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Comparison of Clinical Biochemicals in Sera of Senior Patients with Hyperglycemia

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We analyzed the concentration of Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP), Gamma Glutamyl Transferase (GGT), total protein (TP), albumin, total cholesterol (TC) and triglyceride in sera of patients (n=455) aged 60 years and older with hyperglycemia (≥120mg/dL in serum). The average concentration of biochemicals in patient group was compared with those in reference group. Our data showed that the average concentrations of AST and TC in sera of senior patients with hyperglycemia were significantly increased by 27.5% ($P<0.05$) and 82% ($P<0.05$) in total group, 38.5% ($P<0.05$) and 75.0% ($P<0.05$) in sixty years' group, 16.0% ($P<0.05$) and 89.7% ($P<0.05$) in seventy years' group and 27.0% ($P<0.05$) and 79.5% ($P<0.05$) in eighty years' group, respectively. Patients with hyperglycemia showed a significant decrease in albumin level by 6.7% (total group, $P<0.05$), 4.5% (sixty years' group, $P<0.05$), 8.9% (seventy years' group, $P<0.05$) and 4.5% (eighty years' group, $P<0.05$), respectively. In conclusion, the high concentration of glucose in the senior patients with hyperglycemia may be a cause of severe liver function and lipid metabolism disorder.

Key Words : Hyperglycemia, AST, ALT, ALP, GGT, Cholesterol, Triglyceride

INTRODUCTION

Diabetes is the seventh leading cause of death in the U.S., affecting 16.8 million Americans in 2006 (Mokdad *et al.*, 2009). The prevalence of diabetes among individuals aged 75 years is projected to increase 336% by 2050 (Boyle *et al.*, 2001). This upward trend is attributed mainly to the aging of the population, an increase in obesity, and lifestyle changes (Gregg *et al.*, 2004). Simultaneously, there has been a decrease in the prevalence of several diabetes-related complications as a result of advancements in diabetes management (Chaturvedi, 2007). The occurrence of one or more chronic diseases in the same person occurs frequently among patients with diabetes (Beckman *et al.*, 2002). Currently, integrated diabetes care programs focus on diabetes-related comorbidities like cardiovascular diseases, retinopathy, nephropathy and diabetic foot. However, patients with diabetes do not only have diabetes related comorbidity but also have non diabetes-related comorbidity, such as depression and musculoskeletal diseases (Egede *et al.* 2002). Despite advances in the treatment of patients with hyperglycemia, diabetic complications are still a major concern as the main cause of morbidity and mortality in patients with diabetes. The most devastating complication is diabetic nephropathy, which is associated with a markedly increased risk of end-stage renal failure, cardiovascular disease (Tuomilehto *et al.*, 1998), and premature death (Borch-Johnsen *et al.*, 1985).

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Senior people, defined as individuals 65 years of age, comprise a substantial and growing part of the population in developed countries. Current demographic data in Western societies report that 12~15% of the general population is over the age of 65 years, and this proportion is projected to reach 20~25% by the year 2030 (Centers for Disease Control and Prevention, 2003). The proportion of senior people in Korea is also projected to reach 20.8% by the year 2026 (Kim *et al.*, 2010). Alongside an increase in life expectancy and an explosive growth in the elderly population worldwide, chronic diseases, such as coronary heart disease, cancer, incontinence, pulmonary disease, and diabetes, have become well-known determinants for developing activity of daily living disability (Elia, 2001). Moreover, significant research has illustrated that the effect of chronic diseases on activity of daily living disability varies by gender and increases dramatically for the more senior elderly (Murtagh and Hubert, 2004). The measurement of the concentration of clinical biochemicals is carried for detecting, diagnosing, evaluating severity, monitoring therapy, and assessing the prognosis of the liver and kidney disease and dysfunction. The useful tests for diagnosis of liver function, lipid metabolism and diabetes are the concentration of total protein, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gammaglutamyl transferase (GGT), total cholesterol, triglyceride and glucose in serum (Gitlin *et al.*, 1992; Engelgau, *et al.*, 2000; Dreisbach and Lertora, 2003; Pichette and Leblond, 2003; Nathan *et al.*, 2007). To investigate the health status in elderly patients, we analyzed and evaluated the concentration of clinical biomarkers in sera of elderly patients aged 60 years or older and also made a clinical comparison with those of reference patient group (Burtis and Ashwood, 2006).

MATERIALS AND METHODS

1. Preparation of blood sample

This present study is a comparison of the concentration of biochemical markers in sera of hyperglycemia patients (n=455) aged 60 years and older in Jeonbuk province for the last 2 years (2010 to 2011). After explaining the purpose of this study to the patients, we took the samples under their permission. The patients were divided into four patient groups of 60-69 age group (sixty group), 70-79 age group (seventy group), 80-89 age group (eighty group) and 60-89 age group (total group) by ages. To evaluate the concentration of serum AST, ALT, ALP, GGT, total protein, albumin, cholesterol and triglyceride in hyperglycemia patients, we obtained fasting blood samples from the hyperglycemia ($\geq$120 mg/dL in serum) patients.

2. Analysis of biochemical marker

We isolated sera from bloods and analyzed the concentration of biochemical markers in sera. The activity of AST, ALT, GGT and ALP and the concentration of total protein (TOP), albumin (AL), total cholesterol (TC), triglyceride (TG) and glucose were determined by Hitachi automatic clinical analyzer (Hitachi High Technologies Co., Tokyo, Japan).

3. Statistical analysis

The concentrations of biochemical markers in sera of the patient groups were compared to each other group and reference range (Burtis and Ashwood, 2006). All data are expressed mean $\pm$ SD. Data analyzed by one-way ANOVA using the SPSS statistical software package, Version 8.0 (SPSS Inc., Chicago, IL, USA). A P value less than0.05 was considered statistically significant.

RESULTS

1. Characteristics of participants

The clinical anthropometric characteristics of participants have been displayed in table 1 and 2. Among the 455 patients enrolled in this study, 42.4% (n=193) were men and 57.6% (n=262) were women. The mean age was 70.8±6.7 years. The number of patients in each age group of sixty, seventy, eighty was 44.2%, 44.0% and 11.9% respectively.

2. Statistical comparison of patient groups

We analyzed the each concentration of AST, ALT, ALP, GGT, total protein, albumin, total cholesterol and triglyceride in sera of senior patients with hyperglycemia (Table 1 and 2). We compared the average activity of AST, ALT, ALP and GGT and the average concentration of total protein, albumin, total cholesterol and triglyceride of patients in each age group with those of the average activity of reference group (Fig. 1 and Fig. 2). In comparison of the average activity of AST, ALT, ALP and GGT with those of the average of reference group, the mean activity of AST in each age group ($P<0.05$) and ALT in sixty age group ($P<0.05$) were significantly increased (Table 1). We compared the mean activity in patients groups to those of reference group (Fig. 1). The elevation rate of the mean activity of AST in each age groups was 38.5% (sixty), 16.0% (seventy), 27.0% (eighty) and 27.5% (total) respectively. In the other enzymes we studied, ALT and GGT in sixty age group. ALP and GGT in eighty age group were increased by 15.2%, 11.6%, 11.8% and 6.9%, respectively.

Table 1. The concentration of clinical biochemicals in sera of patients with hyperglycemia and reference

Group	Biochemical			
	AST (U/L)	ALT (U/L)	ALP (U/L)	GGT (U/L)
Reference	20.5±5.0	25.0±7.5	221.0±58.5	45.0±20.0
Total (n=455)	25.5±16.1*	24.7±18.9	215.1±74.6	42.7±6.6
Sixty (n=201)	27.7±18.3*	28.8±22.2*	210.6±65.6*	50.2±7.8
Seventy (n=200)	23.2±12.9*	20.7±12.5*	217.4±86.6	37.8±32.3*
Eighty (n=54)	25.4±17.4*	24.1±22.6	223.6±55.8	48.1±9.8

Data were expressed as mean ± SD.
* $p<0.05$ (compared with the reference group)
Abbreviation: AST, aspartate aminotransferase ; ALT, alanine aminotransferase ; ALP, alkaline phosphatase ; GGT, gammaglutamyl transferase.

Table 2. The concentration of clinical biochemicals in sera of patients with hyperglycemia and reference

Group	Biomarker				
	Total protein (g/dL)	Albumin (g/dL)	Total cholesterol (mg/dL)	Triglyceride (mg/dL)	Glucose (mg/dL)
Reference	7.3±0.6	4.5±0.5	180.0±25.0	100.0±25.0	80.0±7.5
Total (n=455)	7.4±0.5*	4.2±0.3*	186.9±42.6*	182.0±117.3*	159.6±47.9*
Sixty (n=201)	7.4±0.5*	4.3±0.2*	183.6±45.6	175.1±99.2*	163.2±49.8*
Seventy(n=200)	7.3±0.5	4.1±0.2*	189.6±40.6*	189.7±135.9*	154.6±43.6*
Eighty (n=54)	7.3±0.5	4.3±0.3*	189.1±38.0	179.5±104.9*	165.1±54.7*

Data were expressed as mean ± SD.
* $p<0.05$ (compared with the reference group)

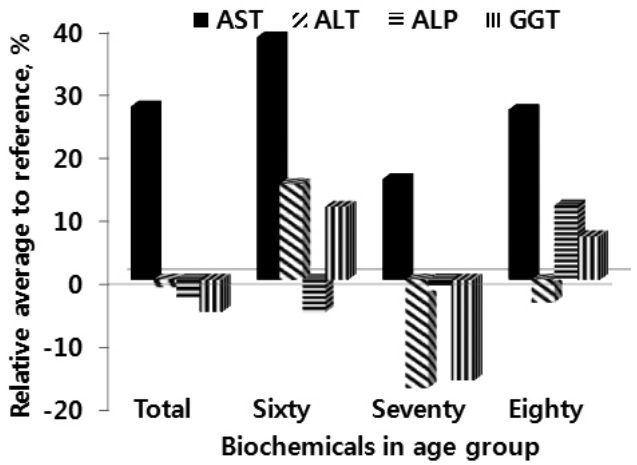

Fig. 1. The relative average activity of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gammaglutamyl transferase (GGT) of patients with hyperglycemia (≥120 mg/dL) in each age group. The percentages were calculated by comparing the average activity of enzymes in patient group to those of the reference group.

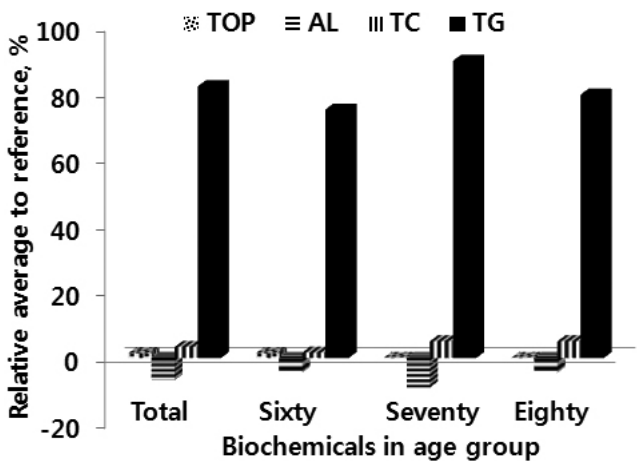

Fig. 2. The relative average concentration of total protein (TOP), albumin (AL), total cholesterol (TC) and triglyceride (TG) of patients with hyperglycemia (≥120 mg/dL) in each age group. The percentages were calculated by comparing the average concentration of biochemicals in patient group to those of the reference group.

In comparison of the average concentration of total protein, albumin, total cholesterol and triglyceride with those of the average concentration of reference group (Table 2), the mean concentration of total protein in sixty group and total group was significantly increased by 1.4% ($p<0.05$). The mean concentration of albumin in each group was significantly decreased by 6.7% (total group, $p<0.05$), 4.5% (sixty group, $p<0.05$), 8.9% (seventy group, $p<0.05$) and 4.5% (eighty group, $p<0.05$), respectively. In total cholesterol and triglyceride, the mean concentration of total cholesterol in total group and in seventy group were significantly increased by 8.3% ($p<0.05$) and 5.5% ($p<0.05$), respectively. The mean concentration of triglyceride in each age group was significantly increased by 82.0% (total group, $p<0.05$), 75.0% (sixty group, $p<0.05$), 89.7% (seventy group, $p<0.05$) and 79.5% (eighty group, $p<0.05$) respectively (Fig. 2).

DISCUSSION

The measuring of the level of biochemicals in blood such as AST, ALT, ALP, GGT, total protein and albumin is useful to evaluate the state of liver disease. In the clinic, the results of these proteins are compared and interpreted according to reference charts containing internationally accepted normal levels for these proteins. Elevation of liver enzymes such as AST, ALT, ALP and GGT indicates hepatic impairment (Sheehan and Haythorn, 1979; Lazo *et al.*, 2008). The results of elevation of the activity of the above enzymes and decrease of the concentration of total protein and albumin may indicate a number of chronic and acute diseases and infections including liver cirrhosis, mononucleosis, hepatitis and heart disease (Williams and Hoofnagle, 1988; Memon *et al.*, 2002).

This present study shows that AST in each age group is elevated significantly from 16.0% to 38.5% and ALT, ALP and GGT in each age group are not increased significantly except for ALT (15.2%) in sixty group (Table I and Fig. 1).

The prevalence of elevated transaminase levels is not known in the Korean senior patients with hyperglycemia. In earlier studies, applying different methodology and enrolling variable population sample sizes as well as considering different cut-off values for AST and ALT readings have yielded variable prevalence rates (Salmela *et al.*, 1984; Erbey *et al.*, 2000; Harris, 2005). Hrris and his coworkers (Harris, 2005) demonstrated that the activity of AST and ALT in Type II diabetes patients were increased by 250IU/L. Another researcher (Salmela *et al.*, 1984) observed that two or more enzymes of AST, ALT, ALP and GGT in diabetes patients showed an abnormal liver function test results. They also observed the presence of elevated ALT and GGT in type II diabetes patients (5.3% and 10.5%) and in type I diabetes patients (22.9% and 23.7%). The tendence for elevation of AST activity in our study is similar to the above observations though not identical rate, but ALT and GGT are not similar to previous report (Erbey *et al.*, 2000). Some previous reports demonstrated that elevation of enzymes such as AST, ALT, ALP and GGT may indicate a number of chronic and acute diseases and infections including liver cirrhosis, hepatitis and heart disease (Williams and Hoofnagle, 1988; Memon *et al.*, 2002). Our data suggest that increasing of AST in the senior patients with hyperglycemia is associated with a risk factor for heart or liver disease. In earlier studies, liver synthesize albumin, therefore the albumin level in blood can serve as an index of liver synthetic capacity. In practice, patients with low serum albumin concentrations is likely to have a hepatic cause for low albumin, such as an acute or chronic inflammatory state of liver (Rothschild *et al.*, 1988; Kamath, 1996). In comparison of albumin and total protein in patient groups with reference average, our findings show that the concentration of albumin in each age group is decreased significantly from 4.5% to 8.9%, but total protein in sixty group is increased 1.4% (Table 2 and Fig. 2). These finding suggest that the high concentration of blood glucose in the senior patients is not correlated with being increased or decreased protein in the patients with hyperglycemia, but the liver synthetic capacity of albumin may be correlated with the high concentration of glucose in patients with hyperglycemia. Bays (Bays *et al.*, 2004) demonstrated that diabetes mellitus enhances lipolysis and inhibits glucose uptake thus increasing triglyceride (TG) formation by adipose tissue. As shown in table 2 and Fig. 2, the senior patients with hyperglycemia in each age group showed significant increase in serum levels of triglycerides from 75.0% to 89.7% ($p<0.05$) and cholesterol in each age group showed a tendency of increase from 3.3% to 5.0% except sixty group. Diabetes is commonly associated with dyslipidemia and hyperglycemia patients (Manzato *et al.*, 1992). Therefore, our study showed significant impaired lipid profile in senior group of the patients with hyperglycemia compared with reference patients. In our results, AST and TG in each patients group are elevated significantly and albumin in each group is decreased significantly. This result suggests that the high concentration of glucose in the senior patients with hyperglycemia may be a cause of severe disorder to liver function and lipid metabolism.

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