Journal of Animal and Veterinary Advances 11 (10): 1552-1554, 2012
ISSN: 1680-5593

Decreased Levels of Ghrelin in Brucellosis

[1]Nermin Kilic and [2]Suleyman Sirri Kilic
[1]Department of Biochemistry and Clinical Biochemistry,
Medical School OMU, Samsun, Turkey
[2]Department of Infectious Disease and Clinical Microbiology,
Samsun Research and Training Hospital, Samsun, Turkey

Abstract: Ghrelin is a growth-hormone releasing lipopeptide that was shown to regulate of lipid and carbohydrate metabolism and appetite. Brucellosis characterized by fever, headache, night sweats, extreme tiredness, chills and weight loss and anorexia. This research aimed to investigate the changes of ghrelin concentrations in blood of brucellosis patients 19 brucellosis patients and 16 healthy subjects with similar ages were randomly selected as control group. Serum levels of acylated ghrelin were evaluated on blood samples of the participants by Radio-Immunoassay Methods. The results showed acylated ghrelin was significantly changed in patients with brucellosis (8.9±2 pg mL^{-1}) compared with controls (39±15.5 pg mL^{-1}). There is no data showing ghrelin in Brucellosis in literature so far. The first evaluated results showed that appetite decrease in Brucellosis might be due to circulating level of ghrelin decrement.

Key words: Brucellosis, headach, sweats, chills, radio-immunoassay, blood

INTRODUCTION

Brucellosis is a relatively rare world wide zoo notic infectious disease caused by the Brucella bacteria. Although, brucellosis is a disease of mainly cattle, swine, goats, sheep and dogs this epidemiologically important infection is transmitted from livestock to humans by direct contact (Seleem *et al*., 2010; Junaidu *et al*., 2006; Abd El-Razik *et al*., 2007; Hawari, 2012).

In humans, brucellosis can cause a range of symptoms that are similar to the flu and may include fever, sweats, headaches, back pains and physical weakness (Solera, 2010). Brucellosis can also cause long-lasting or chronic symptoms that include recurrent fevers, joint pain and appetite lost (Young, 2000; Kilic *et al*., 2005).

Ghrelin, an endogenous ligand for the Growth Hormone (GH) Secretagogue Receptor (GHSR) was originally discovered in extracts of rat and human stomach where it is localized in the endocrine X/A-like (ghrelin cells) cells of the gastric mucosa and is known to act as a signal for food intake. This peptide hormone is composed of 28 amino acid residues, bearing a serine (rarely threonine) residue on the third position where a modification (acylation) is essential for its function. Both forms are present in various tissues and blood where they have important physiological and pathophysiological roles (Katergari *et al*., 2008; Aydin 2007; Kojima *et al*., 1999; Kojima and Kangawa, 2005; Imam *et al*., 2009). This research aimed to investigate the changes of ghrelin concentrations in blood of brucellosis patients. The original aspect of this study was to show how appetite hormone (ghrelin) alters in brucellosis.

MATERIALS AND METHODS

Objectives: The study was carried out on the volunteers whose written consent was taken prior to the study together with the Institutional Ethical Committee approval of the study protocol sampling was from 19 brucellosis patients and 16 healthy controls. All healthy controls had no any health problems as family history of obese, abdominal surgery and gastrointestinal diseases. Brucellosis diagnosis was based on clinical, serologic, bacteriologic and epidemiologic data. The diagnostic criteria for Brucella were as follow: isolation of a *Brucella* species from blood culture (Bactec 9050, Becton-Dickinson Diagnostic Instrument System, Sparks, USA) or a single Brucella titre of ≥1/160 (by standard tube agglutination test or Coombs) confirmed by a 2-Mercaptoethanol test (2-ME) titre of 1/160 in association with compatible clinical findings (Young, 1991). The control groups were all healthy and exclusion criteria for the controls were as follows: pregnancy, use of any drugs, no alcohol consumption and diabetes, use of

Corresponding Author: Nermin Kilic, Department of Biochemistry, Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey

tobacco products, regular intense exercise, chronic medical illness, history of abdominal surgery, history of gastrointestinal diseases and family history of obese. All subjects were advised not to eat, smoke or drink (except water) for the overnight prior to collection of blood samples. Thus, they came to the hospital after an overnight fast and the blood specimens were drawn before breakfast. Approximately, 10 mL bloods were taken from the patients and controls.

Ghrelin assay: Serum ghrelin levels were measured using a commercially available Radioimmunoassay (RIA) kit (Linco Research, St. Charles, MO, USA). This RIA uses an antibody that recognizes active epitops of ghrelin. All samples were read with a gamma counter (LKB-Wallac, MultiGamma 1261, Turku 10, Finland). Ghrelin concentrations were calculated from standard curves generated in the same way with ghrelin.

Statistical analysis: Statistical analysis was done using the SPSS 12 statistical package. The comparison between the groups was determined by the Mann-Whitney U-test. The data are expressed as arithmetic means±Standard Deviation (SD) $p<0.05$ were considered significant.

RESULTS AND DISCUSSION

Biochemical parameters and demographic characteristics study groups are shown in Table 1. Results showed that patients with Brucellosis had >4 fold lower serum level of ghrelin than control (Fig. 1). Significant correlations were observed between ghrelin levels and subjects Body Mass Index (BMI, calculated as kg m^{-2}).

Researchers also found a relationship between ghrelin levels measured patients bearing Brucella and the blood LDL (Low Density Lipoprotein), AST (Aspartate Amino Transferase), ALT (Alanine Amino Transferase), CRP (C-Reactive Protein) and ESR (Erytrocyte Sedimentation Rate) level; those who were lower in controls. This connection was statistically significant ($p = 0.000$).

To the best of the knowledge this is the first study to report serum active ghrelin levels in patients with brucellosis. The level of ghrelin in the brucellosis group was 4 fold lower than in controls. The decreased levels of the appetite hormone (ghrelin) are a new finding of brucellosis.

There has been evidence that plasma ghrelin levels may increase in infections such as with *H. pylori* which is closely associated with the development of chronic gastritis (Osawa, 2008; Ikeda *et al*., 2011). Additionally,

Table 1: Demographic characteristics and biochemical data of groups

Characteristics	Control	Patient
Age	36.25± 6.29	36.88±9.55
Gender (M/F)	9/7	10/9
Body mass index (kg m^{-2})	24.2±2.1	23.3±2.3
HDL (mg dL^{-1})	61.0±6.4	43.3±5.3
LDL (mg dL^{-1})	128.2±25.4	158.8±10.6
AST (U L^{-1})	21.4±3.9	23.8± 4.6
ALT (U L^{-1})	23.9± 4.3	29.5±5.6
ESR (mm h^{-1})	12±5.4	37.8±6.0
CRP (mg L^{-1})	3.2±0.6	36.5±6.4
Ghrelin (pg mL^{-1})	39±15.5	8.9±2.0

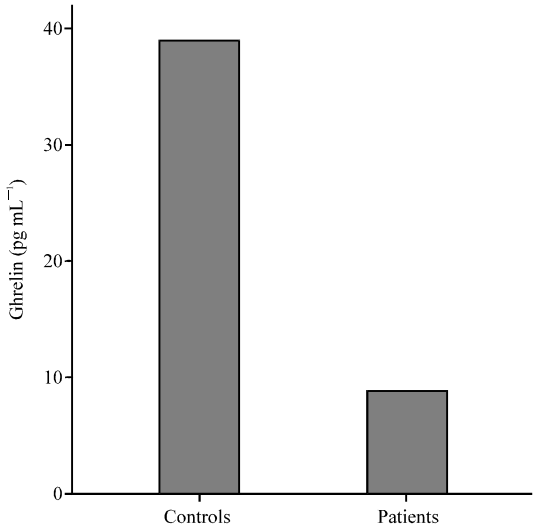

Fig. 1: Serum ghrelin levels

the increased ghrelin levels may mediate immune responses in these patients as suggested to play a regulatory role in innate immune responses to inflammatory infection in oral cavity (Ohta *et al*., 2011). But the decreased levels was observed in this study so, it is unlikely that the changed levels of ghrelin is directly related with infectious process.

The evaluated results should be considered as preliminary and subject to some limitations. First of all, the sample size was too small. The observations need to be confirmed with a larger number of samples in order to find out the mechanism (s) behind the results. Also, researchers could not find any similar research which examined the changes serum in Brucellosis on human thus we are unable to compare the results with other reports. However, based on the results, it could be said that decreased serum acylated ghrelin levels appear to be a new sign of Brucellosis.

CONCLUSION

Researchers tentatively suggest that measuring serum ghrelin levels might be helpful for diagnosing of

Brucellosis beside an elevated C-reactive protein level, ESR level and other classical parameters such AST, ALT. Serum ghrelin level alterations in Brucellosis may have a causal role in the appetite lost and testing these alterations might be aid in the diagnosis of Brucellosis. Since, active ghrelin is known to have important physiological roles in the regulation of food intake (Gallas and Fetissov, 2011).

REFERENCES

Abd El-Razik, K.A., H.M. Desoukey and W.M. Ahmed, 2007. Investigations on brucellosis in Egyptian baladi does with emphasis on evaluation of diagnostic techniques. Pak. J. Biol. Sci., 10: 342-348.

Aydin, S., 2007. Discovery of ghrelin hormone: Researches and clinical applications. Turk. J. Biochem., 32: 76-89.

Gallas, S. and S.O. Fetissov, 2011. Ghrelin, appetite and gastric electrical stimulation. Peptides, 32: 2283-2289.

Hawari, A.D., 2012. Epidemiological studies, seroprevalance and some risk factors of brucellosis in sheep and goats in the South Province of West Bank. Asian J. Anim. Vet. Adv., 7: 535-539.

Ikeda, K., T. Chiba, T. Sugai, K. Kangawa, H. Hosoda and K. Suzuki, 2011. Correlation between plasma or mucosal ghrelin levels and chronic gastritis. Hepatogastroenterology, 58: 110-111.

Imam, S.S., M.E. Kandil, M. Shoman, S.I. Baker and R. Bahier, 2009. Umbilical cord ghrelin in term and preterm newborns and its relation to metabolic hormones and anthropometric measurements. Pak. J. Biol. Sciences, 12: 1548-1555.

Junaidu, A.U., M.D. Salihu and M.L. Gulumbe, 2006. Seroprevalence of brucellosis in sheep in Sokoto city abattoir. Pak. J. Biol. Sci., 9: 2696-2698.

Katergari, S.A., A. Milousis, O. Pagonopoulou, B. Asimakopoulos and N.K. Nikolettos, 2008. Ghrelin in pathological conditions. Endocr. J., 55: 439-453.

Kilic, N., M. Ozden and A. Kalkan, 2005. Lipid peroxidation levels in patients with acute brucellosis. Clin. Exp. Med., 5: 117-121.

Kojima, M. and K. Kangawa, 2005. Ghrelin: Structure and function. Physiol. Rev., 85: 495-522.

Kojima, M., H. Hosoda, Y. Date, M. Nakazato, H. Matsuo and K. Kangawa, 1999. Ghrelin is a growth-hormone-releasing acylated peptide from stomach. Nature, 402: 656-660.

Ohta, K., N.J. Laborde, M. Kajiya, J. Shin and T. Zhu *et al*., 2011. Expression and possible immune-regulatory function of ghrelin in oral epithelium. J. Dent. Res., 90: 1286-1292.

Osawa, H., 2008. Ghrelin and Helicobacter pylori infection. World J. Gastroenterol., 14: 6327-6333.

Seleem, M.N., S.M. Boyle and N. Sriranganathan, 2010. Brucellosis: A re-emerging zoonosis. Vet. Micriobiol., 140: 392-398.

Solera, J., 2010. Update on brucellosis: Therapeutic challenges. Int. J. Antimicrob. Agents, 1: 18-20.

Young, E.J., 1991. Serologic diagnosis of human brucellosis: Analysis of 214 cases by agglutination tests and review of the literature. Rev. Infect. Dis., 13: 359-372.

Young, E.J., 2000. Brucella Species. In: Principles and Practice of Infectious Disease, Mandel, G.L., J.E. Bennet and R. Dolin (Eds). Churchill Livingstone, USA., pp: 2386-2393.