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High Postprandial Triglycerides Serum Levels: Is Obesity a Good Predictor?

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ABSTRACT

The aim of this study was to analyze the correlation between triglyceride (TG) serum levels in obese and non-obese patients in a simulated postprandial state. Both groups showed TG levels < 150 mg/dL when fasting. After 12 h fasting, the subjects ingested a lipid overload diet and blood samples were collected. The variation between fasting and the postprandial TG peak levels were analyzed. The peak of postprandial TG levels occurred 4 h after the lipid overload in both groups. When the subjects were not fasting, the majority of non-obese subjects remained within the range of normal TG values, but the values for the obese group remained elevated. There was a significant correlation between Body Mass Index (BMI) and TG at each time point until 2 h after the meal, but the data did not show a correlation after 3 h. According to the receiver-operating characteristics (ROC) curve, postprandial TG values were not a good predictor of obesity (based on BMI), but they were a predictor of non-obesity. This study reinforces the importance of measuring non-fasting TG levels in obese and non-obese subjects, because some non-obese patients probably had altered fat metabolism, indicating that this examination could be an indicator of metabolic risk.

Key words: body mass index, lipid metabolism, risk factor, ROC curve.

INTRODUCTION

Fats accounts for approximately 30 to 40% of the caloric intake of the occidental diet. An imbalance between caloric intake and energy expenditure results in excessive storage of corporal fat, often resulting in overweight or obesity. This imbalance often produces an altered lipid profile characterized by high TG serum levels, high total cholesterol, high LDL-cholesterol, and low levels of HDL-cholesterol that increases the risk of cardiovascular disease (CAD) (Hu et al. 2000). Generally, the alterations to the lipid profile occur silently over long periods of time. Hyperlipidemic states may lead to undesirable health consequences, such as high blood pressure levels, myocardial infarction, and cerebrovascular accidents (Austin et al. 1998, Miller...
For the prevention of cardiovascular disease, it is extremely important to detect lipid metabolism alterations at an early stage through clinical examinations (Teixeira et al. 2001).

Generally, TG levels are obtained when patients are fasting, and the association between TG levels and cardiovascular disease remains controversial. Bansal et al. (2007) have suggested that postprandial hypertriglyceridemia may play an important role in atherosclerosis. Despite being considered deleterious, postprandial serum hypertriglyceridemia is not identified in many patients with normal fasting lipid serum levels. Consequently, high-risk conditions can be underestimated (Groot et al. 1991, Patsch et al. 1992, Weintraub et al. 1996). For most of the day, humans are not fasting. Consequently, a group that is potentially at high risk for atherosclerosis and coronary artery disease is not identified and is obviously not aware of this risk condition (Patsch et al. 1992, van Wijk et al. 2003). Measuring postprandial lipemia includes both the extent and duration of TG elevation after lipid consumption (Patsch et al. 1992), and determining postprandial plasma TG concentration after a meal is crucially important in identifying the actual lipid metabolism profile.

Three decades ago, Zilversmit (1979) described the importance of postprandial TG studies and hypothesized that the development of atherosclerosis could be a postprandial phenomenon. Stampfer et al. (1996) showed that plasma TG levels measured 3 to 4 h after a meal were better than fasting plasma TG levels at predicting future cases of myocardial infarction. Disturbances in postprandial lipemia have also been observed in type 2 diabetic patients (Chen et al. 1993) and in individuals with visceral obesity or features of metabolic syndrome (Couillard et al. 1998). Obesity is a condition associated with numerous alterations in plasma lipid and lipoprotein concentrations (Björntorp 1992, Kissebah and Krakower 1994), and TG responses to a high-fat meal are exaggerated in obese individuals compared to non-obese individuals (Lewis et al. 1990). In our research, we showed that there are differences in fasting and non-fasting TG states between obese and non-obese patients with basal TG levels <150 mg/dL (which is considered normal [NCEP 2001]). We also analyzed the range of TG variation in relation to the basal TG values in these groups. For this study, we focused on the importance of postprandial TG measurements.

MATERIALS AND METHODS

SUBJECTS

This study included 36 patients between the ages of 18 and 60. The patients were mainly female; there were 25 female (70%) and 11 male individuals (30%) living in the south of Brazil (Ponta Grossa - State of Paraná). There were more female patients because more women than men seek assistance for the treatment of problems related to obesity. All of the patients were treated between 2005 and 2009 and signed informed consent forms before participating in this study. The study was approved by the Ethics Committee of the Vicentino Hospital (Ponta Grossa) and by the Universidade Estadual de Ponta Grossa (COEP authorization number 51/2005).

The study patients were divided into two groups (obese and non-obese) according to their BMI (calculated by dividing body weight in kilograms by height in square meters). In this study, 15 non-obese individuals (BMI <30 kg/m²) (WHO 1998) were used as our control group, and 21 obese patients (BMI ≥ 30 kg/m²) (WHO 1998) also participated. Individuals of both groups had no pre-existing diseases, such as type 2 diabetes mellitus, for example. According to the National Cholesterol Education Program (NCEP 2001), patients can be divided into four groups according to their TG levels: (1) normal TG (< 150 mg/dL), (2) borderline-high TG (≥ 150-199 mg/dL), (3) high TG (≥ 200 - 499 mg/dL), and finally, (4) very
POSTPRANDIAL TRIGLYCERIDES AND OBESITY

According to the NCEP (2001), hypertriglyceridemia is defined as a TG level higher than 150 mg/dL. Patients (non-obese and obese) with TG serum levels < 150 mg/dL in the fasting state were included in this study.

CLINICAL ASSAYS

After a 12 h overnight fast, blood samples (5mL) were collected from all of the patients by venipuncture. Next, while the patients remained seated in the laboratory, a standardized lipid overload (which consisted of 200 g of 25% fat milk cream and 50 g of egg yolk) was administered to them over a maximum time period of 10 minutes. After the meal, blood samples were drawn every 1h for a 6h period; the serum TG levels of the patients were measured by enzymatic methods and compared. No food or drink (except water) was consumed until the exam was finished. The TG levels obtained were compared for both groups in fasting and postprandial states. Additionally, TG values for the obese and non-obese groups were analyzed separately to compare the basal TG levels with the peak levels obtained after the high-fat meal.

STATISTICAL ANALYSIS

Baseline comparisons between the non-obese and obese subjects were made using either Student’s t-test (age and BMI) or Fisher’s exact test (gender). Comparisons between the baseline and postprandial time points were carried out using analysis of variance (ANOVA) for repeated measurements. To compare the two groups (non-obese and obese) at each time point, Student’s t-test was used. The relationship between BMI and TG levels was obtained using the Pearson correlation test at each time point. The area under the ROC curve was determined to evaluate whether TG levels predicted obesity.

The normality of the distribution of the data was confirmed using the Kolmogorov-Smirnov test. When necessary, the raw data were logarithmically transformed. A p-value ≤0.05 was considered to indicate statistically significant differences between the groups. All of the calculations were performed using SPSS® (Statistical Package for the Social Sciences) version 11.5.1 for Windows (SPSS Inc. Chicago, Illinois, USA) and GraphPad Prism® version 5.00 for Windows (GraphPad Software. San Diego, California, USA).

RESULTS

The patients who participated in this study were divided into two groups, obese or non-obese, according to their BMI. Both groups had a similar gender composition (p = 0.465), and there were no significant differences in age between the two groups (p = 0.061). The mean BMI was significantly higher in the obese group than in the non-obese group (p < 0.05) (Table I).

TABLE I
Selected characteristics of the study subjects.
Age and BMI (body mass index) were calculated as the mean ± standard deviation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-obese (BMI &lt; 30 kg/m²)</th>
<th>Obese (BMI ≥ 30 kg/m²)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>32.27 ± 14.51</td>
<td>40.67 ± 11.51</td>
<td>0.061**</td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td>23.28 ± 3.45</td>
<td>38.78 ± 6.41</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Gender†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>6 (40%)</td>
<td>5 (24%)</td>
<td>0.465**</td>
</tr>
<tr>
<td>Female</td>
<td>9 (60%)</td>
<td>16 (76%)</td>
<td></td>
</tr>
</tbody>
</table>

* = Student’s t-test; † = Fisher’s exact test; ** = significant; *m = non significant.

The subjects’ fasting plasma TG levels were considered normal (<150 mg/dL) in both groups. However, the obese patients had higher average lipid levels in the fasting state when compared to the patients in the non-obese group. For the entire period analyzed, the mean TG levels of the obese patients were higher than the mean TG levels of the non-obese patients, reaching a peak level 4 h post-meal in both groups (Figures 1 and 2). For the majority of the non-obese subjects, the TG levels remained <150 mg/dL during the non-fasting
period, unlike the obese group, whose average values did not reach the normal range until 1h after the standardized meal and remained altered for the rest of the measured period.

There was a significant correlation (p<0.05, Pearson correlation) between BMI and TG at baseline and at the 1 and 2h time points (Figure 3). The ROC curve showed that postprandial TG values were not a good predictor of obesity based on BMI; however, they were able to predict non-obesity in the study subjects. Analysis of the ROC curves showed cut-off values for postprandial TG at 149.5 mg/dL (sensitivity: 0.32; specificity: 0.83) and an area under the curve of 0.737 (95% CI: 0.670 to 0.804) (Figure 4).

Figure 1 - Distribution of postprandial TG (triglycerides) (mg/dL) values in non-obese (NO) and obese (O) patients after various time periods (h: hours). The mean values for each group at each assessment time are represented by a horizontal dash (─). The values within the shaded area represent normotriglyceridemic subjects (<150 mg/dL). Comparisons between the NO and O patients revealed significant differences for each time period (*p <0.05, Student's t-test). Comparisons within the same group at different times: NO (#) p <0.05 after 3, 4, 5 and 6 h; (# #) p <0.05 after 4 h; O (+) p <0.05 at 2, 3, 4, 5 and 6 h; (+ +) p <0.05 after 3, 4 and 5 h (repeated ANOVA and post test Tukey measures).

Figure 2 - The mean (standard error) differences in TG (triglycerides) (mg/dL) postprandial levels compared to baseline in non-obese and obese patients after different evaluation periods.
Figure 3 - Pearson correlation test for BMI (body mass index) and TG (triglyceride) at each time point. (*) Indicates a statistically significant correlation.
DISCUSSION

Measurements of serum TG levels, when practiced as a screening method, are generally performed in fasting state generally. Several papers proposed that higher and more harmful TG serum levels were observed in the postprandial states. Unfortunately postprandial exams are complex and time consuming and they are not commonly conducted in clinical practice, preventing the screening of population. Obesity by itself is considered a predictor of adverse lipid metabolism alterations on fasting state; however few studies correlated the obesity with postprandial TG lipid profile.

In this report, the TG level on fasting and on postprandial states of patients in normal weight or carrying different degrees of obesity was analyzed. The relationship between elevated TG concentration and the risk of CAD has been well documented (Krieger 1998, Sharrett et al. 2001); however, the effect of TG levels has been referred to as a “forgotten” risk factor by some authors (Austin 1991, Gotto 1998). Most researchers on plasma lipoprotein levels in obese individuals have used the fasting state, and postprandial lipoproteins are generally neglected (Couillard et al. 1998).

However, postprandial TG measurements are related to the development of atherosclerosis (Bansal et al. 2007). Increased levels of non-fasting TG may indicate the presence of increased levels of atherogenic remnant lipoproteins (Zilversmit 1979), which can penetrate the endothelial cell layer and reside in the sub endothelial space (Patsch et al. 1992, Rapp et al. 1994, Proctor and Mamo 1998, Ginsberg 2002), which constitutes a CAD risk (Kolovou et al. 2011). In our research, we analyzed the TG levels of patients of normal weight and patients with varying degrees of obesity in both the fasting and postprandial states.

An analysis performed after a lipid overload revealed that individuals who apparently presented TG levels above 150 mg/dL (on fasting state), considered normal, had an important increase in their TG levels. The quantification of postprandial lipemia, including both the extent and the duration of higher TG levels after a lipid intake, could be viewed as the most accurate method for measuring TG levels (Patsch et al. 1992). According to Patsch et al. (1992), the postprandial but not fasting TG levels exhibited an association with CAD that was statistically independent and stronger than that of HDL-cholesterol.

Thus, we want to emphasize the importance of measuring lipid profiles when patients (obese or non-obese) are in a non-fasting state. Measuring postprandial lipemia could be considered a powerful tool for studying abnormal lipid profiles. Our results showed that TG levels peaked 4 h after the standardized high-fat meal, corroborating previous studies (Boquist et al. 1999, Bansal et al. 2007). Stampfer et al. (1996) showed that plasma TG levels measured 3 to 4 h after a meal were better than fasting plasma TG levels at predicting future cases of myocardial infarction. Normally, measuring postprandial TG is time-consuming because blood samples are taken for a 6 h period after a lipid overload, but conducting examinations at a fasting baseline and 4 h after the meal could
be sufficient to predict postprandial TG values, according to Kolovou et al. (2011), as can be seen in our study too. Rector et al. (2009) have suggested that an abbreviated single-point method could be a useful addition to clinical risk factor assessments. Furthermore, Patsch et al. (1992) demonstrated that one late postprandial TG measurement may be sufficient to characterize postprandial lipemia, providing a methodology simple enough for future screening. Generally, TG values return to baseline fasting levels 10 h after the lipid overload (Cohn et al. 1988), which could explain the down fluctuation observed in our analysis after 5-6 h, in both groups.

People are in a non-fasting state for most of the day, and even healthy subjects are in a state of postprandial hypertriglyceridemia most of the time due to meal frequency. As observed in Figure 1, even non-obese subjects may have an abnormal lipid profile (TG levels ≥150 mg/dL), another indication of the importance of postprandial studies. Moreover, after the lipid overload, we observed that even some of the non-obese subjects had postprandial responses that exceeded acceptable TG levels (≤220 mg/dL) (Kolovou et al. 2011). Schiavo and colleagues (2003) reported that TG levels can fluctuate depending on which day of the week they are measured. Measurements taken on Mondays were always higher than measurements taken on Fridays, indicating that weekend meals tend to influence the results. Therefore, the 12 h fasting period commonly recommended before testing is not sufficient to explain the lipid profile of a patient (Schiavo et al. 2003).

Our data suggested that there is a correlation between BMI and TG level in the postprandial state at baseline and at 1 and 2 h post-meal. Carneiro et al. (2003) and Cercato et al. (2004) reported that fasting plasma TG levels were higher in individuals with more body fat when compared to leaner individuals. In this present study, the TG level measurements taken after a meal over a 3 h period did not show a correlation with body weight.

TG levels > 150 mg/dL are a primary marker for atherogenic factors as well as components of metabolic syndrome, such as elevated blood pressure, insulin resistance, elevated LDL-cholesterol levels and low HDL-cholesterol levels (NCEP 2001). In some cases of hypertriglyceridemia, there is a genetic defect that alters TG metabolism (Jeppesen et al. 1998). Other influencing factors include oral contraceptives, diuretics, diabetes mellitus, alcohol, and exercise (AbouRjaili et al. 2010). Waist circumference was not recorded during interviews; we used BMI as a substitute for waist circumference. The BMI measurements used in this study are acceptable as per the WHO criteria, but it is not sufficient for the NCEP guidelines. However, the most important aspect of this research is that it represents a new perspective on TG metabolism using postprandial measurements as indicators of metabolic risk. Nevertheless, factors such as environmental, behavioral and genetic characteristics must be considered. Furthermore, we emphasize that all the subjects who participated in this study presented normal glucose blood levels, but we did not measure insulin resistance in order to compare this data with TG levels. Total cholesterol, HDL and LDL-cholesterols levels were not measured either. Some reports indicated that TG levels could be considered an independent risk factor. Jeppesen et al. (1998) reported that fasting hypertriglyceridemia was a strong predictor of CAD independent of other risk factors, including HDL-cholesterol. Other report showed that elevated TG level was associated with a 30% increase in CAD risk in men and a 75% increase in CAD risk in women and adjustment for HDL-C and other risk factors attenuated these risks but did not render them non-significant (Hokanson and Austin 1996).

In conclusion, although the non-obese group had lower levels of postprandial TG than the obese group, some members of the non-obese group also had measurable alterations in their fat
metabolism, even within this small sample. This observation reinforces the importance of testing for hypertriglyceridemia after 4 h of standardized caloric intake.

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**RESUMO**

O objetivo deste estudo foi analisar a correlação entre níveis séricos de triglicérides (TG) em pacientes obesos e não obesos em estado pós-prandial simulado. Os grupos apresentavam níveis de TG em jejum < 150 mg/dL. Após 12 h de jejum, os indivíduos ingeriram uma sobrecarga lipídica e o sangue foi coletado. A variação entre os picos dos níveis de TG em jejum e em estado pós-prandial foi analisada. Os picos pós-prandiais de TG ocorreram 4 h depois da sobrecarga lipídica nos 2 grupos. Após a refeição, grande parte dos indivíduos não obesos permaneceu dentro da normalidade em relação aos níveis de TG, mas os valores para os obesos permaneceram elevados. Houve uma correlação significativa entre Índice de Massa Corporal (IMC) e TG até 2 h após a refeição, mas os dados não mostraram correlação após 3 h. De acordo com a curva ROC (receiver-operating characteristics), os valores de TG pós-prandiais não são um bom indicador de obesidade (baseado no IMC), mas são bons indicadores de não obesidade entre os indivíduos. Este trabalho reforça a importância de se medir níveis pós-prandiais de TG em obesos e não obesos, já que alguns pacientes não obesos provavelmente apresentavam um metabolismo alterado de gordura, indicando que este tipo de exame poderia ser um indicador de risco metabólico.

**Palavras-chave:** índice de massa corporal, metabolismo de lipídeos, fator de risco, curva ROC.

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