Taiwanese vegetarians have higher insulin sensitivity than omnivores

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The present study was designed to examine the effects of habitual consumption of Taiwanese vegetarian diets on hormonal secretion, and on lipid and glycaemic control. Of the ninety-eight healthy female adults recruited from Hualien, Taiwan (aged 31–45 years), forty-nine were Buddhist lactovegetarians and forty-nine were omnivores. Dietary intakes were measured, and blood levels of nutrients and hormones were analysed. Vegetarians consumed less energy, fat and protein, but more fibre than the omnivores. Compared with the omnivores, the vegetarians had, on average, lower BMI and smaller waist circumference. Except for slightly lower levels of thyroxine (T4) in vegetarians, vegetarians and omnivores both showed similar levels of triiodothyronine (T3), free T4, thyroid-stimulating hormone, T3:T4 ratio and cortisol. Compared with the omnivores, the vegetarians had significantly lower levels of fasting insulin (median: 35·3 v. 50·6 pmol/l) and plasma glucose (mean: 4·7 (SE 0·05) v. 4·9 (SE 0·05) mmol/l). Insulin resistance, as calculated by the homeostasis model assessment method, was significantly lower in the vegetarians than in the omnivores (median: 1·10 v. 1·56), while β-cell function was not different between the two groups. BMI and diet were both independent predictors for insulin resistance, and contributed 18 and 15 % of the variation in insulin resistance, respectively. In conclusion, Taiwanese vegetarians had lower glucose and insulin levels and higher insulin sensitivity than did the omnivores. Diet and lower BMI were partially responsible for the high insulin sensitivity observed in young Taiwanese vegetarians.

Vegetarian diets: Thyroid hormones: Insulin: Glucagon: Insulin resistance

Both the beneficial and the adverse effects of vegetarian or plant-based diets on human health have been studied extensively during recent years. Evidence suggests that people who consume vegetarian diets have lower risks of CHD (Thorogood et al. 1994; Szeto et al. 2004), diabetes (Kawate et al. 1979; Snowdon & Phillips, 1985; Ford & Mokdad, 2001; VanDam et al. 2002), cancer (Thorogood et al. 1994) and other chronic diseases than meat eaters. The protective effects of vegetarian diets are possibly due to the presence of monounsaturated and polyunsaturated fatty acids, soya or vegetable proteins, fibre, antioxidant vitamins and a variety of phytochemicals (Segarsothy & Phillips, 1999), which are largely found in vegetables, fruits, whole grains, cereals, nuts, seeds, legumes and soyabeans (Sabate, 2003).

Although some components of Western vegetarian diets have been identified to have hypocholesterolaemic and hypoglycaemic effects, the mechanisms behind these effects remain unclear. One theory proposes that such diets may induce alterations in hormone secretion, which in turn regulate lipid and carbohydrate metabolism and change blood lipid and glucose levels. The interrelationships among diet, hormone levels (particularly thyroid and pancreatic hormones) and blood lipid and glucose concentrations have been studied, but are less clear and less consistent in man than in animals (Forsythe, 1995; Persky et al. 2002; Kuo et al. 2004). For instance, vegetarian diets – specifically their soya and vegetable proteins – have been shown to decrease cholesterol and increase glucagon levels in some studies (McCarty, 1999; Kuo et al. 2004), but to have no effect on these pancreatic hormones or cortisol concentrations in others (Persky et al. 2002). Elevated plasma thyroxine (T4) level could be one mechanism responsible for the hypocholesterolaemic effects of soya protein in animals. However, the effects of soya proteins on levels of T4, free T4, triiodothyronine (T3) and thyroid-stimulating hormone (TSH) are contradictory as reported in hypercholesterolaemic or diabetic patients (Ham et al. 1993; Jayagopal et al. 2002; Persky et al. 2002). Interestingly, Poehlman et al. (1988) found slightly but not significantly lower postprandial T3 levels in vegetarians than in non-vegetarians.

Unlike Western vegetarian diets, which consist mainly of vegetables, fruits, seeds, nuts, dairy products and eggs, a typical Taiwanese vegetarian diet includes mainly rice, grains, vegetables, fruits and significant amounts of soyabeans and soya products. We have recently reported that Taiwanese vegans or lactovegetarians have lower BMI, blood pressure, fasting plasma triacylglycerol, total and LDL-cholesterol

Abbreviations: HOMA-IR, homeostasis model assessment–insulin resistance; T4, thyroxine; T3, triiodothyronine; TSH, thyroid-stimulating hormone; WC, waist circumference; WHR, waist:hip ratio.

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levels, and LDL oxidizability than matched omnivores (Lu et al. 2000; Hung et al. 2002). However, it is not yet known whether the Taiwanese vegetarian diets have the same beneficial effect on disease prevention as do Western vegetarian diets, or whether the Taiwanese vegetarian diets’ beneficial effects on lipid and glycaemic control are hormonally mediated. Therefore, the present study was designed to examine the effects of Taiwanese vegetarian diets on hormone levels and its possible connection to hyperlipidaemic and hyperglycaemic effects observed in our vegetarian subjects (Lu et al. 2000; Hung et al. 2002). Furthermore, the prevalence of diabetes in Taiwan has increased drastically from 4.9 to 9.2% between 1985 and 1996 (Chang et al. 2000; Chou et al. 2001), which makes diabetes and CVD the leading causes of death in Taiwan. Thus, the present study may provide supportive evidence for future studies on the protective potential of Taiwanese vegetarian diets on disease prevention.

Subjects and methods

Subjects

A total of ninety-eight female subjects (forty-nine vegetarians, forty-nine age-matched omnivores) were recruited from Hualien, a city in eastern Taiwan. These subjects were initially recruited for an investigation of the effect of Taiwanese vegetarian diets on risk factors for heart disease (Lu et al. 2000; Hung et al. 2002). The majority of the vegetarians were Tzu-Chi Buddhist nuns; the omnivorous control subjects were mostly employees of local hospitals in Hualien. To be included in the present study, participants had to fulfil the following criteria: (i) aged between 31 and 45 years; (ii) premenopausal; (iii) within 120% of ideal body weight; (iv) no history of chronic disease (heart disease, diabetes mellitus, cancer, hypertension, renal disease); (v) no alcohol intake and no cigarette smoking. About 147 potential subjects were re-screened to find the ninety-eight who completed the study. Among the vegetarians, seven were vegans and forty-two were lactovegetarians who ingested less than 240 ml low-fat or skimmed milk daily. The average history of vegetarian practice was 8 years with a minimum of 2 years. The study protocol was approved by the National Health Research Institute, Taiwan, and was explained to the subjects before they gave their informed consent.

Dietary and clinical assessments

The dietary intake for both groups of subjects was assessed using a 24 h recall method, supplemented with a semi-quantitative food-frequency questionnaire. Nutrient data were calculated using a database for Taiwan food composition. Anthropometric measurements were performed on each subject, and blood samples were collected. Plasma and serum were used for routine biochemical assays and measurements of nutrients and hormones.

Laboratory measurements

Fasting plasma glucose was determined by the glucose oxidase method using a Monarch Chemistry 2000 Autoanalyzer (Instrumentation Laboratory, Oakbrook Terrace, IL, USA). Serum insulin concentration was determined by RIA (Ho et al. 1983). Glucagon levels were assayed by RIA using the DPC double-antibody glucagon kit (Diagnostic Products Corporation, Los Angeles, CA, USA). Serum concentrations of T₃, T₄, free T₄, TSH and cortisol were measured by chemiluminescent enzyme immunoassay using an Immulite automated analyser (Diagnostic Products Corporation; Bason, 1991).

Insulin sensitivity indices

Insulin sensitivity and β-cell function in the subjects were established via the homeostasis model assessment (HOMA) method developed by Matthews et al. (1985), in which fasting serum insulin (FI, µU/ml) and fasting plasma glucose (FG, mmol/l) are used:

\[ \text{HOMA–insulin resistance (HOMA-IR)} = \frac{FI \times FG}{22.5} \]

and

\[ \beta\text{-cell function (}) \%= 20 \times \frac{FI}{(FG - 3.5)} \]

Low HOMA-IR indicates high insulin sensitivity.

Statistical analyses

Data were analysed using SAS Release 8·2 for Windows (SAS Institute, Cary, NC, USA). Results are summarized as means with their standard errors unless otherwise stated. The Anderson–Darling test was performed to determine the normality of the measurements. For normal data, mean differences between vegetarians and omnivores were compared using Student’s t test. For non-normal data, in addition to means and standard errors, median values were calculated and are presented in parentheses in tables. The Mann–Whitney test, a non-parametric procedure, was conducted to compare the median values between the two dietary groups. Pearson’s correlation coefficient was used to estimate the relationship between HOMA-IR or β-cell function and other continuous variables. Multiple regression analysis was used to determine the independent predictors of HOMA-IR and β-cell function. The levels of insulin resistance and β-cell function were positively skewed and were log-transformed in the correlation analysis and the multiple regression analysis. All P values were calculated on the basis of two-sided tests. The significance level for each test was set at P<0·001, instead of 0·05, to adjust for the greater number of tests performed.

Results

Subject characteristics and daily dietary intake data are given in Table 1. Compared with the omnivores of similar age, the vegetarians had similar mean height, waist:hip ratio (WHR) and hip circumference, but had significantly lower mean weight and waist circumference (WC). BMI was relatively lower in the vegetarians than in the omnivores (P=0·025). Energy intake was slightly less in vegetarians, but the energy: weight ratio was not different between the two groups. As shown in Table 1, vegetarians consumed less protein, fat and saturated fat, but more fibre than the omnivores. The daily intakes of unsaturated fat (sum of the intakes of oleate,
linoleate and linolenate) and total carbohydrates were similar in both diet groups.

As shown in Table 2, vegetarians had significantly lower fasting serum insulin and plasma glucose levels than did the omnivores. Insulin:glucagon ratio and HOMA-IR were also significantly lower in vegetarians compared with the omnivores. However, there were no differences in fasting glucagon concentrations and β-cell function between the two dietary groups. Table 3 summarizes the serum concentrations of thyroid hormones and cortisol in vegetarians and omnivores. Vegetarian diets had no effects on serum T3, free T4, TSH levels or T3:T4 ratio, but led to a small decrease in T4 concentration among the vegetarians.

For each of the two dietary groups, Pearson’s correlations were calculated for BMI, WC and WHR with each of the following variables: plasma glucose, serum insulin, insulin:glucagon ratio, HOMA-IR and β-cell function (Table 4). For both vegetarians and omnivores, BMI was found to correlate positively with serum insulin (rveg 0.413; romni 0.323) and with HOMA-IR (rveg 0.395; romni 0.345). A significant positive correlation between BMI and insulin:glucagon ratio was found only in omnivores (r 0.337). β-Cell function was not significantly correlated with BMI, WC or WHR in either dietary group. The pattern of correlations between BMI and the variables described earlier was essentially similar to the pattern of correlations between these variables and WC for both dietary groups. However, there were no statistically significant correlations found between these variables and WHR in either vegetarians or omnivores (data not shown).

Table 5 shows that the percentage increase in HOMA-IR associated with a one-unit increase in BMI is 7 (i.e. e0.065 2 1), while adjusting for type of diet in the regression analysis. As for the effect of diet, the insulin resistance of vegetarians was 30% (i.e. e 0.372 2 1), significantly lower than...
that of omnivores when BMI was held constant. The incremental coefficients of determination ($\Delta R^2$) indicated that BMI alone can explain 18% of the variation in insulin resistance, and that diet increased the percentage of explained variation by 15 from 18 to 33%. The percentage increase in $\beta$-cell function associated with a one-unit increase in BMI was 4, while controlling for the effect of diet in the regression model. Although the dietary effect on $\beta$-cell function was not significant in the analysis, the $\beta$-cell function of vegetarians was estimated to be 12% lower than that of omnivores, when BMI was held constant. The incremental coefficients of determination indicate that BMI alone could account for 7% of the variation in $\beta$-cell function, and that diet increased the percentage of accounted variance by merely 2.

### Discussion

One important finding in the present study is that Taiwanese vegetarians had significantly lower fasting glucose and insulin levels, and lower insulin:glucagon ratio, than did the omnivores. It is known that insulin levels and insulin:glucagon ratio are positively correlated with serum cholesterol levels (Sanchez et al. 1988; Sanchez & Hubbard, 1991). The insulin:glucagon ratio is also sensitive to the plasma amino acid levels that are affected by dietary proteins. Several studies (Sanchez et al. 1983; McCarty, 1999) and our previous report (Hung et al. 2002) have demonstrated reduced levels of lysine, leucine, valine and phenylalanine, all of which stimulate insulin release, in people who consume a vegetarian diet or diet rich in soya protein. Taken together, our data seem to support

### Table 3. Serum levels of thyroid hormones and cortisol in vegetarians and omnivores* (Mean values with their standard errors)

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Vegetarians (n = 49)</th>
<th>Omnivores (n = 49)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Median</td>
</tr>
<tr>
<td>$T_3$ (nmol/l)</td>
<td>1.6</td>
<td>1.61</td>
</tr>
<tr>
<td>$T_4$ (nmol/l)</td>
<td>101.5</td>
<td>2.47</td>
</tr>
<tr>
<td>$T_3/T_4$</td>
<td>0.017</td>
<td>0.001</td>
</tr>
<tr>
<td>Free $T_4$ (pmol/l)</td>
<td>15.3</td>
<td>0.48</td>
</tr>
<tr>
<td>TSH (mU/l)</td>
<td>1.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Cortisol (nmol/l)</td>
<td>267.4</td>
<td>262.1</td>
</tr>
</tbody>
</table>

$t_3$, triiodothyronine; $T_4$, thyroxine; TSH, thyroid-stimulating hormone.

* Student’s $t$ test and the Mann–Whitney test were used respectively for normal and non-normal data, where medians are also shown.

For details of subjects and procedures, see p. 131.

### Table 4. Correlations of log-transformed plasma glucose, serum insulin, insulin:glucagon ratio, homeostasis model assessment–insulin resistance (HOMA-IR) and $\beta$-cell function with BMI and waist circumference (WC) in vegetarians (n = 49) and omnivores (n = 49)

<table>
<thead>
<tr>
<th>Variable</th>
<th>BMI</th>
<th>WC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vegetarians</td>
<td>Omnivores</td>
</tr>
<tr>
<td></td>
<td>Vegetarians</td>
<td>Omnivores</td>
</tr>
<tr>
<td>Plasma glucose</td>
<td>0.082</td>
<td>0.178</td>
</tr>
<tr>
<td>Serum insulin</td>
<td>0.413*</td>
<td>0.323*</td>
</tr>
<tr>
<td>Insulin:glucagon‡</td>
<td>0.258</td>
<td>0.357*</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.395**</td>
<td>0.345*</td>
</tr>
<tr>
<td>$\beta$-Cell function</td>
<td>0.262</td>
<td>0.206</td>
</tr>
</tbody>
</table>

Significance of Pearson’s correlation coefficients: *$P < 0.05$, **$P < 0.01$.

‡ Subject number: forty vegetarians, thirty-six omnivores.

For details of subjects and procedures, see p. 131.

### Table 5. Multiple regression analysis of log-transformed homeostasis model assessment–insulin resistance (HOMA-IR) and $\beta$-cell function using diet and BMI as independent predictors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Regression coefficient ($\beta$)</th>
<th>SE</th>
<th>$P$</th>
<th>Exponential regression coefficient ($e^\beta$)</th>
<th>$\Delta R^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOMA-IR (n = 98)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.065</td>
<td>0.017</td>
<td>&lt; 0.001</td>
<td>1.07</td>
<td>0.179</td>
</tr>
<tr>
<td>Diet: vegetarian v. omnivore</td>
<td>-0.372</td>
<td>0.081</td>
<td>&lt; 0.001</td>
<td>0.70</td>
<td>0.149</td>
</tr>
<tr>
<td>$\beta$-Cell function (n = 98)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.043</td>
<td>0.019</td>
<td>0.023</td>
<td>1.04</td>
<td>0.070</td>
</tr>
<tr>
<td>Diet: vegetarian v. omnivore</td>
<td>-0.132</td>
<td>0.091</td>
<td>0.151</td>
<td>0.88</td>
<td>0.020</td>
</tr>
</tbody>
</table>
Higher insulin sensitivity in vegetarians

an interrelationship between Taiwanese vegetarian diet, reduced insulin level and insulin:glucagon ratio, and decreased blood cholesterol concentration.

Insulin resistance is a fundamental abnormality in the pathogenesis of type 2 diabetes (Shen et al. 1988; Li et al. 2003) and in the development of atherosclerotic CVD (Reaven, 1988). In the present study, a significantly lower insulin resistance, or higher insulin sensitivity, was found in our young vegetarians than in the omnivores. These results are similar to those reported recently in a study of older (>50 years old) Chinese male and female ovo-lactovegetarians in Taiwan (Kuo et al. 2004). In our study, insulin resistance was evaluated by two reliable methods for normoglycaemic subjects, namely HOMA-IR and fasting insulin level (Monzillo & Hamdy, 2003). The values obtained from these two methods were well correlated with one another in either dietary group and in the combined group. Log-transformed HOMA-IR was highly correlated with fasting insulin levels previously observed in our vegetarians (Lu et al. 2000; Hung et al. 2002) may not have been caused solely by the soya protein content in the diets, but was rather due to the combined effects of various food components in the diet on cholesterol levels. Furthermore, the mechanism behind the hypolipidaemic effect of Taiwanese vegetarian diets is probably via pathways on insulin secretion as discussed earlier, rather than via effects on T₄.

It is not clear why T₄ levels were lower in the vegetarians than in the omnivores. Apparently, it is not due to the lower body weight of the vegetarians since body weight has been shown to correlate positively with serum T₄, but not with T₃ (Bray et al. 1976). Although decreased T₃ levels could result from abnormal thyroid function, malnutrition or increased glucocorticoid concentration, there were no signs of malnutrition in our subjects, and they all had normal levels of cortisol, T₃, T₄, free T₃ and TSH.

Dietary factors, such as macro- and micronutrients in the diet, are known to influence insulin sensitivity. A diet containing high levels of fat or saturated fat, high n-6:n-3 ratio or high levels of mono- and disaccharide carbohydrates tend to decrease insulin sensitivity (Daly et al. 1997; Storlien et al. 2000), while a diet rich in mono- or polyunsaturated fat or fibre may increase insulin sensitivity in normoglycaemic subjects (Fukagawa et al. 1990; Storlien et al. 2000). As Table 1 shows, the Taiwanese vegetarian diet is not only low in fat and saturated fat, it is also high in fibre. These characteristics of the diet may be partially responsible for the higher insulin sensitivity observed in Taiwanese vegetarians as compared with the omnivores. Micronutrients, including Mg, Cr, V, Zn, Cu and antioxidant vitamins C and E, have also been shown to change insulin sensitivity by affecting insulin synthesis, release and action (Anderson, 2000). These micronutrients are rich in plant-based diets. We did not measure contents of these trace minerals of the diets in the present study; however, intakes of vitamin C and E were not significantly different between the two groups as previously reported (Lu et al. 2000).

In addition to the macro- and micronutrients, a plant-based diet containing vegetables, fruits, nuts, soya products and whole grains also provides a variety of phytochemicals. The additive and synergistic effects of these phytochemicals were reported to have anti-cancer, anti-heart disease activities (Heber, 2004). However, separate studies are required to examine the effects of the phytochemicals on hormone metabolism and disease prevention.

The potential of a purely vegetarian diet or an increased consumption of plant foods to reduce the risks of type 2 diabetes and CVD has been examined and supported by a number of long-term cohort studies conducted in Western countries (Snowdon & Phillips, 1985; Ford & Mokdad, 2001; vanDam et al. 2002). Our data clearly indicate that Taiwanese vegan and lactovegetarian diets also have effects on lowering insulin resistance and may also have potential effects in reducing the risk of type 2 diabetes in our healthy young adults. Positive effects of plant foods in the treatment of diabetes have also
been reported. A diet high in carbohydrates and fibre but low in fat has been shown to lead to improved blood sugar, cholesterol and triacylglycerol levels (Barnard et al. 1983) and, in some cases, to reductions in insulin and oral hypoglycaemic agent used in type 2 diabetic patients (Nicholson et al. 1999; Jenkins et al. 2003).

Taiwanese vegetarians consist mainly of rice, grains, vegetables, fruits, a significant amount of soybeans and many varieties of soybean products. This study determines the dietary pattern different from Western vegetarian diets, which contain more nuts, seeds, dairy products and eggs. Analysis of our diets reveals that the daily protein intake of Taiwanese vegetarians, 4.7 g/d or 0.91 g/kg, is higher than the Dietary Reference Intake in both Taiwan and the USA of 0.9 and 0.8 g/kg, respectively. The higher protein consumption probably is a direct result of the high levels of soy and vegetable proteins, as well as the small amount of milk contained in the diet. Our omnivores consume 64.5 g protein/d or 1.16 g protein/kg, which is acceptable for that age group. The energy sources of both vegetarian and omnivorous diets may be compared as follows. Protein, total fat, saturated fat and polyunsaturated fat for the vegetarian diet, as a percentage of energy, are 12.2, 22.7, 4.9 and 11.5, respectively; and for the omnivorous diet are 15.2, 26.4, 8.6 and 9.5, respectively. Although there are obvious differences between the two groups, the percentage energy from total fat in both (22.7 and 26.4) is within the international nutritional recommendation of 20–30% for women; the percentage energy from saturated fat (4.9 and 8.6) also fits the recommendation of <10. The percentage energy from polyunsaturated fat (11.5 and 9.5) is close to the international recommendation of 6–10%, but the vegetarians’ intake is slightly higher. The polyunsaturated fat:saturated fat ratio is 1.1 in omnivorous diets and 2.3 in vegetarian diets, which is higher than the value of 1.0–1.7 reported in Western vegetarian diets (Sacks et al. 1985; Draper et al. 1993).

Based on the main components of Taiwanese vegetarian diets and their known effects on reducing lipids, blood glucose and other risk factors related to CVD and diabetes, Taiwanese vegetarian diets have promising potential benefits for the prevention and treatment of diabetes and CVD. This possibility must be explored further in non-diabetic and diabetic patients in Taiwan.

In conclusion, our data suggest that Taiwanese vegetarian diets consumed by healthy young female vegetarians significantly lower levels of fasting plasma glucose and serum insulin, and significantly decrease HOMA-IR. Thus, the Taiwanese vegetarian diet may have significant clinical implications, as future studies may demonstrate its potential not only to prevent but also to treat type 2 diabetes and its complications.

Acknowledgements

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