OBJECTIVES: Irisin (OPN) is required for osteoclast recruitment. We hypothesized that AD exacerbates bone erosion by inducing OPN expression in synovial tissue. This study aimed to evaluate a novel role for AD in RA.

METHODS: The serum levels of AD and OPN were determined in 38 RA, 40 osteoarthritis (OA) patients, and 20 healthy controls using enzyme-linked immunosorbent assay (ELISA). AD, OPN production were measured by double immunofluorescence of RA and OA synovial tissue. Quantitative real-time PCR and immunofluorescence were used to evaluate the mRNA and protein expression levels of OPN in RA synovial fibroblasts (RASFs) and OA synovial fibroblasts after preincubation with AD, respectively. Migration of the RAW264.7 osteoclast precursors cell line was assessed using the Transwell migration assay and co-culture system. Bone destruction and osteoclastogenesis were assessed by immunohistochemistry, microcomputed tomography, and tartrate-resistant acid phosphatase (TRAP) staining in AD-treated collagen-induced arthritis (CIA) mice with antibody (Abadie, C) and their control groups (Abadie, C).

RESULTS: Our results indicated that the AD and OPN expression levels increased noticeably and were associated with each other in the RA serum. The AD distribution was coincident with that of OPN in the RA synovial tissue. AD stimulation of RASFs increased OPN production in a dose-dependent manner. AD-treated RASFs promoted RAW264.7 cell migration, and the effect was blocked with a specific antibody against OPN. Silencing of OPN using lentiviral-OPN shair-p RNA reduced the number of TRAP-positive osteoclasts and the extent of bone erosion in the AD-treated CIA mice. When bound to integrin α1β3, OPN functions as a mediator of AD and osteoclasts.

CONCLUSIONS: Our study provides new evidence of AD involvement in bone erosion. AD induces the expression of OPN, which recruits osteoclasts and initiates bone erosion. These data highlight AD as a novel target for RA treatment.

Disclosure of Interest: None declared


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SERUM IRISIN AND MYOSTATIN LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

J.M.D.S. Silva1,2, R. C.D.E. Santo1,2, E.C. Freitas1,2, N.F.T. Braz3, A.C.S. Silva3, A.M. Kakehashi3, R. M. Xavier4, L. Oliveira de Doenças Autoimunes de Clínicas de Porto Alegre; Universidade Federal do Rio Grande do Sul, Porto Alegre; Laboratório Interdisciplinar de Investigação Médica, Universidade Federal de Minas Gerais; Serviço de Reumatologia, Hospital das Clínicas da Universidade Federal de Minas Gerais; Universidade Federal de Minas Gerais, Belo Horizonte; Serviço de Reumatologia, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

BACKGROUND: Rheumatoid arthritis (RA) patients have loss of muscle mass. The balance between muscle protein synthesis and degradation is regulated by cytokines and growth factors, named myokines, such as irisin and myostatin. Myokines are mainly expressed by skeletal muscle and exert systemic effects as a mediator of AD and osteoclasts.

OBJECTIVES: To evaluate serum levels of irisin and myostatin and body composition of RA patients and controls.

METHODS: 122 female patients with RA, mean age 53 years, mean disease activity score (DAS28) 4.09, mean disease duration 11.2 years and mean body mass index 27.33 kg/m² were included. 69 age and sex-matched healthy subjects were enrolled as control group. Irisin (Phoenix Pharmaceuticals) and myostatin (R and D Systems) serum levels were evaluated by ELISA. Fat mass index (FMI; Kg/m²) and appendicular lean mass index (ALMI;Kg/m²) were assessed by total body dual-energy x-ray absorptiometry. Student’s t test and Spearman correlation were performed. Significance was set at p<0.05.

RESULTS: RA patients had decreased serum levels of irisin (25.61±8.25 vs 30.36 ±10.95 ng/ml; p<0.05) and myostatin (3011.28±1271.11 vs 4049.08±1610.01 pg/ml; p<0.05), decreased ALMI (6.09±0.88 vs 6.50±1.10; p<0.05) and increased FMI (11.26±3.30 vs 9.44±2.65; p<0.05), compared to controls. No correlations were observed among irisin and myostatin levels and ALMI and FMI. Of the 122 RA patients, 40 were analysed for the use of biologic medication. Serum levels of irisin and myostatin were different between RA patients treated and non-treated with biologics (table 1).

CONCLUSIONS: RA patients presented loss of lean mass and gain of fat mass, as well as lower irisin and myostatin serum levels, in comparison with controls. Additionally, the use of biologic medication by patients impacted on myokines serum levels. Further analyses are needed for a better comprehension of irisin and myostatin roles in RA, and to verify their correlation to other RA features.

REFERENCES:

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