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EFFECT OF LOW GLYCAEMIC INDEX MEALS ON INSULIN SECRETION IN DIABETIC AND APPARENTLY HEALTHY SUBJECTS

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ABSTRACT
One of the potential effects of low glycaemic index (low-GI) diets is to reduce insulin secretion in patients with type 2 diabetes. The effects of low GI meals (Acha, Rice and Eba) on serum insulin were elicited in diabetic type 2 subjects. Ten diabetic and 6 healthy individuals participated in the study. Fasting blood samples were taken and after consumption of the reference (glucose) and test meals (Acha, Rice and Eba) every 30 minutes until two and half hours post - consumption. Serum blood glucose level was determined using glucose oxidase method while insulin level was determined using Enzyme-Linked Immunosorbent Assay (ELISA). Insulin responses to the various meals in the diabetic subjects were initially lower ($p<0.05$) compared to those in the control and also the insulinogenic indices were significantly lower in the diabetics than the control ($p<0.05$). In the type 2 diabetic patients however, despite higher increments of serum glucose, only modest changes of plasma insulin occurred initially but later the insulin responses continued to increase up to two and half hour but the hyperglycaemia continued leading to a much lower ratio. This is to show that there is a state of impaired pancreatic beta-cell function since insulinogenic index is a measure of β -cell secretary function and also the insulin produced is not effective. Therefore, diabetic individuals consuming low glycaemic meals may not be producing effective insulin to clear the hyperglycaemia being produced by these meals.
Keywords: type 2 diabetics, low glycaemic index, insulin, insulinogenic indices

INTRODUCTION

Dietary intake can influence insulin levels, especially among individuals who are insulin resistant due to factor such as obesity. Dietary glycaemic load (GL), which is a quantitative measure of the glycaemic effect of food, has been associated with triglycerides and high-density lipoprotein levels (Brand-Miller, 1994: Liu *et al.,* 2001and Ford and Liu, 2001), as well as the risk of diabetes (Salmeron *et al.,* 1997a; Salmeron *et al.,* 1997b) and heart disease (Liu *et al.,* 2000). Postprandial insulin responses are not always proportional to blood glucose concentrations or to a meal's carbohydrate content (Holt *et al.,* 1997). It has been shown that when low-glycaemic carbohydrates are incorporated into an energy-deficient diet, there is a greater fall in insulin resistance than can be accounted for by weight loss alone (Slabber *et al.,* 1994).

One of the potential effects of low-GI diets is to reduce insulin secretion in patients with type 2 diabetes and to reduce daily insulin requirements in patients with type 1 diabetes. Wolever *et al.* (1994) observed a 30% reduction in urinary C-peptide levels in subjects with type 2 diabetes on a low-GI diet, indicating reduced endogenous insulin demand. The wider implementation of a low-GI diet will depend on the continuing identification of low-GI foods.

Diets with a low-GI or glycaemic load elicit lower postprandial insulin responses and produce better clinical outcomes compared with diets with higher GI or GL (Mckeown *et al.,* 2004; Barclay *et al.,* 2008; Reynolds *et al.,* 2008). Carbohydrate counting and knowledge of the GI of foods provide the most accurate prediction of likely insulin response (Kaufman *et al.,* 1999; Gilbertson *et al.,* 2001). A physiologic basis for classifying all foods according to their postprandial insulin response is of both theoretical and practical significance. In individuals at risk of developing type 2 diabetes, diets that provoke excessive insulin secretion may increase oxidative stress and accelerate the course of β - cell failure (Porte, 2001).

Although carbohydrate is the primary stimulus for insulin secretion, it is not the only one. Protein-rich foods also elicit a significant insulin response and, when combined with carbohydrate, act synergistically to raise insulin concentrations and reduce glycemia (Gannon *et al.,* 1988). Similarly, addition of fat to a carbohydrate rich meal reduces postprandial glycemia but not the insulin response (Gannon *et al.,* 1993; Collier *et al.,* 1988). Several insulinotropic factors are known to potentiate the stimulatory effect of glucose and mediate postprandial insulin secretion. These factors include specific amino acids and fatty acids and gastrointestinal hormones such as gastric inhibitory polypeptide, glucagon-like peptide 1, glucagon, and cholecystokinin (Collier *et al.,* 1988; Frid *et al.,* 2005).

Evidence has accumulated during the last decade on the significant roles of both decreased insulin sensitivity and β -cell dysfunction in the pathogenesis of type 2 diabetes mellitus (DM).

Both insulin secretion and insulin sensitivity are genetically and environmentally controlled and the impairment of both has individually or together been associated with increasing risk of developing type 2 DM (Pimenta *et al.,* 1995; Polonsky *et al.,* 1996; Weyer *et al.,* 1999).

It has been reported that during each stage of the development of type 2 DM, decreased insulin sensitivity and insulin secretory dysfunction are independent predictors of worsening glucose tolerance (Weyer *et al.,* 2001). Indeed, fasting hyperinsulinaemia, known to reflect decreased insulin sensitivity, together with decreased insulin secretion are the strongest independent predictors of type 2 DM (Haffner *et al.,* 1997).

Therefore, the classification of the relative insulinaemic effects of different foods is of both theoretical and practical significance. Postprandial blood glucose responses have been the focus of much research because of their importance for glycaemic control in patients with diabetes. In a bid to expand the existing information on glycaemic index and insulin responses of the local meals in our nation, this study was conducted to systematically compare postprandial insulin responses to known low glycaemic index meal in diabetic and non - diabetic subjects, so that dietary variety and palatability are not compromised.

MATERIALS AND METHODS

Ten diabetic subjects and six healthy subjects participated in each meal on two different mornings after 10-12 hours fasting. Informed consent for inclusion into the study was obtained from the subjects who fulfilled the inclusion criteria. The nature of the study was explained to the subjects in the language spoken by him or her. The subjects were instructed not to change their physical activity patterns during the period of the study because that might influence peripheral sensitivity to insulin and thus might have an effect on the glycaemic and insulinaemic indices. The protocol and procedure was approved by the scientific and ethical committee of Ahmadu Bello University Teaching Hospital Shika, Zaria.

Meals

The test meals acha (*Digitaria exelis Stapf*) rice *(Oryza sativa* L*)* and eba (*Manihot esculanta* Cranz) were prepared according to the usual Nigerian methods. Food Macronutrients were calculated using food composition table by Enwere, (1998). **Analytical methods**

The fasting blood sample was collected into plain tubes and was left to clot for about 15 minutes which was promptly centrifuged at 1,500 revolutions per minute (rpm) using a centrifuge (Hettich, Universal) for 15 minutes. The serum was analyzed for glucose on the same day of collection and the remaining serum was stored in plain bottles. Sera samples were aliquots into 2 ml tubes which were kept on ice, then stored at -20°C until further analysis for insulin assay. The serum glucose concentration were determined using the enzymatic colorimetric method of Randox (Cat. no. GL 2614 Randox Laboratories Ltd., Antrim,UK) while plasma insulin concentrations were measured by a commercially available enzyme linked Immunosorbent Assay (ELISA) human insulin kit manufactured by DEMEDITEC Diagnostics GmbH D.24145 Kiel Germany (2006).

Following the fasting blood samples, the glucose (standard) solution or meals was given and completely eaten within 15 minutes by each subject. The time of complete consumption was recorded as zero minutes. Blood samples were taken at times of 30, 60, 90,120 and 150 minutes after consumption of the meals. Analysis for glucose and insulin were carried out as for the fasting.

Glycaemic index (GI)

The GI from the two and half hour glucose area of acha, rice and eba meals were determined by using standard protocol (FAO/WHO, 1998) with anhydrous glucose as the reference food (glycaemic index = 100).

Incremental areas under the concentration-time curve (IAUC) were calculated by the trapezoidal method for serum glucose (Wolever *et al.,* 1991). The IAUC obtained for glucose was considered to correspond to a glycaemic index (GI) of 100,

The glycaemic index was expressed as a percent of the response to the same amount of carbohydrate from a standard food taken by the same subject. GI values were classified as low (<55) (Brand- Miller *et al.,* 2003), and the GI of meals in both subjects were calculated based on their incremental area under the curve (IAUC) expressed relative to the reference IAUC of the glucose. The GI for each food was taken as the average of all 10 individuals' values for diabetic subjects and average of all 6 individuals' value for control subjects.

Insulinogenic index

The incremental insulin area under the curve (AUC) over 150 min for each meal was calculated according to the trapezoidal rule with the fasting concentration as the baseline (Wolever *et al.,* 1991). Area below the fasting concentration was ignored. For each subject, an individual relative insulin response was calculated by dividing the insulin AUC value for the test meal by his or her average insulin AUC value for glucose (tested twice). Insulinogenic index was calculated as the ratio incremental value of serum insulin level divided by the relative net increase of serum glucose level.

Statistical Analysis

Statistical analyses were carried out using SPSS 17.0 Software (Statistical Package for Social Sciences, Inc, Chicago, IL, USA). Data was presented as mean plus or minus standard deviation of the mean for GI, serum insulin and insulinogenic indices. Paired student t test was used to compare the effects of glucose versus meal in diabetics, glucose versus meal in healthy subjects. Unpaired student t test was used to find the differences between the healthy and diabetic subjects. The significance level was set at $P<0.05$.

RESULTS

The glycaemic index and glycaemic loads in both diabetic and control groups are shown in Table 1. The mean insulin response to acha was significantly higher in the control at 30 minutes than the type 2 diabetic subjects $p<0.05$ (Table 2).

Meanwhile the mean insulinogenic indices to acha were significantly lower at 30 - 120 minutes for the diabetic subjects than the control p<0.05 (Table 3). The overall insulinogenic index to acha was significantly lower in diabetic subjects than the control p<0.05. The fasting serum insulin level was significantly lower in the diabetic subjects than control subjects at (p<0.05) in the group that consumed eba. Also after ingestion of eba the mean serum insulin level was significantly lower at 30 minutes in the diabetic subjects than control subjects, but at 120 and 150 minutes it became significantly higher in the diabetic subjects than control subjects (p<0.05) (Table 2). The insulinogenic indices of eba meal were significantly lower in type - 2 diabetic subjects at 30 - 60 minutes than control subjects (P<0.05) (Table 3).
The mean serum insulin levels in diabetic and control subjects after consumption of rice are shown in Table 2. After the consumption of rice the control subjects had significantly higher insulin responses at 30 minutes, but by 150 minutes the diabetic subjects had significantly higher insulin production when compared to control subjects (p<0.05). The insulinogenic indices were significantly lower in the diabetics from 30 -120 minutes than control subjects (p≤0.05) (Table 3).

Table 1: Glycaemic indices and glycaemic loads of meals fed to diabetic and control subjects

	Glycaemic Index N = 10		Glycaemic Load# N = 6	
Meals	**Diabetes subjects**	**Control subjects**	**Diabetes subjects**	**Control subjects**
Acha	49.28±11.52	35.38±22.32	24.5	17.5
Rice	52.14±8.11	40.24±16.43	26.0	20.0
Eba	52.51±6.45	49.87±10.38	26.5	25

Values are presented as mean ± standard deviation. # = values are calculated from the GI. N = number of subjects

Table 2: Mean serum insulin level of Type 2 diabetics and control subjects fed with Acha, Rice, and Eba meals

	Diabetic subjects N -10			Control subjects N = 6		
Time (Min)	**Acha meal**	**Rice meal**	**Eba meal**	**Acha meal**	**Rice meal**	**Eba meal**
0	4.03±0.09	6.41±0.92^{b}	7.51±0.07^{s}	3.67±1.50	1.39±0.37^{b}	2.93±1.83^{s}
30	7.91±1.55^{a}	9.11±1.15^{c}	9.90±0.95^{d}	24.27±9.91^{a}	38.25±15.17^{c}	43.64±10.67^{d}
60	11.39±2.83	10.12±1.28	15.95±2.25	19.02±7.77	18.25±4.86	27.81±6.98
90	16.23±3.80	13.30±3.18	20.72±3.28	15.78±6.44	13.64±4.28	16.93±3.91
120	10.27±1.87	17.12±3.30	26.38±4.27^{f}	12.07±4.93	12.42±4.15	10.46±3.34^{f}
150	17.62±5.17	20.07±5.12^{e}	29.05±5.55^{g}	7.51±3.07	4.77±2.72^{e}	5.34±2.90^{g}

Values in µIU/ML are means ± SD. Values in the same row with same superscripts are significantly different (p<0.5). N = number of subjects

Table 3: Insulinogenic indices of Type 2 diabetics and control subjects fed with acha, rice, and eba meals

	Diabetic subjects			Control subjects		
Time (Min)	**Acha meal**	**Rice meal**	**Eba meal**	**Acha meal**	**Rice meal**	**Eba meal**
30	0.84±0.32^{a}	0.53±0.10^{b}	0.57±0.24^{c}	15.54±5.33^{a}	20.76±9.68^{b}	25.03±10.90^{c}
60	1.18±0.43^{d}	0.38±0.08^{e}	1.41±0.40^{f}	6.48±1.93^{d}	7.93±3.89^{e}	9.88±3.16^{f}
90	1.80±0.49^{g}	0.67±0.26^{h}	2.49±0.99	8.38±3.82^{g}	3.48±1.41^{h}	6.19±3.09
120	1.06±0.43^{k}	1.43±0.38^{l}	2.26±0.72	6.03±2.16^{k}	4.84±1.59^{l}	4.02±1.76
150	1.63±0.66	3.02±1.11	5.13±1.77	2.50±1.48	1.99±1.27	6.16±2.84

Values in the same row with same superscripts are significantly different (p<0.5). Values are presented as mean ± standard deviation. N = number of subjects

DISCUSSION

These three meals used in this work were reported as low glycaemic index meals by Alegbejo *et al.* (2009a, 2009b and 2011) and also all the meals had high glycaemic load. It has been shown that when low-glycaemic carbohydrates are incorporated into an energy-deficient diet, there is a greater fall in insulin resistance than can be accounted for by weight loss alone (Slabber *et al.,* 1994). Also, diets with a lower glycaemic index or glycaemic load produce better clinical outcomes and elicit lower postprandial insulin responses when compared with diets with higher GI or GL (Barclay *et al.,* 2008; Mckeown *et al.,* 2004; Reynolds *et al.,* 2008) but it was not the case in this study because the diabetic subjects responded initially to the meals by producing lower quantity of insulin and gradually increased in the production then became higher consistently compared to the control subjects.

Prolonged or high degrees of postprandial insulinemia are thought to contribute to the development of insulin resistance and associated diseases (Gannon *et al.,* 1993; Collier *et al.,* 1988 Frid *et al.,* 2005). Hyperinsulinemia, a marker of insulin resistance (Ronnemaa *et al.,* 1991), has been demonstrated to be a strong predictor for type 2 diabetes (Lillioja *et al.,* 1987; Eriksson *et al.,* 1989; Martin *et al.,* 1992; Henriksen *et al.,* 1994; Haffner *et al.,* 1995; Mykkänen *et al.,* 1993). Type 2 diabetic subjects are usually characterized by peripheral insulin resistance, β -cell failure, and increased hepatic glucose production (1988). The physiologic importance of postprandial hyperinsulinemia is unknown, particularly if the corresponding level of glycemia is low, as in this case. Hyperinsulinemia may be pathogenic when associated with dyslipidemia, hypertension, impaired fibrinolysis and other features of the metabolic syndrome (Stout, 1996).

Low GIs is characterized by slower rates of digestion and absorption in the small intestine, nutrient receptors in the gastrointestinal tract are stimulated for a longer period of time, resulting in prolonged feedback (through signals such as cholecystokinin and glucagon-like peptide-1) to the satiety center in the brain (Lavin *et al.,* 1998). Reducing the rate of digestion of carbohydrate spreads the absorption of carbohydrate along a longer portion of the small intestine (Balfour and McTavish, 1993; Jenkins and Wolever 1981), and tends to increase the amount of carbohydrate which escapes digestion in the small intestine (Jenkins *et al.,* 1981). For example, the amount of carbohydrate from lentils entering the colon is 2.5 times as great as carbohydrate from bread. Increasing the delivery of starch to the colon has many implications which include those on the health of the colon itself and on systemic metabolism. It is believed that starch entering the colon is completely and rapidly fermented, mostly in the caecum (Cummings and Macfarlane, 1991). The fermentation of starch produces relatively more butyrate than the fermentation of dietary fibre (Cummings and Macfarlane, 1991) and resistant starch produces somewhat different fermentation products than readily digested starch (Nordgaard *et al.,* 1995).

The insulin response varied between the meals in both the diabetic and the control subjects but the insulin production remained high in the diabetic subjects even at two and half hour, yet there was hyperglycaemia. Insulinotropic factors, such as protein- and fat-rich foods, may induce substantial insulin secretion despite producing relatively small blood glucose responses (Krezowski *et al.,* 1986; Peter and Davidson, 1993). In this study the meals contained all the macronutrients and this may also contribute to more insulin production. Although carbohydrate is the primary stimulus for insulin secretion, it is not the only one. Protein-rich foods also elicit a significant insulin response and, when combined with carbohydrate, act synergistically to raise insulin concentrations and reduce glycaemia (Gannon *et al.,* 1988), but the glycaemia was not reduced in the diabetic subjects. In a study comparing glucose to insulin response to foods, the authors reported that although the two scores were highly correlated, the glycaemic response accounted for only 23% of the variability in insulinaemia (Holt *et al.,* 1997). It has long been recognized that the chronic hyperglycemia associated with type 2 diabetes (glucose toxicity) leads to impairment in insulin secretion and a possible defect in glycogen synthesis but it was not the same in this study (Rosetti *et al.,* 1990).

In this study, control subjects had consistently higher mean insulinogenic indices than their type 2 diabetic subjects. Insulinogenic indices represent dynamic interactions between changing levels of plasma insulin and changing levels of plasma glucose. The control subjects expectedly had significantly and consistently higher indices than their type 2 diabetic counterparts. Nondiabetic pancreases self-regulate the amount of insulin secreted, acting in response to changes in blood glucose concentration that result from the ingestion of food. In people with diabetes, however, bolus and basal glucose levels are increased; In addition, a study of type 2 diabetic Japanese patients recently showed that decreased insulin secretion had a more pronounced impact on glucose tolerance than insulin sensitivity (Fukushima *et al.,* 2004). Both glucose toxicity and lipotoxicity have been reported to contribute to β - cell dysfunction. Furthermore, decreased β - cell function may exist already at normal fasting blood glucose levels (Godsland *et al.,* 2004).

This study showed that both β - cell dysfunction and insulin resistance may be responsible for the hyperglycaemia associated with type 2 diabetes mellitus. The clients that were enrolled prior to treatment randomization, into the United Kingdom Prospective Diabetes Study, underwent 3 months of non-pharmacological treatment with emphasis on life-style changes. Therefore, implementation of a healthier life style with an increase in physical activity and a reduction of body weight, based on the regulation of calories and fat intake, are the basis for the prevention of type 2 diabetes (Tuomilehto *et al.,* 2001; Knowler *et al.,* 2002; Laaksonen *et al.,* 2005) and the same principles apply to basic treatment of type 2 diabetes (Pastors *et al.,* 2002; Sigal *et al.,* 2004). Low-GI foods may benefit weight control in 2 ways: *1*) by promoting satiety and *2*) by promoting fat oxidation at the expense of carbohydrate oxidation. These 2 qualities of low-GI foods stem from the slower rates at which they are digested and absorbed and the corresponding effects on postprandial glycaemia and hyperinsulinemia. Even when appearance and nutrient content are matched, low-GI foods typically induce higher satiety than do their high-GI counterparts and are followed by less energy intake at subsequent meals (Ludwig, 2000).

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