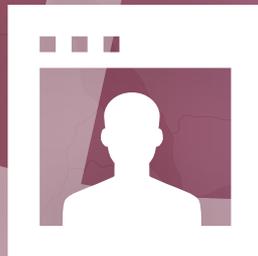


WORLD CONGRESS
ON OSTEOPOROSIS,
OSTEOARTHRITIS AND
MUSCULOSKELETAL
DISEASES

VIRTUAL CONGRESS

August 20-22, 2020



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AbstractBook

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XANTHINE OXIDASE, XANTHINE DEHYDROGENASE, AND SUPEROXIDE DISMUTASE ACTIVITIES IN RHEUMATOID ARTHRITIS WITH EXTRA-ARTICULAR MANIFESTATIONS: ENZYMATIC PROFILING OF BLOOD PLASMA

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Objective: To study xanthine oxidase (XO), xanthine dehydrogenase (XDG), superoxide dismutase (SOD) activities in plasma of rheumatoid arthritis (RA) patients with extra-articular manifestations.

Methods: We obtained samples from 71 RA patients (46 females and 25 males) and 30 healthy controls. Diagnosis of RA had been established using ACR/EULAR 2010 criteria. Extra-articular manifestations were found in 30 (42,2%) RA patients. 30% of them had cardiovascular involvement, 23.3% – pulmonary involvement, and 23.3% had renal involvement. Enzymatic activities in plasma were determined by spectrophotometric assay. Statistical comparison tests were selected in line with common guidelines, differences were considered significant when $p < 0.05$.

Results: Reference intervals ($M \pm 2\sigma$) for XO activity were 2.28-5.12 nmol/min/ml, for XDG activity – 3.96-7.24 nmol/min/ml, for SOD activity – 3.13-6.58 units. Significantly increased plasma XO and SOD activities dominated in the enzymatic patterns of RA patients. Articular lesions were found to be associated with elevated activity of all the enzymes: XO ($p \leq 0.001$), XDG ($p = 0.019$), and SOD ($p \leq 0.001$). XO activity ($p < 0.001$) are further increased in RA patients with extra-articular manifestations comparing to selective articular RA type. SOD activity ($p = 0.022$) is lower in RA patients with extra-articular manifestations form in RA patients than with articular form.

Conclusion: RA is characterized by activation of both oxidative and antioxidant metabolic pathways including significant changes of plasma XO, XDH, and SOD activities. Overall increase of all three plasma enzymatic activities is found to be characteristic for RA patients. The difference between selective articular and visceral types of organ involvement also exists. One of eventual sources of "rheumatic" anticitrulline antigens is newly discovered neutrophil extracellular traps. Their induction is influenced by some enzymes of purine/oxidative metabolism, such as xanthine oxidase, xanthine dehydrogenase, and superoxide dismutase.

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SPONTANEOUS AND INDUCED NEUTROPHIL EXTRACELLULAR TRAPS FORMATION IN RHEUMATOID ARTHRITIS PATIENTS

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Objective: To study the ability of peripheral blood neutrophils to generate extracellular traps spontaneously and after inductor exposure in rheumatoid arthritis (RA) patients.

Methods: The study included 15 patients with verified RA according to the ACR/EULAR 2010 criteria. Neutrophils were isolated with one-step centrifugation procedure using double-layer ficoll-amidotrizoate density gradient with density of upper and lower layers 1080 kg/m³ and 1090 kg/m³, respectively. The types of cells in the resulting fractions were identified by means of light microscopy, the extent of neutrophil activation was measured using common nitro-blue tetrazolium test. The generation of neutrophil extracellular trap (NETs) was stimulated by phorbol-12-myristate-13-acetate (PMA). The shape and size of NETs was assessed using fluorescence microscopy with SYBR green.

Results: RA disease activity assessed using DAS28 score did not exceed 2.6 in every patient. 15 healthy people were included as a control group. The mean age of RA patients was 56.2±3.4 y, mean disease duration 1.4±0.5 y. Anticitrullinated protein antibodies (ACPA) were detected in 60% of RA patients. Mean purity of neutrophil fraction in RA group was 93.3%, cell viability in every sample was above 95%. Spontaneous NET formation was observed in neutrophils isolated from RA patients and healthy controls. Spontaneous and induced NETosis in RA patients was significantly increased comparing to healthy controls. Neutrophils from ACPA-positive RA patients demonstrated increased spontaneous and induced NETs formation compared from ACPA-negative RA patients.

Conclusion: We have revealed enhanced spontaneous and induced NET formation by neutrophils from RA patients, suggesting that circulating neutrophils may be primed to NETosis through autoimmune inflammation. Thus, NETs can be used as potential biomarkers of RA.