a difference was found to be statistically not significant ($p = 0.06$). Post-meal plasma glucose levels (the two bars on right) were equal to 156.96 ± 8.45 mg/dl before FPP use, and to 144.84 ± 22.07 mg/dl after FPP use. Such a difference was found to be statistically significant ($p = 0.01$).

In detail, five out of these clinically-healthy subjects needed particular attention, after one month of FPP use, in the mid afternoon (at about 6 p.m.), because of the fact that they showed clear hypoglycaemic signs, caused by levels of plasma glucose on average at 60 mg/dl.

Type 2 diabetic patients

As shown in Figure 2, fasting sugar plasma mean levels (the two bars on left) were equal to 144.64 ± 12.22 mg/dl before FPP use, and to 125.36 ± 18.81 mg/dl after FPP use. Such a difference was found to be statistical significant ($p<0.001$). Post-meal plasma glucose levels (the two bars on right) were equal to 184.68 ± 20.98 mg/dl before FPP use, and to 166.48 ± 21.36 mg/dl after FPP use. Such a difference was found to be statistically significant ($p<0.005$).

In detail, eight patients needed to lower the glybenclamide dose, and, interestingly, one patient could suspend the OAD therapy.

Discussion

The results of this scientific study confirm our empirical observation that the use of FPP can induce dropping of fasting and post meal plasma sugar levels. Such a phenomenon systematically occurs in both the healthy subjects and non-insulin dependent diabetic patients.

Additionally, the present results, examined on a personal basis, indicate that the FPP use can induce a substantial decrease of circulating glucose during the mid-afternoon hours is some of the clinically-healthy and diabetic patients

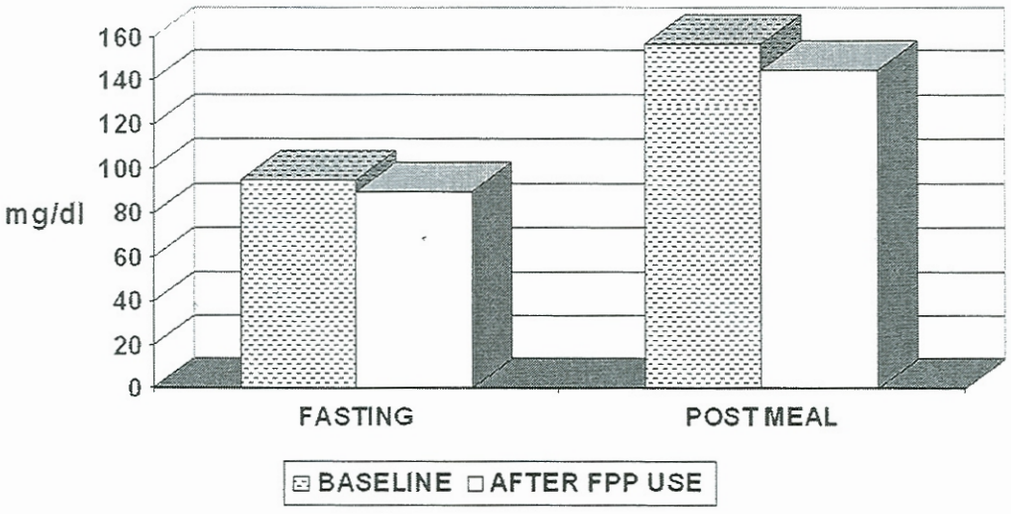

Fig. 1. Fasting and post-meal plasma glucose mean levels in clinically-healthy subjects, before and after two months of use of a Fermented Papaya Preparation (FPP). The differences for plasma glucose levels before and after FPP use are not significant for fasting levels ($p = 0.06$), and significant for post meal levels ($p = 0.01$).

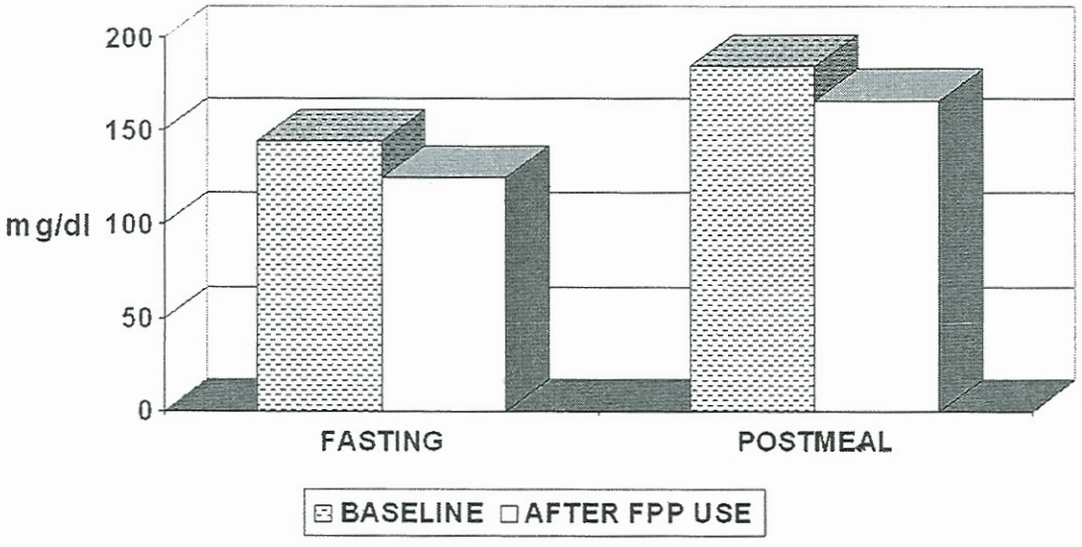

Fig. 2. Fasting and post-meal plasma glucose mean levels in type 2 diabetic patients, before and after two months of use of a Fermented Papaya Preparation (FPP). The differences for plasma glucose levels before and after FPP use are significant for both the fasting levels ($p < 0.001$), and post meal levels ($p < 0.005$).

investigated. Because of this FPP-induced effect on the carbohydrate metabolism, some of the diabetic patients were obliged to reduce the dosage of OAD that they were taking, already for a long time, and, more surprisingly, one of the diabetic patient had the unexpected opportunity to suspend such a therapy.

This clinically-oriented investigation makes us not capable to explain the mechanisms by which the FPP exerts its hypoglycaemic effects. Speculatively and tentatively, it can be said that the oxidative stress and the circulating glucose levels are closely correlated (13). In fact, in order to decrease the number of diabetes complications and to postpone their development, the use of biologic active component and plants is already recommended. The most important biologic active substances for this purpose are vitamins and minerals, lectins, saponins and flavonoids. According the literature data, the mostly used plants are: Ginkgo biloba, Allium sativum, Silybum marianum, Panax Ginseng, Carica papaya, Vaccinium myrtillus, Phaseolus vulgaris. All these plants are proposed, as adjuvants, for treatment of diabetic complications for their ability to stabilize membrane through antioxidant and radical scavenging actions (14).

However, whatever the mechanism might be, the present study authorizes us to declare that the FPP, in that is able to lower the circulating levels of glucose in fasting and post meal conditions, could be used as an adjuvant drug in the

treatment of type 2 diabetes mellitus, with the secret hope that its continuative administration could help in ameliorating the carbohydrate metabolism, letting the dosage of the OAD to be in some way reduced or, even more fortunately, revoked.

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