REVISTA BRASILEIRA DE REUMATOLOGIA

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Original article

Higher nitric oxide levels are associated with disease activity in Egyptian rheumatoid arthritis patients

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ARTICLE INFO

Article history:
Received 10 April 2013
Accepted 6 July 2014
Available online 23 October 2014

Keywords:
Rheumatoid arthritis (RA)
Oxidative stress
Nitric oxide (NO)

ABSTRACT

Background: Oxidative stress generated within inflammatory joints can produce autoimmune phenomena and joint destruction. Radical species with oxidative activity, including reactive nitrogen species, represent mediators of inflammation and cartilage damage.
Objectives: To assess serum nitric oxide as a marker of oxidative stress in Egyptian patients with rheumatoid arthritis and its relation to disease activity.
Methods: Eighty patients with rheumatoid arthritis were divided into 2 groups, according to the DAS-28 score: Group I: 42 patients with disease activity, and Group II: 38 patients with no disease activity. Forty age- and sex-matched individuals were included as control group (Group III). Routine laboratory investigations were done, and nitric oxide was measured using Elisa. Hand plain radiographies were done for radiological status scoring using the Sharp method.
Results: A comparison between nitric oxide in all three groups showed a highly significant difference ($p < 0.001$), significantly higher levels were obtained among rheumatoid arthritis patients in comparison to controls, and higher levels were obtained in patients with active disease (mean ± SD 82.38 ± 20.46) in comparison to patients without active disease (35.53 ± 7.15). Nitric oxide in Group I showed a significant positive correlation with morning stiffness (r = 0.45), arthritis (r = 0.43), platelet count (r = 0.46), erythrocyte sedimentation rate (r = 0.83), C-reactive protein (r = 0.76) and Disease Activity Score (r = 0.85). Nitric oxide showed a significant positive correlation (r = 0.43) with hand radiographies (Sharp score) in Group I.
Conclusion: There are increased levels of nitric oxide in the serum of patients with rheumatoid arthritis. Nitric oxide correlates significantly with disease activity, inflammatory markers and radiological joint status.

DOI of original article: http://dx.doi.org/10.1016/j.rbr.2014.07.003.
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http://dx.doi.org/10.1016/j.rbre.2014.07.002

Níveis de óxido nítrico mais elevados estão associados à atividade da doença em pacientes egípcios com artrite reumatoide

Palavras-chave:
Artrite reumatoide (AR)
Estresse oxidativo
Óxido nítrico (NO)

RESUMO

Introdução: O estresse oxidativo produzido no interior de articulações inflamadas pode produzir fenômenos autoimunes e destruição articular. As espécies radicais com atividade oxidativa, incluindo espécies reativas de nitrogênio, representam mediadores de inflamação e de lesão cartilaginosa.

Objetivos: Avaliar o óxido nítrico sérico como marcador de estresse oxidativo em pacientes egípcios com artrite reumatoide e sua relação com a atividade da doença.

Métodos: Oitenta pacientes com artrite reumatoide foram divididos em dois grupos, de acordo com a pontuação DAS28: Grupo I: 42 pacientes com doença ativa, e Grupo II: 38 pacientes com doença inativa. Quarenta indivíduos equiparados por idade e gênero foram incluídos como grupo controle (Grupo III). Foram realizados exames laboratoriais de rotina e o óxido nítrico foi medido usando Elisa. Radiografias simples das mãos foram feitas para a pontuação do estado radiológico utilizando o método de Sharpe.

Resultados: A comparação do nível sérico de óxido nítrico entre os três grupos mostrou uma diferença altamente significativa ($p < 0{,}001$). Obtiveram-se níveis significativamente mais elevados entre os pacientes com artrite reumatoide em comparação com os controles. Os níveis mais elevados foram obtidos em pacientes com a doença ativa (média ± DP 82,38 ± 20,46) em comparação com aqueles com a doença inativa (35,53 ± 7,15). O óxido nítrico no Grupo I exibiu uma correlação positiva significativa com a rigidez matinal (r = 0,45), artrite (r = 0,43), contagem de plaquetas (r = 0,46), velocidade de hemossedimentação (r = 0,83), proteína C-reativa (r = 0,76) e Índice de Atividade de Doença (r = 0,85). O óxido nítrico mostrou uma correlação positiva significativa (r = 0,43) com as radiografias das mãos (índice de Sharpe) no Grupo I.

Conclusão: Observa-se um aumento nos níveis séricos de óxido nítrico em pacientes com artrite reumatoide. O óxido nítrico se correlaciona significativamente com a atividade da doença, marcadores inflamatórios e estado radiológico das articulações.

Introduction

Nitric oxide (NO) is an endogenously produced small molecule that has critical roles in cellular signaling and is involved in a variety of physiological processes. NO can have opposite biological effects, depending upon various environmental and pathophysiological conditions.[1]

Oxidant stress generated within an inflammatory joint can produce autoimmune phenomena and connective tissue destruction within the synovium. Radical species with oxidative activity, which include reactive nitrogen species and reactive oxygen species, represent the mediators and effectors of cartilage damage.[2]

NO mediates many different cell functions at the site of synovial inflammation, including signal transduction, mitochondrial function and apoptosis.[3]

NO has emerged as an important mediator in rheumatoid arthritis (RA) synovium. Increased levels of NO in serum and synovial fluid have been reported in patients with RA, ankylosing spondylitis and osteoarthritis.[4]

The aim of this work is to assess NO level as a marker of oxidative stress in Egyptian patients with RA and to correlate it with various disease parameters and disease activity.

Methods

In a cross sectional study, 80 patients with RA, diagnosed according to the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) criteria,[5] were divided into 2 groups according to disease activity: Group I: 42 patients with disease activity, and Group II: 38 patients with no disease activity. A third group was included: Group III: 40 age and sex matched healthy individuals as control. All patients were recruited from the Rheumatology Outpatient Clinic and Internal Medicine Ward at Ain Shams University Hospital. Informed consents were obtained from all participants, and the study was approved by the Ain Shams Medical ethics committee. The nature of the present study was explained, and laboratory and radiological procedures represent standard care posing no ethical conflicts. For all the patients, the following were done:

I. Detailed medical history and thorough clinical and musculoskeletal examination with assessment of disease activity by using DAS28-ESR:[6]

Detailed history of disease duration and progression and constitutional symptoms and signs of fever, weight loss and fatigue were assessed, and a thorough musculoskeletal examination was performed.