WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 4, Issue 2, 59-64. Research Article ISSN 2277– 7105

SYNOVIAL MUCOSAL CYTOKINES AND CHAPEROKINE IN STAPHYLOCOCCUS AUREUS HUMAN SEPTIC A RTHRITIS

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Article Received on
03 Dec 2014,

Revised on 25 Dec 2014,
Accepted on 15 Jan 2015

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ABSTRACT

Human septic arthritis were clinically proven by the orthopedician in this team. S. aureus was reported in association of 27 neutrophilic synovitis out of 400 arthritis patients. Such patient infections induces local production of synovial cytokines TNF alpha, INF gamma, IL4 and the chaperokine heat shock protein HSP 70 to high levels than that of controls. The proinflammatory; TNF alpha, INFgamma, balanced by the anti-inflammatory IL4 and HSP70 representing the TH1/TH2 balance state. Hence, S. aureus initiate natural neutrophilic, humoral and cellular responses in the synovial compartment of the common mucosal immune system during the septic human arthritis.

Keywords: Septic arthritis, synovum, common mucosal immune system, TH1/TH2 balance.

INTRODUCTION

The pathogenesis of human arthritis can be mapped into three pathways. The haematogenous, the lymphogenous and the direct osteogenic infection spread from the local affected boney tissues.[1] In comparison, the immunopathogensis of septic arthritis may be triggered by the immunodominant epitope(s) of the infectious agent which might be of; an immunogenic, allergenic and /or autoimmunogenic natures resulting in immune response, allergic response and autoimmune response.[2] Such responses actually are of mucosal as well as systemic nature.[3] Excess antibodies and /or excess cytokines may take part in the local immunopathogenesis of human septic arthritis through the immune tissue injury they cause it.[4] The objective of the present work was to assess the local cytokine levels of TNF alpfa,

INF gamma, IL4 and the heat shock protein HPS70 in S. aureus septic arthritis in human beings.

MATERIALS AND METHODS

Four hundred human arthritis cases were clinically proven. The synovial fluids of these patients were aspirated by the senior orthopedicians in this team .Synovial Giemsa[5] stained films reveals 27 of which were of neutrophilic nature. These 27 cases were yielding variable degrees of growth density ranging from scant to heavy growth and marked purity of S aureus as identified by manual standard and Vitic system.[6,7] The clarified synovial fluids were assessed for TNF alpha, INF gamma, IL4 and HSP70 using eliza technique and in accordance with the manufacturer instructions(USBIO,USA).Twenty control synovial fluids were assessed as in the test group as controls.

RESULTS

1-TNF alpha

The 27 patients were showing higher concentration means reaching 35.81 ± 3.423 as compared to 1.687 ± 0.1351pg/ml. in controls Table 1.

2-INFgamma

The concentration means of INF gama was 29.63 ± 2.135 in patients as compared to 1.678 ± 0.137pg/ml. in controls. Table2.

3-IL4

The patients have shown IL4 mean concentrations of 19.51 ± 0.667 as compared to 0.7925 ± 0.116 pg/ml. in controls.Table3.

4-HSP70

The concentration means of HSP70 in patients were 34.34 ± 2.973 as compared to 11.70 ± 1.064 ng/ml. in controls. Table 4.

5-Cytokine balance

The synovial high levels of cytokine concentration means for the pro inflammatory may balance the anti-inflammatory IL4 and HSP70 in the synovial compartments of septic arthritis patients Tables1, 2, 3, and 4.

Table 1: The synovial TNF alpha concentrations among septic arthritis patients.

Test groups	Number of subjects	Concentration means pg/ml. ± SE	Significance
Patients	27	35.81 ± 3.423	< 0.05
Controls	20	1.187 ± 1.34	

Table 2: The synovial INF gamma concentrations among septic arthritis patients.

Test groups	Number of subjects	Concentration mean pg/ml. ± SE	Significance
Patients	27	29.63 ± 2.135	< 0.05
Controls	20	12.15 ± 0.504	

Table 3: The synovial Interleukine 4 concentrations among septic arthritis patients.

Test groups	Number of subjects	Concentration means pg/ml. ± SE	Significance
Patients	27	19.51 ± 0.667	<0.05
Controls	20	0.7928 ± 0.116	

Table 4: The synovial heat shock protein 70 concentrations among septic arthritis patients.

Test groups	Number of Subjects	Concentration means ng/ml. ± SE	Significance
Patients	27	34.34 ± 2.973	<0.05
Controls	20	11.70 ± 1.064	

DISCUSSION

The cytokine IL1B is the main effecter molecule that may promote optimal TNF alpha induced osteoclastogenic osteoclast.[8] Though the main effects of TNFalpha, IL6 and IL1B is to induce inflammatory response through the neutrophils recruitment mechanism into the site of the inflammation where being they initiate the starting of production of collagenases and prostrglanidins by chondrocytes which initiates the synthesis and triggering of monocytes to produce excessive cytokines which can be terminated by cartilage and bone damage that are finalized by the attainment of secondary osteoitis.[9] INFgamma do the act of macrophage activation and associated with Th1 responses.[10] INF gamma has shown to be of arthritogenic potential in septic arthritis and the local administration of INF gamma into the joint, it promotes the development of arthritis.[11] IL4 has beneficial role to chondrocyte viability through; necrosis, apoptosis, proliferation and nitrus oxide NO production. IL4 can inhibits the effect of IL1B, TNF alpha on the production of NO and proliferation of chondrocytes. The cytokines IL1, IL6, TNF alpha stimulate joint inflammation and distruction and can be detected in high concentrations in synovial fluids of septic arthritis

patients, such increase is correlated with the presence of leukocytes in the synovial membranes.[12] IL4 may have a dual function during the immune responses on the mucosal surfaces. The first function is through inhibiting the intracellular killing by phagocytes promoting systemic spread of the infection and second through the down regulation of the local levels of the proinflammatory cytokines and kemokines. Such dual function appears to be positively influences the progression of bacterial arthritis.[13] It was proposed that IL4 promotes polymorphism which might modify the TH1/TH2 responses and thereby to trauma and sepsis development in bacterial arthritis patients.[14] Heat shock proteins of 70KD family are the major chaperokines of most cells and tissues.[15] HSP70 provides a mechanism for controlling the excessive expression of an inflammatory response after monocyte activation through the joint infection with a bacterial pathogens like S.aureus.[16] Hence, the increasing of IL4 and HSP70 in the septic arthritis synovial fluid might protect from joint distruction induced by TNFalpha, INFgamma cytokines.[17,18] The rise up of the TNFalpha, INFgamma are somewhat is balanced by the increase of IL4 and HSP70 in the mucosa of the synova during septic human arthritis as compared to normal controls Tables,1,2,3,and4.

CONCLUSIONS

1-Natural neutrophilic synovial response is evident in S. aureus arthritis.

2-S.aureus induces pro and anti-inflammatory cytokines and chaperokine.

3-HSP70 and IL4 may equivocate TNF alpha and INF gamma levels on synovial mucosa during S. aureus human septic arthritis.

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