- [4] Scorza R, et al., 2001.
 [5] Higuchi T, et al., 2015.
 [6] Hassoun PM, et al. 2015.

Disclosure of Interests: clara crescioli: None declared, Valeria Riccieri: None declared, Katia Stefanantoni Consultant for: Only 1 scientific advice for Italfarmaco in 2016, clarissa corinaldesi: None declared, massimiliano vasile: None declared, francesco marampon: None declared, Guido Valesini: None declared, andrea lenzi: None declared, luigi di luigi: None declared, cristina antinozzi: None declared
DOI: 10.1136/annrheumdis-2019-eular.7161

THU0021 CLINICAL SIGNIFICANCE OF WEIGHT LOSS ON THE LEVEL OF PROINFLAMMATORY CYTOKINES IN PATIENTS WITH OSTEOARTHRITIS

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Background: Obesity is a condition that prolongs chronic inflammation and promotes synthesis and secretion of pro-inflammatory factors by adipose tissue, such as classical cytokines, tumor necrosis factor- α (TNF- α), adipokines (leptin, adiponectin, resistin) and other newly identified proinflammatory factors (hemerin, lipokain, serum amyloid protein 3) [1,2,3,4,5]. Nowadays one of the most actively studied adipokines is nicotinamide phosphoribosyltransferase (visfatin, Nampt).

Objectives: We investigated the relationship the effect of weight loss over 5 kg on the clinical manifestations of OA and Nampt serum levels in patients with OA.

Methods: We observed 160 patients with different forms of OA ranged in age from 36 to 78 years, of whom there were 104 (65%) women (mean age 52.08 $\pm$ 1.58 years), and 56 (35%) of men (mean age - 54.07 $\pm$ 2.0 years) and the control group (60 healthy persons) with no complaints of pain in the joints over a lifetime, and without clinical signs of OA. Nampt level in serum was determined by ELISA using a commercial test systems.

Results: As overweight patients were recruited in the study, hypocaloric diet low in animal fats and physiotherapy has been recommended to all participants. The positive dynamics in body weight loss over 5kg within 3 months has been achieved by 36 patients (23%). All patients were divided into two groups to study the effect of weight loss on the clinical manifestations of OA. These data proves that obesity may be an important risk factor for OA progression. As a result, weight loss results in decreasing metabolic disorder severity. In the second group of patients we have seen a decrease in all the parameters, but a significant difference has been observed only in the level of CRP, level of pain at rest and during walking according to VAS scale and total index on the WOMAC. However, patients with weight loss over 5 kg had significantly greater positive dynamics of clinical parameters than in the second group without weight loss. This fact is probably explained by the decreased activity of inflammatory process after OA therapy and weight reduction.

Conclusion: Thus, as a result of our study patients with OA with weight loss of more than 5 kg had more obvious pain relief than patients with the original weight. These findings suggest that there is a possible role of visfatin in the pathogenesis of osteoarthritis. All patients with OA with a BMI over 25 kg/m² are recommended to lower their weight to decrease the mechanical stress on the joints, and also to reduce the severity of inflammation and metabolic disorders.

REFERENCES:

- [1] Akhverdyan, Y. et al. Adipokines as new laboratory markers in osteoarthritis//Ann Rheum Dis 2013. – Vol.72 (Suppl. 3):702.
- [2] Degtiarev, V.K.; Aleksandrov, A.V. et al. The influence of general magnetic therapy on the psychological status of the patients presenting with osteoarthritis//Voprosy kurortologii, fizioterapii, i lechbenno fizicheskoy kultury 2013, №3, P.27-30.
- [3] Zavadovsky, B. V. et al. The efficacy and safety of etoricoxib versus meloxicam in the treatment of patients with gonarthrosis//Terapevticheskii Arkhiv Volume: 88 (12), P.: 78-81.
- [4] Papichev, E. V. et al. Fetuin-a level and secondary osteoporosis in women with rheumatoid arthritis//Osteoporosis International, 2018, Vol.:29 S.239.

- [5] Polyakova J. et al. Pathogenic relationship between osteoarthritis, overweight and inflammation//Annals of the Rheumatic Diseases. 2015. :. 74. №S2. C. 372.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.2048

THU0022 ETANERCEPT INCREASES AUTOPHAGY AND REDUCES APOPTOSIS INDUCED BY TNF- α EXPOSURE IN ENDOTHELIAL CELLS IN VITRO

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Background: Rheumatoid arthritis (RA) is associated with high incidence of cardiovascular events, mainly due to accelerated atherosclerosis and endothelial dysfunction (1). Apoptosis in endothelial cells has been associated with vascular wall damage, contributing to atherosclerotic plaque formation (2). At the contrary, autophagy may play a protective role in preventing development of atherosclerosis. However, the exact mechanism which controls the autophagy of endothelial cells is still unknown. Tumor necrosis factor alpha (TNF- α) is one of the leading cytokines involved in the pathogenesis of RA. Several evidences suggest a pro-atherogenic effect of TNF- α in patients with RA. Etanercept (ETA) and other TNF- α inhibitors are effective treatments for joint inflammation in RA, but their effect on endothelial dysfunction is still not well understood.

Objectives: The aim of this study was to investigate *in vitro*, the effects of ETA treatment on endothelial cells exposed to TNF- α , with particular attention on apoptosis levels and autophagy pathway.

Methods: *In vitro* effects of ETA and TNF- α on endothelium were evaluated using human umbilical vein cell line EA.hy926. Cells were treated with ETA (15 μ g), TNF- α (10 ng/ml), alone or in combination. An untreated control cell culture was also performed. After 24 hours, apoptosis levels and autophagy have been evaluated. Apoptosis was analyzed by flow cytometry using a FITC-conjugated annexin V and propidium iodide apoptosis detection kit (3); autophagy was analyzed by western blot for the expression level of the autophagic markers LC3-II and p-62 (4).

Results: TNF- α treatment significantly increased apoptosis in endothelial cells compared both to untreated and ETA-treated cells ($p=0.0067$ and $p=0.00187$ respectively) [Figure 1]. The co-treatment with TNF- α and ETA significantly reverted the increase of apoptosis levels ($p=0.001$ versus TNF α alone). Both ETA and TNF α treatments significantly increased the expression level of LC3II in treated cells when compared to untreated cells ($p=.18$ and $p=.3$ respectively). The co-treatment induced an additive effect on autophagy levels ($p<0.0001$ versus untreated cells). At last, the expression level of p-62 showed an inversely proportional trend to LC3II levels [ETA ($p=0.0001$), TNF- α $p=.1$), ETA+TNF- α $p=.5$) versus untreated cells, respectively] [Figure 2].

Conclusion: Our results show that treatment with Etanercept have a protective effect on endothelial cells *in vitro*, reversing the apoptosis induced by TNF- α . Moreover, this is the first study that supports a possible effect of Etanercept in increasing autophagy level in endothelial cells. Reducing TNF α -induced apoptosis, Etanercept treatment may lead to an improvement of endothelial function and to a reduction of accelerated atherosclerosis.

REFERENCES:

- [1] Hürliemann D, Forster A, Noll G, Enseleit F, Chenevard R, Distler O, et al. Anti-tumor necrosis factor- α treatment improves endothelial function in patients with rheumatoid arthritis. *Circulation*. 2002;106:2184–2187
- [2] Fukuo K, Nakahashi T, Nomura S, Hata S, Suhara T, Shimizu M, et al. Possible participation of Fas-mediated apoptosis in the mechanism of atherosclerosis. *Gerontology*. 1997;1:35–42.
- [3] Alessandri C, Barbati C, Vacirca D, Piscopo P, Confalonni A, Sanchez M, et al. T lymphocytes from patients with systemic lupus erythematosus are resistant to induction of autophagy. *FASEB J*. 2012;26:4722–4732.
- [4] Barbati C, Alessandri C, Vomero M, Vona R, Colasanti T, Vacirca D, et al. Autoantibodies specific to D4GDI modulate Rho GTPase mediated cytoskeleton remodeling and induce autophagy in T lymphocytes. *J Autoimmun*. 2015;58:78–89.