The Effects of Weight Loss on Normal Transaminase Levels in Obese Patients

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ABSTRACT: *Background:* Obesity is associated with insulin resistance, which is the main pathogenic factor for nonalcoholic fatty liver disease (NAFLD). NAFLD can progress without associated elevations in liver enzymes. Therefore, we investigated the effects of weight loss on normal transaminase levels in obese subjects who are at risk for NAFLD. *Methods:* Thirty-seven obese patients with normal ALT levels were evaluated. All patients received an individualized low-calorie diet over at least 6 months. Twenty-two patients who achieved weight loss of at least 5% body weight were identified as the study group and the others as the control group. Transaminases, insulin resistance, and body mass index were compared before and after the intervention. *Results:* Hepatic steatosis was found in 83.8% of obese patients. ALT was correlated with HOMA-IR in all patients at baseline ($r = 0.363$, $P = 0.027$). At the end of the follow-up, mean weight loss achieved in the study and control groups were 9.2% (8.7 ± 3.0 kg) and 0.3% (0.5 ± 2.8 kg), respectively. In the study group, HOMA-IR and ALT decreased from 4.0 ± 1.8 to 2.4 ± 0.9 and from 21.4 ± 6.6 IU/L to 16.8 ± 5.5 IU/L, respectively ($P = 0.005$ and $P = 0.044$). *Conclusions:* The results demonstrate that weight loss results in a decrease in normal ALT levels as well as insulin resistance. Therefore, the normal range for ALT may need to be reassessed. **KEY INDEXING TERMS:** Obesity; Transaminases; Insulin resistance. **[Am J Med Sci 2007;334(5):327–330.]**

Obesity is a chronic disease that has many medical complications. It is associated with resistance to the effects of insulin on peripheral tissues and is frequently observed in patients with nonalcoholic fatty liver disease (NAFLD).[1] Conversely, although the pathogenesis of NAFLD is multifactorial, its main association is with insulin resistance.[2,3] Insulin resistance can be estimated by the homeostasis model assessment of insulin resistance (HOMA-IR).[4] Monitoring alanine aminotransferase (ALT) monitoring in the management of chronic liver diseases, including NAFLD, is a usual clinical practice. However, serum ALT levels of patients with NAFLD are not necessarily elevated.[5] Studies in patients with NAFLD have confirmed that weight loss[6–8] or drugs enhancing insulin sensitivity[9,10] decrease the serum aminotransferase levels. However, the effects of weight loss on the liver enzymes in obese patients, who may be at risk for NAFLD, are not known, especially when ALT levels are within normal limits. For this reason, we conducted this study to investigate the effects of weight loss on normal ALT levels in obese patients.

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Methods

This protocol was approved by the medical ethics committee of the Afyon Kocatepe University Hospital and conducted according to the Helsinki Declaration of 1975. The current study was planned prospectively and has been performed between September 2004 and April 2006 in Internal Medicine Clinic of Afyon Kocatepe University Hospital.

Study Population

Seventy-nine obese patients (body mass index [BMI] >30 kg/m^2) were evaluated in outpatient settings. Seventeen patients were excluded: 7 had serum levels of ALT >40 U/L for male and >30 U/L for female in at least 1 measurement of 2 consecutive blood samples obtained 4 weeks apart, and 10 had type 2 diabetes mellitus. Of the 62 patients, 25 were excluded from subsequent analysis because of loss to follow-up. Those patients who achieved weight loss of at least 5% body weight were identified as study group (group I). For purposes of comparison, group I was compared with the control group (group II) who had achieved less than 5% weight loss.

Clinical and Laboratory Data

Blood samples for measurements of fasting glucose, insulin, and ALT were obtained after an overnight fast at baseline. Insulin resistance was measured by HOMA-IR. Body mass index was calculated and is defined as weight (kg)/height (m^2). All patients also underwent hepatic ultrasonography, which was performed by the same operator. Steatosis was graded as 0, 1, 2, or 3. An individualized low-calorie diet was initiated to promote a goal of 0.5 kg weight loss per week and patients were followed by the same dietician throughout the study. The energy requirements were individualized based on height, weight, age, sex, and physical activity level. The diet contained 60% of energy as carbohydrate, 25% protein, and 15% fat.

Liver function tests, HOMA-IR, body weight measurement and hepatic ultrasonography were repeated after group I had achieved a weight loss of at least 5%. In group II, who had achieved less than 5% weight loss, all measures and tests, except hepatic ultrasonography, were repeated after at least 6 months.

Both baseline and final values of BMI, HOMA-IR, and ALT were compared between groups. We also compared baseline values with final values in both groups, and investigated the effects of weight loss on normal ALT levels. Additionally, in group I only, we evaluated the degree of change in steatosis after weight reduction. The serum biochemical indexes were examined by an autoanalyzer based on standard protocols.

Statistical Analysis

All clinical parameters were summarized by descriptive statistics. Categorical parameters were compared by χ^2 and Fisher's exact test. Comparisons of continuous clinical parameters between subjects with different categorization by weight loss were made by Student t test and Mann-Whitney U test. Correlations between variables in the study group were assessed using Pearson's correlation analysis. The differences within groups, before and after study period, were analyzed for statistical significance using the paired t test and Wilcoxon test. Two-tailed P values of less than 0.05 were considered to indicate significance. Statistical analysis was performed by SPSS for Windows software (Version 10.0).

Results

During the study, 22 patients achieved at least 5% weight reduction (group I). Although the dietary intervention, 15 patients did not succeed in losing weight, and were accepted as control group (group II). The obese patients who lost weight (6 male, 16 female) had a mean of age 46.5 ± 10.2 (27 to 66) years, whereas the mean age of the control group (3 male, 12 female) was 47.9 ± 11.2 (30 to 68) years. At baseline, there were no significant differences in age, BMI, or ALT levels between groups except HOMA-IR, which was significantly higher in group II than in group I ($P = 0.049$). Steatosis was found in 86.4% of study group subjects and 80% of control subjects (Table 1). Alanine aminotransferase levels were correlated with HOMA-IR in all patients at baseline ($r = 0.363$, $P = 0{,}027$).

With respect to their baseline and final values, no significance was found in BMI, HOMA-IR, or ALT levels of group II. However, in group I, BMI, HOMA-IR, and ALT values decreased significantly ($P < 0.001$, $P = 0.005$, and $P = 0.044$, respectively). Although 17 patients had no change in steatosis grade among group I patients at the end of the follow-up period, 5 had an improvement in hepatic steatosis (1 of 2 grades, and 4 of 1 grade). This improvement in hepatic steatosis was significant ($P = 0.034$) (Table 2). The correlation between ALT and HOMA-IR, which had decreased after weight reduction, also persisted ($r = 0.523$, $P = 0.001$).

The follow-up period was significantly higher in group II than in group I ($P = 0.009$). At the end of the follow-up period, group I achieved a mean weight loss of 9.2% (8.7 ± 3.0 kg). Of 15 patients in group II, 4 patients experienced weight gain of 3.7% (3.2 ± 1.9 kg) and 11 patients achieved weight loss of 1.8% (1.9 ± 1.4 kg). The mean weight loss in control subjects was 0.3% (0.5 ± 2.8 kg). In addition, we found

Table 1. Data in Obese Subjects of Both Study Group and Controls at Baseline*

Variables	Study Group (n = 22)	Control Group (n = 15)	*P*
Male, No. (%)†	6 (27.3)	3 (20)	0.613
Age (yr)	46.5 ± 10.2	47.9 ± 11.2	0.691
BMI (kg/m^2)	35.8 ± 7.1	39.1 ± 7.0	0.177
HOMA-IR	4.0 ± 1.8	5.5 ± 2.4	0.049
ALT (U/L)	21.4 ± 6.6	21.6 ± 6.7	0.933
AST (U/L)	21.1 ± 6.8	20.7 ± 5.4	0.847
ALP (U/L)	173.6 ± 79.5	157.6 ± 68.2	0.534
GGT (U/L)	18.1 ± 7.4	22.9 ± 9.7	0.109
Those with hepatosteatosis, No. (%)‡	19 (86.4)	12 (80.0)	0.468

BMI, Body mass index; HOMA-IR, homeostasis model assessment for estimating insulin resistance; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transpeptidase.
** All parameters expressed as mean ± SD and analyzed by Student t test, unless otherwise stated.*
† Comparison by χ^2.
‡ Comparison by Fisher's exact test.

Table 2. Data of Study Group (n = 22) Before and After the Intervention Period*

Variables	Before	After	*P*
BMI (kg/m^2)	35.8 ± 7.1	32.3 ± 6.2	<0.001
HOMA-IR	4.0 ± 1.8	2.4 ± 0.9	0.005
ALT (U/L)	21.4 ± 6.6	16.8 ± 5.5	0.044
AST (U/L)	21.1 ± 6.8	16.1 ± 7.5	<0.001
ALP (U/L)	173.6 ± 79.5	88.0 ± 46.2	0.005
GGT (U/L)	18.1 ± 7.4	14.0 ± 5.0	<0.001
Grade of hepatic steatosis (n)			0.034
Grade 0	3	4	
Grade 1	12	15	
Grade 2	5	2	
Grade 3	2	1	

BMI, Body mass index; HOMA-IR, homeostasis model assessment for estimating insulin resistance; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma glutamyl transpeptidase.
**All parameters expressed as mean ± SD and analyzed by paired t test, unless otherwise stated.*
† Tested by Wilcoxon.