PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
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Pakistan Journal of Nutrition 4 (6): 389-392, 2005
ISSN 1680-5194

Correlation of Serum Leptin with Circulating Anti-Helico Bacter Pylori IgG Antibodies in End-Stage Renal Failure Patients on Regular Hemodialysis

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Abstract: Leptin is synthesized mainly by the adipose tissue. Leptin also is detected in gastric chief cells. To consider the association of serum leptin with helicobacter pylori- IgG antibodies as parameters of nutritional status, on a group of hemodialysis patients, serum Leptin and serum helicobacter pylori specific IgG (H. Pylori-IgG) antibody titer were measured. Total patients were 36. In all patients there were a significant positive correlation of serum leptin with BMI and a near significant positive correlation of serum leptin with age. In the diabetic HD group a significant inverse correlation of helicobacter pylori IgG antibody titer and serum leptin was seen. This is the first report of the association of serum leptin with pylori-IgG antibodies in hemodialysis patients which may explain nutritional problems that is frequently seen in diabetic hemodialysis patients .More research is needed regarding the clinical consequences of this association.

Key words: Hemodialysis, helicobacter pylori IgG specific antibodies, leptin

Introduction

Leptin is a 16-kDa protein synthesized mainly by the adipose tissue and plays a crucial role in homeostasis of body weight by reducing appetite and increasing energy expenditure (Zhang *et al*., 1994; Coleman, 1978). Originally thought to be a satiety factor, leptin is a pleiotropic bioactive molecule (Faggioni *et al*., 2001; Sanchez-Margalet *et al*., 2003). Contrary to initial reports, leptin production is not restricted to adipocytes. It is also detected in human placenta, muscles and gastric chief cells (Faggioni *et al*., 2001; Sanchez-Margalet *et al*., 2003; Bado *et al*., 1998; Azuma *et al*., 2001; Sobhani *et al*., 2000). Several recent studies have demonstrated that leptin is cleared principally by the kidney. Thus serum leptin concentrations are increased in patients with chronic renal failure and those undergoing maintenance dialysis (Wolf *et al*., 2002), and it has been speculated that hyperleptinemia may contribute to uremic anorexia and malnutrition (Stenvinkel, 1999). Helicobacter pylori a bacteria first described in 1984, since that time is linked with chronic gastritis and duodenitis. Dyspeptic symptoms and chronic gastritis are common in patients with chronic renal failure (Zwolinska *et al*., 2000) and helicobacter pylori (H. pylori) infection has been found in dialysis patients (Aguilera *et al*., 2001). Malnutrition is a problem in a large proportion of dialysis population and is associated with an increased morbidity and mortality (Lin *et al*., 2002; Nasri and Baradaran, 2005; Baradaran and Nasri, 2005). It is well known that Helicobacter pylori play an important role in gastritis and peptic ulcer disease in the general population (Ozgur *et al*., 1997). However it seems that among dialysis patients, the proportion of H. pylori-positive patients is low (Nasri and Baradaran, 2005; Baradaran and Nasri, 2005; Ozgur *et al*., 1997) or as high as that for the non-renal disease group (Nakajima *et al*., 2004; Breidert *et al*., 1999). Leptin levels have also been found in the gastric mucosa of patients with helicobacter pylori associated gastritis(Breidert *et al*., 1999). A study on the effect of H. pylori infection on gastric leptin expression, demonstrated that gastric leptin may play a role in weight gain after eradication of H pylori infection (Azuma *et al*., 2001). Studies concerning the association of H. pylori infection and serum leptin in hemodialysis population are scarce they are the parameters of nutritional status in hemodialysis patients. We therefore aimed to conduct a study on the association of serum leptin in hemodialysis patients with anti helicobacter pylori IgG antibodies to recognize the effect of leptin on H. pylori infection in these patients in order to find all aspects of factors which induce and develop malnutrition in hemodialysis patients.

Materials and Methods

This is a cross-sectional study that was conducted on patients with end-stage renal disease undergoing maintenance hemodialysis treatment with acetate basis dialysate and polysulfone membranes (HD group). All patients had various upper gastrointestinal complaints consisting of epigastric pain, epigastric burning, postprandial fullness, early satiety, bloating and belching. Exclusion criteria for patients were the use of H_2 proton pomp inhibitors and antibiotics as well as active or chronic infection during the last month before

Table1: Patients' data

Total patients n=36	Minimum	Maximum	Mean±SD	Median
Age (years)	16	80	45±17	41.5
DH* (months)	2	156	32±36.5	20
Dialysis dose sessions	18	1584	259±367	145
BMI kg/m^2	16	33	21±4	20.5
H.Pylri-IgG	0.50	33	8.2±10	2
Leptin ng/ml	0.10	52	8±9.5	5.75
Non diabetics n=26				
Age (years)	16	80	42.6±17	40.5
DH* (months)	2	156	38±41	21.5
Dialysis dose sessions	18	1584	352±450	156
BMI kg/m^2	16	33	21±4.6	19
H.Pylri-IgG	0.50	32	8.2±9.8	2
leptin	0.10	52	7.25±10	3.7
Diabetics n=10				
Age (years)	27	79	52±16.6	55
DH* (months)	6	24	14.4±6.7	12
Dialysis dose sessions	54	216	120±56	99
BMI kg/m^2	20	25	22.4±1.9	22.5
H.Pylri-IgG	0.50	33	8±11.7	1.5
leptin	0.20	23.8	9.6±6.7	9.4

*Duration of hemodialysis

the study. After 12-hour fasting, levels of serum Leptin (normal range of values for males is 3.84±1.79 and for females 7.36±3.73 (ng/ml) were measured by the enzyme-linked immunosorbent assay (ELISA) method using DRG of USA. and serum Helicobacter pylori specific IgG antibody titer (titer >10 U/ml was interpreted as positive according to the manufacturer's instructions) was measured by the ELISA method also with a standard kit. The body mass index (BMI) was calculated using weight and height (kg/m^2) (http://www.halls.md/body-mass-index/av.htm). Duration and doses of hemodialysis treatment were calculated from patients' records. The duration of each hemodialysis session was four hours. For statistical analysis descriptive data are expressed as Mean±SD. Comparison between groups were considered using T test. For correlations partial correlation test was used .Statistical analysis was performed on total HD, females, males, diabetics and non diabetics population separately. For some correlations the logarithm of data were also used .All statistical analysis was performed using the SPSS (version 11.5.00). Statistical significance was inferred at a p value< 0.05.

Results

The total hemodialysis (HD) patients were 36 (F=15M=21) with 26 (F=21 M=13) non diabetic hemodialysis and 10 (F=4M=6) diabetic hemodialysis patients with upper gastrointestinal symptoms. Table 1 shows patients' data. Mean±SD of age of total HD patients were 45±17 years. Mean±SD of age of diabetic and non diabetic dialysis patients were 52±16.6 and 42.6±17 years respectively. The duration of hemodialysis treatment was 32±36.5 months (median:20). The value of serum helicobacter pylori (H. Pylori) specific IgG antibody titer of total HD patients was 8.2±10 U/ml (median:5.75). The value of serum H. Pylori specific IgG antibody titers of diabetic and nondiabetic-dialysis patients were 8±11.7 (median:1.5) and 8.2±9.8 (median:2) U/ml respectively. The value of serum leptin of total HD patients was 8±9.5 ng/ml (median:5.75). The value of serum leptin of diabetic and nondiabetic-dialysis patients were 9.6±6.7 (median:9.4) and 7.25±10 ng/ml (median:3.7) respectively. In this study no significant differences of serum H. pylori -IgG antibodies between diabetic and non diabetic HD population and also no significant diferrences of serum helicobacter pylori -IgG antibodies between male and female groups were seen (*P.* N.S.). In this study also no significant differences of serum leptin between diabetic and non diabetic HD patients and also no significant differences of serum leptin between male and female population were seen (P. N.S.) too. In all patients there were no significant correlations between H. pylori -IgG antibodies and the values consisting of age, the BMI, duration and dosage of hemodialysis were seen (*P.* N.S.). In all patients there were no significant correlations between serum leptin and the values consisting of age, duration and dosage of hemodialysis (*P.* N.S.).Significant positive correlations of serum leptin with BMI (r =0.40 P= 0.018) (adjusted for age), and a near significant positive correlation of serum leptin with age (r = 0.34 P = 0.058) (Adjusted for BMI, gender, DM, duration and dosage of dialysis) were seen. Statistical analysis on the male

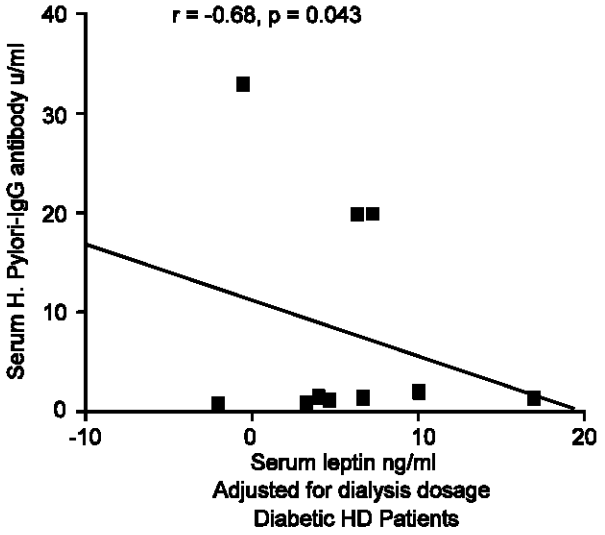

Fig. 1: Significant inverse correlation of helicobacter IgG antibody titer and serum leptin

hemodialysis population showed significant positive correlations of serum leptin with duration (r =0.48 P= 0.040) and dosage of hemodialysis treatment (r=0.48 P= 0.044) (adjusted for age, BMI and DM for two correlations). In the male population a significant positive correlation of serum leptin with ages of the patients was found (r = 0.62 P= 0.004). In the diabetic HD group a significant inverse correlation of helicobacter pylori IgG antibody titer and serum leptin was seen (r = -0.68 P= 0.043; Fig. 1) whereas correlation of serum H. pylori -IgG antibody titer and serum leptin in other groups was not significant (*P*. N.S.).

Discussion

In this study we found no significant differences of serum H. pylori IgG antibodies between the diabetic and non diabetic HD population and also no significant differences of serum H. pylori IgG antibodies between male and female groups existed. No significant differences of serum leptin between diabetic and non diabetic HD patients and also no significant diferrences of serum leptin between male and female population were seen either. In all patients there were no significant correlations between helicobacter pylori IgG antibody and the values consisting of age, duration and dosage of hemodialysis were seen. In the total number of patients also no significant correlations between serum leptin and the values consisting of age, duration and dosage of hemodialysis were seen. Significant positive correlations of serum leptin with BMI and a near significant positive correlation of serum leptin with age were seen. In the male hemodialysis population significant positive correlations of serum leptin with duration and dosage of hemodialysis were found. In the diabetic HD group a significant inverse correlation of helicobacter pylori IgG antibody titer and serum leptin was seen. whereas correlation of serum H. pylori -IgG antibody titer and serum leptin in other groups was not significant (*P*. N.S.). Helocobacter pylori is thought to play an important role in the pathogenesis of active gastritis and other upper gastrointestinal mucosal lesions. Sezer *et al.* (2004) in a study showed an association of H. pylori infection and nutritional status in hemodialysis patients and the study also demonstrated that patients involved by H. pylori infection had lower BMI (Sezer *et al.*, 2004). Bado *et al.*, 1998 reported that leptin mRNA and leptin protein were present in the rat gastric epithelium, and that cells in the glands of the gastric fundic mucosa were immunoreactive for leptin (Bado *et al.*, 1998) Immunoreactive leptin cells were found in the lower half of the gastric fundic glands in humans, and leptin mRNA was also detected in human gastric mucosa by RT-PCR. (Lin *et al.*, 2002; Nakijama *et al.*, 2004). In a study conducted by Azuma *et al.* (2001) showed the presence of leptin in the human gastric mucosa. Azuma concluded that gastric leptin may play a role in weight gain after eradication of H. pylori infection and gastric leptin may have a local rather than systemic action. Azuma, showed a significant increase in gastric leptin expression in patients with H. pylori infection, and a significant reduction in gastric leptin expression with a concomitant increase in BMI after successful eradication therapy. On the other hand serum leptin levels did not change significantly after eradication of H. pylori infection (Azuma *et al.*, 2001). To examine the effect of H. pylori eradication on serum leptin levels and BMI, Shimzu *et al.* (2002) conducted a study on 15 children with H. pylori infection .In this study serum leptin levels and BMI were evaluated before and six months after eradication therapy. There were no significant differences in serum leptin levels or BMI before and after eradication of H. pylori. However, serum leptin levels increased in 7/9 patients who showed an increase in BMI, and decreased in 5/6 patients who showed a decrease in BMI. The study demonstrated a significant positive correlation between serum leptin levels and BMI in patients after eradication of H. pylori infection (Shimzu *et al.*, 2002). Eating and appetite disorders are frequent complications of the uremic syndrome which contribute to malnutrition in dialysis patients and several studies showed that hyperleptinemia may contribute to uremic anorexia and malnutrition (Aguilera *et al.*, 2004; Stenvinkel, 1999). As to our knowledge this is the first report of association of serum leptin with helicobacter pylori IgG antibody titer in hemodialysis patients. In the diabetic HD group we found a significant inverse correlation of serum leptin with helicobacter IgG antibody titer that may explain nutritional problems which is frequently seen in diabetic hemodialysis patients. More research is needed regarding the clinical consequences of this association.

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