

The Correlation between Rheumatoid Factor, Chloroquine Phosphate in Osteoarthritis

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Abstract

Osteoarthritis (OA) is a series of aggressive destructive inflammatory processes. Synovitis is common both at an early and a late phase. This disease may be uniquely singular in some site but phylogenetically related at some point in time to produce a common outcome of dysfunction, disability, socioeconomic destruction and sometimes socioeconomic failure. Articular cartilage, subchondral bone and synovial membrane are the site of major abnormalities in this disease process. Rheumatoid factor (RF) represents one of the routine laboratory tests that made for all patients have joint complaints. Chloroquine phosphate (CQP) is agent belong to disease modifying osteoarthritic drugs (DMOADs). Chloroquine and their derivatives have been used for their anti-inflammatory effect in juvenile chronic arthritis, Sjogren's syndrome, discoid and systemic lupus erythematosus. The aim of this trial depend on using this drug in osteoarthritic patients for two months then estimate the level of RF check and RF(A,G,M). The result showed a significant correlation between CQP and RF check as well as RF type M in patients suffered from OA, so the level of these two parameters are decreased significantly in period of treatment thus leads to ameliorate the patients status and the joints pain will decreased.

Key words: Chloroquine, osteoarthritis, rheumatoid factors.

الخلاصة

ألفصال العظمي عبارة عن سلسلة من العمليات الهادمة العدائية الالتهابية للمفاصل . التهاب الغشاء المصلي ممكن حصوله في المراحل المتطورة او المتأخرة من هذا المرض . هناك نوعين من اسباب حصول الفصال العظمي قد يكون متميزا ووحيداً في بعض الاماكن او معتمداً على التطور النوعي في مواضع اخرى مما يسبب العجز وعدم الكفاءة في اداء الوظائف والعوز الاجتماعي الاقتصادي مؤدياً لفشل حركة المفاصل والعظام المحيطة بها كذلك الغشاء المصلي لحصول تغييرات لاطبيعية فيه. تعيين عامل الروماتيزم من التحليلات المختبرية المعمول بها للمرضى الذين يعانون من مشاكل في المفاصل. عقار فوسفات الكلوركوين اثبت استعماله كعامل مغير ومضاد للالتهاب في الفصال العظمي. اما عقار الكلوركوين النقي ومشتقاته استعمل سابقاً في امراض عديده منها الالتهابات الرثوية المزمنة الولادية، متلازمة جوجرين، داء الذئبة الاحمراريه الجهازى و القرصى. هدف هذه التجربة هو استخدام فوسفات الكلوركوين لفترة شهرين لغرض تعيين عامل الروماتيزم المرتبط الكلى والخاص بكل بروتين مناعي نوع (أى، جى، أم) . اظهرت النتائج بان هناك علاقه وثيقه ومعنويه بينهما. أجريت التجربة على ٢٥ متطوعاً من الأصحاء و ٦٥ مريضاً في مستشفى مدينة الطب/قسم الروماتيزم والتأهيل الطبى تم تحليل دم المرضى والأصحاء لتعيين نسبة العامل الرثوي الكلى ثم اجراء تحليل آخر على المرضى الذين يكون لديهم تركيز هذا العامل أعلى من ٢٠ مايكرو/مل من الدم للكشف على المكونات المفصلة من البروتينات المناعية المحتوية على الغلوبين وتعيين مستوياتها و أنواعها. صرف للمرضى عقار الكلوركوين لمدة شهرين بجرعة ٢ حبة يومياً من قبل الطبيب الاختصاصي بعدها عينت تراكيز هذه البروتينات. لوحظ أن هناك انخفاض ملحوظ و معنوي في نسبتها مما يقلل من تهدم الأنسجة العظمية والغضروفية وتحسن حالة المرضى اضافة الى تقليل الالم .

Introduction

Osteoarthritis (OA) is the most common form of arthritis, the major cause of pain and disability in older people as well as is a condition of synovial joints characterized by focal loss of articular hyaline cartilage with proliferation of new bone and remodeling of joint contour^(1,2,3,4,5). According to American College of Rheumatology (ACR)⁽⁶⁾, many signs and symptoms such as (age over 50, stiffness less than 30 minutes , crepitus , bony enlargement & tenderness ,no palpable warmth

,erythrocyte sedimentation rate less than 40 mm/ hour, RF & synovial fluid examination) at least five of them associated with OA in addition to pain. Rheumatoid factors (RFs) is a laboratory test used to detect the antibodies (Abs)⁽⁷⁾. Although these factors have been associated with a person who had arthritis they are also present in normal individual ⁽⁸⁾. The titers were elevated in many cases such as viral infection, acute and chronic inflammation and lymphoproliferative disease^(9,10).

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Chloroquine CQ and their derivatives were classified as anti-malarial agents or disease modifying osteoarthritic drugs (DMOADs). The mechanism of these agent were complicated through interfering with many pro-and anti-inflammatory mediators that directed to breakdown cartilage also playing important role in decreasing and antibodies production as their immune effects^(11,12,13,14,15). In this study attempted to use chloroquine phosphate as DMOADs that has an ability to prevent, retard or reverse some signs and in OA in humans by decreasing the titer of RF check especially RF type M.

Patients and Methods

Twenty-five healthy peoples (27.77)% as control and sixty-five patient (72.22%), all of them were male selected randomly by Rheumatologist. The study began in January – December (2007) , the patient's age range from (50 to 55) year with their mean age (54.51±2.35). Detailed history of patient including : Age, weight, body mass index ,occupation, duration of disease, past history of disease or operation and the use of non steroidal anti-inflammatory drug was obtained. X-ray was observed by Rheumatologist and classified according to Kellgren and Lawrence grading criteria which start from grade (0 to IV) so the first grade represent no feature of OA and the last one is joint space greatly impaired with sclerosis of subchondral bone⁽¹⁶⁾. CQP 150mg tablet were dispensed to the patients for two month, twice daily after meal.

RFs value were assessed quantitatively by Enzyme Linked Immune Sorbent Assay ELISA (Aida-RF chelal and A, M, G kits) were purchased from Aida GmbH (auto immune diagnostic assay).The aim of this study is to measure the real effects of CQP on RF titer and take care dispensing corticosteroids or other agents because the age of patients related with chronic diseases such as hypertension and diabetes. Serum samples were estimated by ELISA RF- check kit, if the concentration of sample is more than 20 µ/ml, the RFs - AGM must done in order to determine each immunoglobulin separately^(17,18).Forty five (69.23%) from the total samples be above 20µ/ml. RFs check and AGM were calculated as mean ± standard error of mean (M±SEM) paired ±test.The analysis was done in central public health laboratory in immunological department.

Results

In this study the presented data showed the level of RFs of patients and healthy subjects. Table (1) include RFs check for all individuals and RFs AGM for patients who their RFs check were above 20 µg/ml, also there are comparisons before and after 2 months of CQP treatment. Figure (1) show the level of RFs check only between control, all patients before treatment and after 2 months figure (2) show the level at RFs AGM for control, (69.23%) of total patients before and after using the drug.

Table 1: The serum level of RFs check and RFs AGM for control and patients.

	Control (C)	Patients before using CQP (P ₀)	P value (C+ P ₀)	Patients after 2 months of using CQP (P ₂)	P value (C+ P ₂)
No. of subjects Percentage(%)	25 22.77%	65 77.22%		20 30.76%	
RFs check µ/ml	18.73±1.22	30.49±2.89	P<0.05 ^s	19.12±1.27	P<0.05 ^s
RFs check > 20 µ/ml Percentage(%)		45 males from 65 (69.23%)		45 males (All) (100%)	
IgA µ/ml	2.07±0.31	2.87±0.13	P>0.01 ^{NS}	2.39±0.13	P>0.01 ^{NS}
IgG µ/ml	9.99±0.45	10.12±0.79	P>0.01 ^{NS}	7.54±1.01	P<0.001 ^s
IgM µ/ml	6.76±0.68	37.95±1.02	P<0.005 ^s	10.45±1.62	P<0.001 ^s

S : significant

NS : non-significant

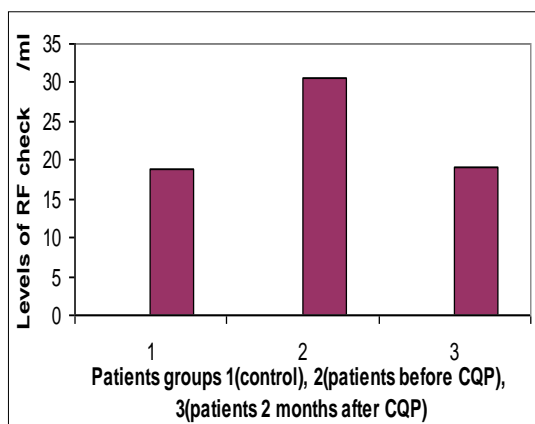


Figure 1: Levels of RF check in patients

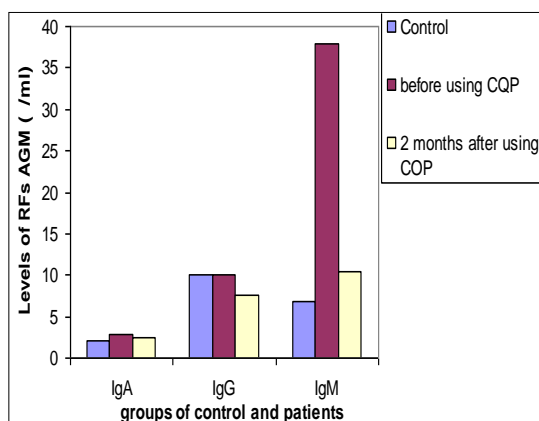


Figure 2: Levels of RFs AGM in control and patients before and after 2 months of CQP treatment

Discussion

In this study the presented data showed the level of RFs of patients and healthy subjects as control. Table (1) include RFs check for all individuals and RFs AGM for patients who their RFs check were above 20 $\mu\text{g/ml}$, also there are comparisons before and after 2 months of CQP treatment. Figure (1) show the level of RFs check only between control (C) and all patients before treatment (P0) and after 2 months (P2) while figure (2) show the level at RFs AGM for control, (69.23%) of total patients before and after using the drug. The correlation between RFs values and OA at the same time of using this agent appeared to be significant depending on the mode of action of chloroquine through ameliorating the signs and symptoms of the patients. This drug classified as weak base so has direct effect on lysosomes and stabilization of lysosomal membrane by increasing pH inside this part of cell as well as interfering with enzyme activity dependant on acidic environ, impairment of endocytosis and processing of antigen by macrophages, antigen

presentation, posttranscriptional modification of protein and cytokine secretion also suppress the responsiveness of T- lymphocytes and decrease polymorphnuclear cell chemotaxis, inhibit of immune complex formation through decrease the secretion of interleukin one alpha by monocyte and interleukin six by monocyte and T- cell⁽¹¹⁻¹⁵⁾. OA defined as a condition characterized by a series of inflammatory processes 50% synovitis is common, both as an early and late phase^(20, 21). Clinically OA is a disorder of diarthrodial joints lead to pain, activity limitation⁽²²⁾. Radiography show the presence of osteophytes and joint space narrowing, while histopathologic find the alteration in cartilage integrity⁽²³⁾. The pathologic feature of OA is a progressive loss of articular cartilage as well as affect synovial joints, subchondral bone, synovium, meniscus, ligaments, and supporting neuromuscular apparatus in addition to cartilage^(2,3). RFs are auto antibodies (AAb) directed against antigenic determinants on the fragment crystalizable (FC) of IgG molecule^(17,23). The production of RFs is induced during the course of many acute and chronic inflammatory diseases^(2,3) where as IgM RFs predominant in most of these condition, IgG RFs are occasionally produced⁽²⁴⁾. CQ was previoualy used as DMOADs to treat rheumatic diseases such as rheumatoid arthritis, discoid and systemic lupus erythromatosis also has anti inflammatory effects in juvenile chronic arthritis and Sjogren syndrome⁽¹¹⁻¹⁴⁾. Before five years many investigations studied the effects of CQP on OA as disease modifying agent and as decrease many pro inflammatory (IL1,6,8), tumor necrosis factor-alpha (TNF- α), complements, C-reactive protein⁽²⁵⁻²⁸⁾.

Conclusion

The levels of serum RFs combined and separated were determined by ELISA in OA before and two months after using CQP, this factor usually used for rheumatoid arthritis but in this study for osteoarthritis with follow up of using chloroquine for two months. At zero time RF-check (combined Ig AGM) measure high titer due to disease (significant increase). This increasing followed by a decrement in RFs-check or RF AGM after 60 days of taking the drug that play a role in acting as anti inflammatory also as a disease modifying anti rheumatic agent.

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