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The effect of chloroquine phosphate on C-reactive protein and erythrocyte sedimentation rate measurement in knee osteoarthritic patients.

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الخلاصة:

الفصال العظمي مرض شائع في أنحاء العالم يصيب المفاصل والغضاريف نتيجة لسلسلة من الفعاليات الميكانيكية والبايولوجية التي تؤدي إلى تغير وتحوير كل من الغضاريف والعظام التي تحيط بها.

استشاريو الروماتيزم يطلبون من المرضى إجراء فحص روتيني لمعدل ترسيب الكريات الحمراء وقياس نسبة البروتين التفاعلي – سي في الدم لاعتبارها مؤشر مختبري لقياس مدى الالتهاب الرثوي.
أدوية الملاريا استعملت سابقاً لعدد من الامراض الروماتيزية ويعتبر عقار فوسفات الكلوراكوين إحدى العلاجات التي تؤثر على المرض وتحاول تقليل شدته وقد أوضحت هذه الدراسة إلى أن استعمال هذا الدواء سوف يقلل من نسبة معدل ترسيب الكريات الحمر وكذلك البروتين التفاعلي– سي في مرض الفصال العظمي وقد أجريت دراسة متزامنة معها تؤكد تأثير هذا الدواء على نسبة انترلوكين واحد (الفا وبيتا) وعامل الورم التعفني – الفا على نفس المجموعة من المرضى.

أجريت الدراسة على 50 شخصاً من الأصحاء (30 أنثى و 20 ذكر) و 60 مريضاً (40 أنثى و 20 ذكر) في مستشفى مدينة الطب /العيادة الاستشارية للروماتيزم والتأهيل الطبي للفترة من كانون الثاني إلى أيلول 2008) شخصّ المرض حسب الدستور الأمريكي لمبحث الرثية.

سحبت عينة من دم الأصحاء والمرضى قبل العلاج ثم عينة أخرى للمرضى بعد العلاج المتمثل بأخذ أقراص فوسفات الكلوراكوين 250 ملغم مرتين باليوم بعد الأكل لمدة شهر.

تم قياس نسبة الكريات الحمراء المترسبة والبروتين التفاعلي – سي في المصل وقد لوحظ تقليل نسب هذه العوامل في الدم بصورة معنوية وملموسة.

Abstract:

Osteoarthritis (OA) is the most common articular disease world wide. It is the result of both mechanical and biological events that destabilize the normal coupling of degeneration synthesis of articular cartilage and subchondral bone.

Rheumatologist often routinely order tests for rheumatoid factor and erythrocyte sedimentation rate (ESR) for all patients with joint complaints as well as C - reactive protein (CRP) as a laboratory marker important in the

assessment of inflammation. Anti malarial drugs are used for treatment of many rheumatic diseases. Chloroquine phosphate (CQP) was used previously as a disease modifying anti rheumatic drug and in this study its effect appears through decreasing the measurement of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in knee osteoarthritic patients (KOA).

Abbreviation: HCQ, hydroxy chloroquine; CQ, chloroquine; DMARD, disease modifying anti rheumatic drug; APP, acute phase protein; ACR, American College of Rheumatology; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; RF, rheumatoid factor.

Introduction

OA is a disease characterized by a progressive articular cartilage destruction, osteophyte formation, subchondral bone sclerosis and secondary synovitis[1,2]. The acute phase response is a major pathophysiologic phenomenon that accompanies acute and chronic inflammation [3,4]. CRP is one of APPs that influence one or more stage of inflammation so it has both pro inflammatory and anti inflammatory action [5,6]. ESR is an indirect measurement of plasma APPs concentration and can be greatly influenced by many factors [7]. Rheumatologist often routinely order tests for RF, ESR for all patients with joint complaints [8]. However neither the presence of RF nor mildly elevated ESR excludes a diagnosis of OA in elder patient [4]. CQ is an amino-quinoline derivate drug that previously used in treatment of malaria. It has a beneficial therapeutic effect in SLE, RA and viral infection [9, 10, 11, 12]. Phosphate salt of CQ is used in this study to ameliorate the signs and symptoms of disease by reducing blood level of ESR and CRP.

Materials and Methods:

Sixty patients (40 female and 20 male) are classified as KOA by Rheumatologist according to ACR criteria [13], in Out Patient Clinic in Baghdad Teaching Hospital, Medical Center, Baghdad, from January to September 2008 with fifty healthy people (30 female and 20 male). The patient ages are ranged from (55 to 67) years, their mean values ± standard mean of error are (62.7± 5.2). CQP is used for one month to treat all patients, two tablets are taken daily after meal (Medoquine 250 mg /Medochem Company equivalent to 150 mg CQ base).

CRP was assessed by antigen-antibody reaction technique (quantitative turbidity metric method). ESR was estimated by Wintrob's Haematocrit tube [14]. Whole blood was used to determine ESR while the serum was used to determine CRP.

Results:

In this study, the presented data showed a significant ($p<0.01$) differences between control and patients groups before using CQP, also showed a significant ($p<0.05$) differences between patients group before and after treatment.

	Control		Baseline	P-value control-baseline	After one month	P-value pre-post treatment
CRP mg/L	T	1.05±0.09	4.3±0.36	P<0.01	2.02±0.2	P<0.05
	M	5.4±0.01	3.8±0.65		1.8±0.32	
	F	1.2±0.1	4.63±0.41		2.17±0.23	
ESR mm/h	T	5.1±0.21	15.61±1.23	P<0.01	8.61±0.6	P<0.05
	M	3.2±0.17	12.48±1.6		7.45±0.71	
	F	6.9±0.2	17.62±1.67		9.36±0.86	

Table-1: The level of (CRP) and (ESR) before and after treatment by using (CQP) in KOA as well as control.

Were:

T = Total patient
M = Male
F = Female
The result are calculated as mean ± standard of mean, paired t-test

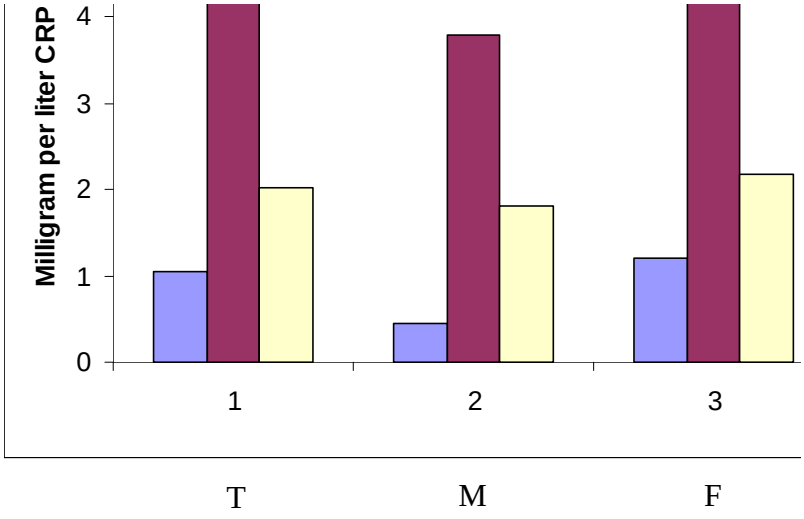

Figure-1: The level of serum CRP in control and KOA patients.

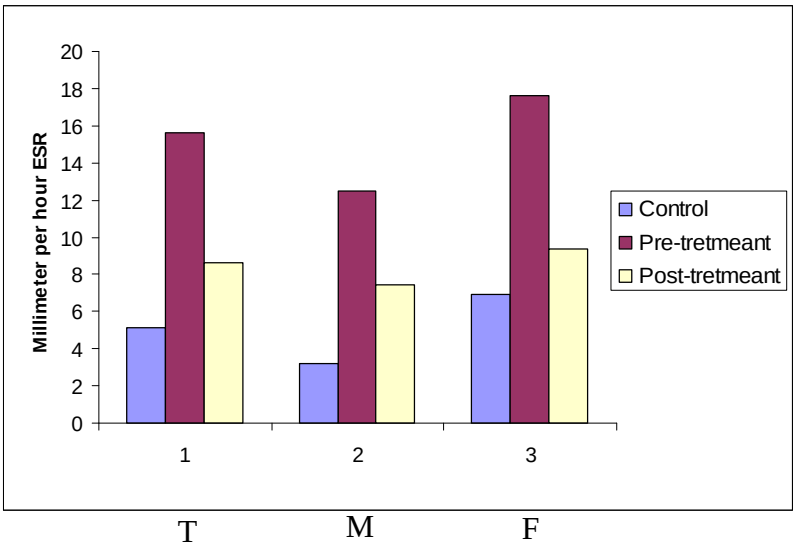

Figure-2: The level of blood ESR in control and KOA patients.

Discussion:

CQ is a well - known lysosomontropic agents, it can pass the plasma membrane preferentially concentrates in the acidic cytoplasmic vesicles leading to increase its PH.The elevation may influence endocytosis, exocytosis and phagocytosis [15], as well as other cell functions like antigen presentation [16], and iron metabolism [17].

CQP is present in trace concentration in the plasma of all humans. It a pentamer consisting of 5 - identical, non - covalently linked 23- KD subunit [18]. In the assessment of inflammation CRP represents an important laboratory maker as well as serves a predictor and indicator of response to therapy in addition to over all outcome in various disorder [19], so it combines phospholipids that is released from damaged tissue to become an activator of the complement pathway [20] and is useful in early detection of low-grade inflammation [21].

CQ may inhibit protein(positive APP) secretion and intracellular processing of. protein precursors such as complement precursor pro–C_3 [22], decreases lymphatic proliferation and interferes with natural killer cell activity [23] and inhibits phospholipase [24]. Jawad et al previously assessed the serum level of CRP in patients with KOA at baseline and three month later of using CQP, their results showed a slight decrease ($p > 0.05$) in this laboratory marker [25]. The presented data in this study shows a significant decrease in CRP level ($P<0.05$), (Table-1), figure (1). As result, all finding, fact and trial about the

CRP serum level assessment are in agreement with this research and support it. CRP and ESR may be useful diagnostically, in helping to differentiate inflammatory from non inflammatory conditions, in patient management since they may generally reflect the response to and need for, therapeutic intervention [26].

Measurement of ESR and CRP of the patient with rheumatic disease indicates the progression and prognosis of it, as well as the elevation of both markers are associated with radiographic progression at [6,7,8,9,10,11,12] after study entry [27,28], and the time-integrated values of ESR and CRP correlate significantly with disease progression over periods of up to 20 years [29, 30], as well as their levels are significantly associated with early synovitis and erosion as detected by MRI [31] with cellular infiltrates on synovial histologic specimens [32], osteoclastic activation and reduced bone mineral density [33] and work disability on long term follow up [34].

CQ and HCQ are used previously as a DMARD, they inhibits the inflammatory response through their effects on T-cell which plays an important role in initiation and perpetuation of rheumatoid inflammation and disease progression [35, 36]. In 2004, Miranda et al studied the effect of two DMARDs combination in treatment the early onset RA, their result showed a decrease in ESR serum level after six months of using the therapy [37]. Cytokines and other inflammatory mediators are decreased because the secretion of protein is inhibited by CQ or HCQ through their lysosomotropic and non lysosomotropic action [24].

In this study the presented data showed a significant decrease in ESR measurement ($p < 0.05$), (Table-1), figure (2), and the result is in agreement with all findings, trials and mode of action of CQ.

Conclusion:

CQP alleviates the signs and symptoms of patients with KOA by decreasing their serum level of CRP and the blood measurement of ESR.

Further studies are needed to detect other markers and mediators in the blood and synovial fluid in relation with CQP therapy in osteoarthritic patients.

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