International Journal of Research in Orthopaedics
Joshi AK et al. Int J Res Orthop. 2016 Dec;2(4):350-353
http://www.ijoro.org

Original Research Article

DOI: http://dx.doi.org/10.18203/issn.2455-4510.IntJResOrthop20164167

Study of inflammatory markers in idiopathic osteoarthritis of knee

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Received: 01 September 2016
Accepted: 01 October 2016

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ABSTRACT

Background: The aim of the present study was to analyse inflammatory markers in idiopathic osteoarthritis of knee and to formulate reliable disease markers in the diagnosis and prognosis of the disease.
Methods: This prospective study was conducted for 2 years in a tertiary care center in 60 patients with idiopathic osteoarthritis of knee and compared them with 60 controls that had no signs of osteoarthritis.
Results: The hematological markers to study inflammatory basis of idiopathic osteoarthritis of knee suggested that ESR (erythrocyte sedimentation rate) was more than 20 mm/hour in 83.3%. Serum rheumatoid factor (RF) and CRP (C-reactive protein) was positive in 8.3% and 13.3% patients respectively. Antinuclear antibody (ANA) was positive in 2 (3.3%) patients and negative in 58 (96.7%) patients. Synovial fluid analysis was done in 44 patients with RF positivity in only 1 patient. The control group has ESR less than 30 mm/hour and CRP was (<3 µg/ml). In the control group RF and ANA were similar to the normal population.
Conclusions: Synovial fluid analysis is of value to rule out crystal arthropathies and pyogenic arthritis. The study indicates that ESR, CRP and RF collectively can serve as surrogate markers in idiopathic osteoarthritis of knee. Further studies need to be done to formulate reliable disease markers in idiopathic osteoarthritis of knee.

Keywords: Osteoarthritis, Erythrocyte sedimentation rate, C-reactive protein, Rheumatoid factor, Antinuclear antibody

INTRODUCTION

Osteoarthritis (OA) is the most common cause of long-term disability in most of the people over 65 years of age. The pathology of OA manifests as loss and erosion of articular cartilage, subchondral sclerosis, and osteophytes formation. OA is of multifactorial etiology and it can be primary or secondary to some other disorder. Arthritic conditions can be classified as low-inflammatory or high-inflammatory types. Patients with the low-inflammatory type have low leukocyte counts in the synovial fluid and laboratory findings are consistent with low-level inflammatory activity. The affected joint often shows focal degeneration. Those with the high-inflammatory type have high leukocyte counts in the synovial fluid, laboratory findings consistent with high-level inflammatory activity, and usually show a more diffuse degeneration of the involved joints. OA is a chronic degenerative cartilaginous joint disorder with variable etiopathogenesis. OA is thought to be derived from defective chondrocyte metabolism thus lack large-scale systemic response. The inflammatory surrogate markers may be produced directly during disease process or indirectly as biological end points of cytokines produced during cartilage degradation and joint destruction. OA

has been classically defined as an age related degenerative wear-and-tear disease, but recent work indicated that it has as an immunological component on a spectrum between healthy condition and rheumatoid arthritis.[1] Although OA is classified as non-inflammatory synovitis, recent studies indicate osteoarthritis may have mild to moderate inflammation. The immune system plays a significant role in OA and RA, but DMARDs, tumor necrosis factor α (TNFα) and interleukin-1 (IL-1) inhibitors, effective in the treatment of RA, are unsuccessful in treating OA. On the basis of this background, the present study was conducted to find out the inflammatory basis of OA.

METHODS

This prospective study was conducted for 2 years in 60 patients and compared them with 60 controls that had no signs of OA. In the diseased group the male female ratio of 1:1.5. The patients were included according to criteria of American Rheumatism Association (ARA, 1986).[2] The detailed history was taken and general physical examination was done. The anteroposterior (weight bearing and non-weight bearing) and lateral radiographs of knee were performed. The serum levels of ESR, CRP, RF and ANA were measured in 60 patients, however in 44 patients synovial fluid analysis was done for cytology and RF. In 60 controls serum levels of ESR, CRP, RF and ANA were analysed.

The institution adheres to the basic principles of the Declaration of Helsinki of the World Medical Association. As human participant were involved, a statement of approval by institutional review board (IRB) and the participant's informed consent was taken. A copy of the IRB approval is provided to the lead author to keep received in his/her personal file.

RESULTS

Among 60 patients 24 (40%) were males and 36 (60%) were females. The disease prevalence and severity was more common in perimenopausal or postmenopausal women than in men. Out of 44 patients RF was positive in only 1 (2.5%) patient. The hematological markers to study inflammatory and immunological profile in idiopathic OA of knee included serum levels of ESR, CRP, RF and ANA. ESR was more than 20 mm/hour in 83.3% cases. Serum RF was positive in 5 (8.3%) patients and negative in 55 (91.7%) patients. CRP was found positive (>3 µg/ml) in 8 (13.3%) patients while negative (<3 µg/ml) in 52 (86.7%) cases. ANA was positive in 2 (3.3%) patients and negative in 58 (96.7%) patients as given in Table 1. Out of 60 patients synovial fluid (SF) analysis was done in 44 patients for cytology and RF. The cytology revealed mild leukocytosis with predominance of mononuclear cells. In the control group the ESR was less than 30 mm/hour. CRP was negative (<3 µg/ml) in all controls. The RF was seronegative in the all participants of control group, but the titers of RF showed an increasing trend with the age. ANA positivity in control group was similar to that of normal population.

Table 1: Haematological markers in osteoarthritis.

Serological markers	No. of patients	Percentage
ESR (mm/hour)		
<20	10	16.7
20-40	37	61.7
>40	13	21.6
RF		
Negative	55	91.7
Positive	5	8.3
CRP		
Negative	52	86.7
Positive	8	13.3
ANA		
Negative	58	96.7
Positive	2	3.3

DISCUSSION

Analysis of synovial fluid showed only 1 (2.5%) case with RF positivity as compared with serum RF of 8.3%. there was no correlation between serum RF and synovial RF. The cytology of synovial fluid revealed mild leukocytosis with a predominance of mononuclear cells. This coincided with findings of Dieppe et al having 80% and Altman and Gray with >72% of mononuclear cells predominance in synovial fluid.[3,4] The importance of SF tests lies in its rationalisation and improved quality control. Further investigation is recommended into the contribution of SF inspection and white cell counts to diagnosis, as well as of the specificity and sensitivity of SF microbiological assays, crystal identification, and cytology.[5] SF analysis was most useful for patients likely to have gout, pseudogout, or infectious arthritis. The derived therapeutic thresholds were consistent with recommended medical practice, for example, with a lower threshold for possible septic arthritis (20%) than for possible gout (65%).[6] Findings of the present study suggest that 83.3% patients of osteoarthritis had ESR 20 mm/hr moreover Serum RF and CRP were positive in 8.3% and 13.3% respectively. These findings correlate well with suggestion by Sipe that there is a modest rise in ESR and the concentration of CRP are elevated in osteoarthritis but to a lesser extent than rheumatoid arthritis.[7] CRP is raised in OA compared to normal population, and is correlated with rheumatic disease signs and symptoms, including HAQ (health assessment questionnaire) disability, joint count, and pain. ESR was not associated with clinical signs or symptoms except for a weak association with functional disability. An inflammatory component associated with OA can be detected in the serum.[8] ESR and high-sensitivity CRP were raised in patients with knee osteoarthritis and were correlated with clinical features.[9] Moreover it correlates well with the study of deOliveira et al that concentration of acute phase protein (APP) and CRP were raised in

osteoarthritis when compared with normal population.[10] Antinuclear antibody (ANA) was positive in 2 (3.3%), one showed borderline positivity and in other it was strongly positive. The present study correlates with the study of Robitaille et al suggesting incidence of ANA positivity was similar to that of normal population.[11] The results were comparable with the study of Cooke that four of 59 were RF positive; five (10%) of 48 cases were ANA positive.[12] In addition to the ability of inflammatory cytokines to induce cartilage catabolism, many cytokines can also promote OA progression by inhibiting anabolic processes critical to cartilage homeostasis.[13] Our current knowledge shows that the inflammatory process involves recruitment of receptors and activation of the complement mechanism by degradation products of extracellular matrices of cartilage and other joint tissues. This leads to synovial reaction which releases a wide variety of cytokines and chemokines. These inflammatory mediators in turn have catabolic effects on chondrocytes. Now a day's therapeutics in osteoarthritis is targeting these inflammatory mediators to reduce both symptoms and structural joint damage in OA.[14] The osteoarthritic joint is considered as a chronic wound, in which the innate immune response is triggered by molecular signals of tissue damage.[15] The more aggressive symptoms of OA knee were seen with increased CRP levels may be mechanically linked to a more inflammatory synovial response in the diseased joint.[16] The systemic CRP levels suggest synovial inflammation in OA patients, probably due to synovial IL-6 production.[17] IgM RFs are sometimes seen in healthy elderly people, which indicate that it may be a result of the age related immune deregulation.[18] RFs may be the result of the immune response to inflammation and probably have regulatory effects on immunoglobulin production by controlling B cell activation.[19] The prevalence of rheumatoid factor positivity in general population increases with age and smoking status. The study indicated that CRP and RF with around 10% of detectability are unsuitable to be recommended as marker in OA. The more severe the clinical and radiographic finding, the ESR is more than 30 mm/hr and CRP are strongly positive. The normal level of ESR increases with age, and up to 29 mm/hr can be accepted as normal limit in elderly population.

However the present results do not match with a study which found ANA positive in 57.5% in osteoarthritis compared to rheumatoid arthritis (28.5%) and normal (10%) controls.[20] Synovial fluid analysis is of value to rule out crystal arthropathies and pyogenic arthritis. The study indicates that raised levels of ESR, RF and CRP collectively indicate that there is some inflammatory component associated with OA. However CRP and RF with around 10% of detectability are unsuitable to be recommended as marker in idiopathic OA of knee. The incidence of ANA in idiopathic osteoarthritis of knee was similar to that of normal population. Further studies need to be done to find valuable inflammatory markers for diagnosis and prognosis of idiopathic osteoarthritis of knee. It may be useful if other biomarkers can be defined.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Joshi AK, Singh V, Hatwal D, Singh M, Joshi C. Study of inflammatory markers in idiopathic osteoarthritis of knee. Int J Res Orthop 2016;2:350-3.