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DPP-4 Inhibition in Diabetic Rheumatoid Arthritis Patients
Diabetik Romatoid Artritli Hastalarda DPP-4 İnhibisyonu

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Abstract

Rheumatoid arthritis (RA) is a common disorder that affects the synovium with an autoimmune reaction. Additionally, the prevalence of diabetes mellitus (DM) in RA patients is higher compared with normal population. Chronic systemic inflammation is a characteristic feature of RA and also has been associated with both insulin resistance and type 2 DM. A recent research by Ospelt et al. showed that inhibition of fibroblast activation protein and dipeptidylpeptidase increases cartilage invasion by rheumatoid arthritis synovial fibroblasts. Furthermore, Jacobs et al. has suggested in a recent publication that the use of a dipeptidylpeptidase inhibitor in the setting of RA is a precious contribution in a determination of the role of RASFs in disease progression. The recent guidelines for the treatment and management of diabetes from the American Diabetes Asoociation, American Association of Clinical Endocrinologists and the National Institute for Health and Clinical Excellenge include DPP-4 inhibitors, a new therapeutic option. However, the available data on the inhibition of dipeptidyl peptidase in RA suggest that we should be careful in terms of the use of DPP-4 inhibitors in the treatment of diabetic patients with RA. *Turk Jem 2013; 17: 81-2*

Key words: Diabetes mellitus, DPP-4 inhibitors, rheumatoid arthritis

Özet

Romatoid artrit (RA) otoimmun reaksyon ile synoviayı etkileyen, sık görülen bir hastalıktır. Buna ek olarak diabetes mellitus prevelansı RA'lı hastalarda normal populasyona göre daha yüksektir. Kronik sitemik inflamasyon romatoid artritin karakteristik bir özelliğidir, insülin direnci ve tip 2 diabetes mellitus ile ilişkilidir. Ospelt ve arkadaşlarının son zamanlarda yaptıkları bir çalışmada fibroblast aktivatör protein ve dipeptidilpeptidaz inhibisyonunun romatoid artrit synoviyal fibroblastları ile kartilaj invazyonunu arttırdığı gösterilmiştir. Ayrıca Jacob ve arkadaşları romatoid artritte dipeptidil peptidaz inhibitörlerinin rolünü değerlendirmişler, romatoid artritte sinovyal fibroblastların hastalık ilerleyişinde önemli katkılarının olduğunu ortaya koymuşlar ve yakın zamanda yayınlamışlardır. ADA, AACE ve NICE'nin son diabet tedavi kılavuzları yeni tedavi seçeneği DPP-4 inhibitörlerini içermektedir. Bununla birlikte RA'de dipeptidilpeptidaz inhibisyonu ile ilgili ulaşılabilen veriler, diabetik RA'lı hastalarda DPP-4 kullanılmasında dikkatli olunması gerektiğini göstermektedir. *Turk Jem 2013; 17: 81-2*

Anahtar kelimeler: Diabetes mellitus, DPP-4 inhibitörleri, romatoid artrit

Dear Editor;

Ospelt et al. was recently performed a study that evaluate the effect of L-glutamyl L-boroproline (PT-630) on rheumatoid arthritis synovial fibroblasts (RASFs) and their invasive attitude in joint cartilage of healthy human and in a severe combined immunodeficient (SCID) mouse (1). Results of the study showed that fibroblast activation protein and dipeptidylpeptidase increases cartilage invasion by rheumatoid arthritis synovial fibrobalsts. In a recent report Jacobs et al. suggested (2) that a dipeptidylpeptidase inhibitor in the setting of rheumatoid arthritis (RA) is a precious contribution in a determination of the role of RASFs in disease progression (2). However, these well conducted studies bring up some consideration about the use of DPP-4 inhibitors in diabetic patients with RA.

Insulin resistance and type 2 diabetes mellitus has been related with chronic systemic inflammation. An important question have to answered if the prevalence of DM is raised in RA patients. A few trials was target this question although the results of these

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reports have been inconsistent. Han et al.,was performed a population based research and showed a higher prevalence of type 2 DM in patients with RA contrast to matched controls (3). Nevertheless, conflicting results were represented from two clinical trial. The research revealed by Solomon et al. did not find a proof of correlation between RA and DM in a prospective cohort study (4).While another cohort study del Rincon et al. showed a higher rates of diabetes in RA patients compared with the controls (5).

Supraphysiologic concentrations of exogenous glucagon-like peptide-1 (GLP-1) can decrease blood glucose in type 2 DM. There has been great interest at decreasing the DPP4 activity in humans to raise plasma GLP-1 level. Since the Food and Drug Administration (FDA) approved the use of dipeptidyl peptidase-4 (DPP-4) inhibitors for the treatment of diabetes in 2006, the latest guidelines of ADA, AACE and NICE involve the DPP-4 inhibitors for the treatment of type 2 DM.

Ospelt et al. have shown that inhibition of DPP-4 increases cartilage invasion by rheumatoid arthritis synovial fibroblasts. As mentioned above, the prevalence of DM in RA patients is higher than in the general population and intermittent or continuous glucocorticoid use is difficult to treat this group of patients. Since the symmetrical joint deformities are a predominant characteristic and undesired feature of the disease. Accumulation of this data raised a question about the DPP4 inhibitor treatment in diabetic RA patients. Furthermore, the important problem arises whether DPP-4 inhibition contribute to the occurrence of deformities in patients with RA. Ideally, large-scale, prospective studies are required to elucidate the exact effect of DPP-4 inhibitor therapy on RA patients. In addition, in a near-future ADA, AACE and NICE guidelines may give special consideration for diabetic patients with RA.

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