MP2-17

Anti-inflammatory effect of Obestatin in Experimental Rat Autoimmune myocarditis model

Erciyes University School of Medicine Division of Pediatric Cardiology (1), Erciyes University School of Veterinary Division of Histopathology (2) Erciyes University School of Medicine Division Biochemistry(3)Erciyes University School of Veterinary Division of Physiology(4)

Background and aim:
Obestatin is a popular endogeneous peptide, known to have autoimmune regulatory effect on energy metabolism and gastrointestinal system. The studies regarding the anti-inflammatory effect of obestatin are limited in number. In this study we aimed to show anti-inflammatory effect of obestatin in experimental rat autoimmune myocarditis model.

Material and Methods:
Experimental autoimmune myocarditis was induced in Lewis rats by immunization subcutaneously twice at a 7-day interval with porcine cardiac myosin in an equal volume of complete Freund’s adjuvant supplemented with Mycobacterium tuberculosis. Intraperitoneal pretreatment with obestatin(50μg/kg) was started before the induction of myocarditis, and continued for 3 weeks. The severity of myocarditis was evidenced by clinical, echocardiographic and histological findings. In addition by-products of neutrophil activation, lipid peroxidation, inflammatory and anti-inflammatory cytokines were measured in serum.

Results:
Obestatin significantly ameliorated clinical and histopathological severity of autoimmune myocarditis. Therapeutic effect of obestatin in the myocarditis was associated with reduced lipid peroxidation, suppression of PMNL infiltration and enhancement of glutathione synthesis [malondialdehyde (MDA), myeloperoxidase (MPO), glutathion peroxidase (GSH) activities], inhibition of serum inflammatory(IL-1β, IL 6, TNFα), and activation of anti-inflammatory cytokines (TGFβ, IL-10). Histopathologically; there was obvious cavity dilatation and a increase in wall thickness in left ventricle, widespread lymphocytic and histocytic infiltrate (arrow) is associated with myocyte damage Severe infiltration of relatively large mononuclear cells (solid arrow) was observed myocardium. Large areas of necrosis and myofiber degeneration were present(Figure1) in myocarditis. These histopathological changes were all shown to be decreased in obestatin treated rats. Minimal focal inflammatory lesion is shown macroscopically in Figure 2. There was mild dilatation and a in wall minimal thickness in left ventricle. Myocardial inflammatory infiltration (arrow) was also seen but decreased in comparision to myocarditis group (figure 2).

Conclusion:
This study demonstrated novel anti-inflammatory effect of obestatin in an experimental model of autoimmune myocarditis. Consequently, obestatin administration may represent a promising therapeutic approach for myocarditis and so for the dilated cardiomyopathy in the future.