The role of Chloroquine phosphate on rheumatoid factor in patients with knee osteoarthritis

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Summary:

Fac Med Baghdad 2009; Vol.51, No1 Received June, 2008 Accepted Nov., 2008 **Background:** Osteoarthritis (OA) is disorder of diarthrodial joints characterized clinically by pain and functional limitation. Rheumatoid factor (RF) represents one of routine laboratory tests that done for all patients have joint complaints. Chloroquine phosphate (CQP) is a disease modifying antirheumatic drug (DMARD) used for patients suffer from knee osteoarthritis (KOA) in order to reduce their RF value and improves the disease status.

Objective: To evaluate the effect of chloroquine phosphate on rheumatoid factor (RF) level in serum of patients with knee osteoarthritis KOA)

Design: case report.

with COP for one month.

Subjects and methods: RF value were assessed quantitatively by ELISA technique before and after treatment for a total of fifty five patients with KOA (30 femal and 25 male) their age ranged from (50-66 years) selected randomly from out patient clinic in Baghdad Teaching Hospital, Medical City Baghdad; suffering from KOA. All patients were treated with oral dosage form of CQP for one month twice daily. **Results:** Mean serum RF level was significantly reduced (p<0.05) in serum of patients after treatment

Conclusion:CQP is a disease modifying antirheumatic drug (DMARD) used for patients suffering from KOA in order to reduce their RF value and improves the disease status.

Key words_ Chloroquine phosphate, Knee osteoarthritis, Rheumatoid factor, Immunoglobulin and DMARD

Introduction:

OA is the most common form of arthritis, is characterized clinically by joints pain, tenderness, limitation of movement, crypitus, occasional effusion and variable degree of local inflammation but without systemic effect (1). Radiologically finds bony proliferation at joint margin, asymmetric joint—space narrowing and subchondral bone sclerosis developed as diseas progress.(2) CQ is used for treatment of RA ,SLE, and malaria.(3)

In this study CQP is dispensed for KOA patients as DMRAD in order to decrease RF value and to improve the sign and symptom of this disorder.

Subjects and methods:

Fifty –five patients (30 female and 25 male) are selected randomly from the out patient clinic in Baghdad Teaching Hospital , Medical center , Baghdad whom age ranged from (50-66)years , their mean are (56.92 ± 4.12) .

According to signs , symptoms and radiographic evidence , all patients are treated with CQP tablet

(Medoquine 250mg 150 chloroquine base), Medochem company, twice daily for one month .

This treatment is prescribed by a rheumatologist. RF value was assessed quantitatively by ELISA technique. Serum samples are incubated in the microplates coated with specific antigen (Ag). Patients antibodies (Ab), if present in the specimen, bind to Ag. The unbound fraction is washed off in the following step .After wards anti-human Ig conjugated to hoarseradish peroxidase (conjugate) are incubated and react with the Ag-Ab complex of the samples in the microplates. Unbound conjugate is is washed off in the following step Addition tetramethylbenzidine(TMB) substrate generate an enzymatic colorimetric (blue) reaction, which is stopped by diluted acid (color change to yellow). The rate of color formation from the chromogen is a function of the amount of the respective Ab in the patient sample (4).

AIDA, RF-check kit was purchased from aida gmba (autoimmune diagnostic assay).

Results:

Rf –check value is calculated as Mean \pm standard error of mean, paired t-test, M \pm SEM.

S=significant Pvalue (P<0.05).

RF value

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U/ml	Baseline	1 month	Pvalue
T	22.1 <u>+</u> 2.18	10.29 <u>+</u> 0.8	S
M	21.25 <u>+</u> 3.65	10.01 <u>+</u> 1.46	S
F	22.65+2.79	10.47+0.93	S

T=Total patients

M=Male

F=Female

Discussion:

Rf , first was described in 1940 as antibodies reacting with gamma globulin , are autoantibodies directed against C-terminal part of constant region of the IgG heavy chain as IgG–Fc (5).

Rf are found both in the healthy population and several diseases , so the diseases commonly associated with high Rf concentration are RA , Sjogren's syndrome and SLE .The presence of IgM RF in the serum has been regarded as the most important serological indicator for RA as well as IgG and IgA subclass(4).

Pathologically in KOA, an affected joint experiences a progressive loss of cartilage, the slippery material that cushion the end of bones as result the bone beneath the cartilage undergo changes that lead to bony overgrowth and the tissue lines the joint can become inflamed, the ligaments can loosen and the associated muscle can woken(6).

The initiation of OA process is accompanied with enzymes proteases and their inhibitors releases, in addition to proinflammatory cytokines and acute phase proteins such as IgG, IgM, IgA (1).

CQP is used previously as DMARD in KOA patients (8).It's role to improve the patients' status depending on it's ability to enter lysosomes (9).

Immune effects of CQP include, a decrease in lymphocyte proliferation interference with natural killer cell activity (10) and possibly alteration of autoantibody production (11).

Non-lysosomotropic effects include the inhibition of phospholipases, antagonization of PG and stabilization of lysosomal membrane in synoviocytes(12) (13)(14).

The presented data in this study showed a significant decrease (P<0.05) in Rf value in patient taking CQP for one month .table(1.1).

The result in this study in agreement with the mode of action of CQP (immune effect) that tend to decrease RF value level in the serum through it's effect on IgG, M, A concentration .

Conclusion:

RF value include (Ig G, M, A) represent a part of acute phase protein that is increased in KOA.

Chloroquine phosphate is a DMARD decreases the serum level of RF value significantly in patients with KOA and thus improves their signs and symptoms. In further studies are needed to assess other parameters

such as enzymes and their inhibitors in synovial fluid and blood.

References:

1.Hochberg MC: osteoarthritis, B.Clinical features. In: Klippel JH, Crofford LJ, Weyand CM, (eds). Atlanta, Georgia = Athritis foundation, 2001; p 289-293.

2.Schnitzer TJ :osteoarthritis (degenerative bone disease).In Bennett JC, Plum F (eds).Cecil Text book Of medicine.20th(ed)volume 2.W.B. Saunders company,1998;p 1517-152`.

3.Ahmed MH, Osman MM (why does chloroquine impair renal function?.Medical hypotheses, 2007; 68, 140-143.

4.Peter JB ,Shoenfeld y :Autoantibodies .Elsevier Sciences B.V. ,Amsterdam ,1996.

5.Witte T, Hartung K, Sachse C, Matthias T, Fricke M, Khalden JR et al .Rheumatoid factors in systemic lupus erythrematous :Association with clinical and laboratory parameters .SLE study group.Rheumatol Int, (2000); 19,107-111.

6.Brandt KD: Osteoarthritis .In: Harrison's Principle of Internal Medicine 6th ed. Kasper DL (ed):McGraw Hill companies.(2005),p 2036-2045.

7.Kidd BL ,Photion A ,and Inglis JJ :The role of inflammatory mediators on nociception and pain in arthritis Novartis Found .Symp. 2004;260:122-123.

8. Jawad HH , Salmans , Mohammed L: The effect of chloroquine phosphate as disease modifying agent in osteoarthritis, a Ph D Thesis submitted to Baghdad College of Medicine and the committee of postgraduate studies in clinical pharmacology, 2004.

9.Petri M: Heydroxychloroquine use in the Baltimore Lupus cohort: Effects on lipid, glucose and thrombosis , Lupus, 1996; 5, 516

10.Karres I, Kremer JP, Dietl I, et al. (Choroquine inhibits proinflammatory cytokines release into human whole blood. Am J Physiology/ Regul Integ Comp Physiol, 1998; 274, 1058-1064.

11.Fox RI, Kang HI: Mechanism of action of antimalarial drugs: inhibition of antigen processing and presentation. Lupus, 1993; 2, 59.

12.Fox RI: Antimalarial Drugs: Possible mechanisms of action in autoimmune disease and prospects for drug development. Lupus, 1996; 5, 54.

13. Wallace DJ: Antimalarial therapies In: Dubois Lupus erythematosus, 5th ed, Wallace DJ, Hahn BH (eds), Williams Wilkins, Baltimore, 1997; P 117.

14.Stuhimeier KM: Mepacrine inhibit matrix metalloproteinases-1 (MMP-1) and MMP-9 activation in human fibroblast-like synoviocytes. J Rheumatol. 2003; 30, 2330.