Some Physiological and Clinical Changes in Temporomandibular Joint in Patients with Systemic Rheumatoid Arthritis

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Abstract

The rheumatoid arthritis is one of the most common autoimmune disease, characterized by systemic chronic inflammation of joints. This study done in marjan hospital in rheumatology centre in AL-Hilla City. The total number of subjects involved in the study was 200 (130 patients & 70 control). Tempromandibular joint effected with RA found clinical physiological symptom such as pain, clicking hearing , limitation of mouth opening. The radiographic examination occur within normal, other have varies change such as flatting of condylar, abnormal or loss of normal shape or diminished thickness of condylar cartilage or complete destruction of condylar.

The results showed for hematological studies found the WBC and platelet count elevated when compared with healthy control that result from chronic inflammation, and another sample taken from same patient to analysis immunolgical studies (interleukin-1B, tumer necrotic factor alfa and serotonin) which highly elevated when compared with healthy control that leading increase clinical symptom in TMJ and condylar erosion with change of vertical dimension and occlusion.

الخلاصة

التهاب المفاصل الروماتويدي هو أحد أمراض المناعة الذاتية الأكثر شيوعا، يتميز التهاب المفاصل المزمن في النظام. هذه الدراسة أجريت في مستشفى مرجان في مركز أمراض الروماتيزم في مدينة الحلة. وكان العدد الإجمالي للمواضيع المشاركين في الدراسة ٢٠٠ (١٣٠ مريضا وغير مصابين ٧٠). وجد تاثرالمفصل الفكي الصدغي بالروماتزم وقدظهرت أعراض سريرية الفسيولوجية مثل الألم، وقرقعة ، التحدد في فتح الفم. والفحص ألشعاعي وجد بعض بالحالة الطبيعية، وأخرى تختلف تغيير مثل flatting of condylar ، غير طبيعي أو فقدان الشكل الطبيعي أونقص في سمك غضروفcondylar أو التدمير الكاملcondylar .

ان النتائج بينت عدد كريات الدم البيض وعدد الصفائح الدموية متزايدة عندة مقارنتها بالغير مصابين والسبب التهاب مزمن،وعينة أخرى أخذت من المريض نفسه لغرض التحاليل المناعية (interleukin-1B, tumer necrotic factor alfa and serotonin).

وجدت متزايدة عندة مقارنتها بالغير مصابين وهذا يفسر ظهور ألاعراض سريرية في المفصل الصدغي الفكي وتآكلcondylar مع التغير vertical dimension and occlusion.

Introduction

Rheumatoid Arthritis is one of the more common systemic autoimmune disorders, affecting approximately 1% of the general population worldwide[1]. The incidence of RA is 2–3 times higher in females than males and rises with increasing age [2].

Patients with RA may present haematological abnormalities can be broadly categorized into areas of anaemia, neutropenia, thrombocytopenia, thrombocytosis,

eosinophilia, and haematological malignancies eosinophilia in RA reflects active disease or hypersensitivity to drugs[3].

The temporomandibular joint is commonly influenced in patients with rheumatoid arthritis and is usually among the last joints to be affected[4]. Involvement and dysfunction of the TMJ in RA patients has been described, but the incidence varies greatly from 2-86%[5]. Manifestations are diverse and include pain, restricted range of motion, tenderness on palpation of the joint and the masticatory muscles[6]. Radiography may reveal joint space narrowing, condylar head flattening, and subchondral bone cysts there is progressive softening and loss of cartilage of the TMJ[7].In RA patients Interleukin-1 (IL-1B)was associated with clinical sign of TMJ bone tissue destrtuction by bind to specific cell surface receptors resulting in cell activation in the TMJ synovial fluid[8]. Tumer necrotic factor-α(TNF-α) is strong inflammatory mediator, modulating the destruction of cartilage and bone, it has direct modulatory effects on pain[9]. The TNF-α is elevated plasma and synovial fluid of patient with RA[10,11]. The pain in maximum mouth opening had high level of TNF-α in TMJ synovial fluid[10].

Serotonin is mediator of pain and inflammation, the relation between the serum Serotonin and TMJ pain on maximum mouth opening and suggested that serotonin from blood is also involved in the modulation of this pain entity[12].

The Aim of study in this thesis to investigate TMJ pain, radiographic change of the joint, impacted of TMJ pain on daily activity and influence pain to tissue destruction of inflammatory markers and Measurement of inflammatory markers and mediators(tumuor necrotic factor alpha, interleukin 1-B and serotonin) in serum and compared with healthy control and measurement the patient's blood count (white blood cell and platelet) and study the change with rheumatoid arthritis.

Patients and Method

Patients

The study was conducted in in Marjan teaching hospital in Al-Hilla City, the total number of them involved in the study was 200, they classified into patients & control groups (130 patients & 70 control). The age distribution for females starting form youngest patient who was (20) years to the oldest who was (71) years with age mean (50.31±11.759), while the youngest male patient was (35) years and oldest was (72) years with age mean (54.77±8.512).

Methods

Clinical Examination

The clinical examination additional information to help confirm or rule out structures involved in a patient's complaints and other suspected disorders that may contribute to these complaints, facial topography for finding any change in patient's expiration such as asymmetry, swelling, cutaneous lesion, muscle flexing or flashing. All subject examined with Palpation, and TMJ Noise [13].

Computed Tomography

Computed tomography (CT) (figure:1) computed tomography (CT) for evaluation of bony morphology and pathology of the joint, mandibular ramus, and condyle as well as a 3D reconstruction and analysis of the joints for determining the actual dimensions of the structures[14].Bilateral TMJ image were obtained with CT apparatus PHILIPS, Brilliance16 ((protocol name facial bone volume/head, patient

position head fist prone, scan options Helix, slice location -31.5mm)

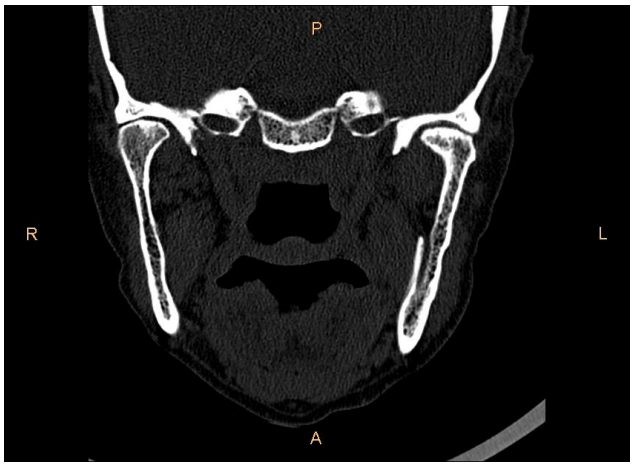

Figure 1 CT image(Coronal section)for rheumatoid patient explain narrowing with condylar space (Marjan Teaching Hospital in Al-Hilla City) .

Blood samples collection

Blood samples were obtained from the patients and controls. Blood samples of five ml were taken by an anticubital vein venopuncture, two ml of blood was delivered in to Ethylene diamine tetra acetic acid (EDTA) tube; the tube was inverted several type to mix the blood with anticoagulant to be used for hematological tests **(White blood cell count and differential Leukocyte, Platelet count)** [15]. The remaining three ml blood delivered in to clean plane tubes and after that centrifugation separate the serum and the sera obtained were put in another disposable sterile plain tubes and stored in deep freeze (-20 C^0) to be used for biochemical tests **(Measurement of Human Interleukin-1Beta, human Tumor Necrosis Factor Alfa and Serum Serotonin)** [15].

Statistical Analysis

Statistical Package for Social Science (SPSS) program was used in this study. All values were expressed as mean ± standard deviation (SD). Independent t-test was used to estimate differences between groups. The differences were considered significant when the probability (P) was less than 0.05 ($P<0.05$) and highly significant when the probability (P) was less than 0.01 ($P<0.01$) [16].

Results

The majority of the patients with rheumatoid arthritis aged 50-59 years old is about(38.5%) and duration of RA disterbuted from<1 year is about5.4%, 1-10 years is about64.6% and 11-20years is about30%.

The distribution depending on sex result in a female to male ratio (4/1) effected with rheumatoid arthritis (100 females constituting 77% and 30 males constituting 23%) and healthy control (52 females and 18 males)**.**

Physical Examination for Rheumatoid Patients found that limitation of mouth opening level different in both sex and it distributed occur in female (66.4%) and in male (73.5%), The TMJ sound (clicking) is 62% in female and 68% in male, Rheumatoid patient suffer with tenderness with or without palpation in TMJ in female about 60% and in male about 68%.

The Radiographic result reach for this study after examination about (30) RA patients with computer tomography scan found different change to TMJ due RA if compared

with healthy control, distributed patients in three groups depending on duration of effected, the RA patient with less than one years have no radiographic change it is about (10%),the RA patients with (1-10 years) show normal TMJ is about (30.6%), others have change with condylar (including flattening, change in contour of bone or joint-space narrowing) is about (16.6%), and lastly, patients have condylar erosion is about(3.4%). The RA patients with (11-20 years) show normal TMJ is about (16.8%), others have change with condylar (including flattening, change in contour of bone or joint-space narrowing) is about (16.8%) and lastly patients have condylar destruction (condylar erosion) is about(6.6%).

Hematological (total White Blood Cell platelet and Differentiated)result

The mean of the white blood cell and platelet count for female and male with RA in comparison to female and male controls show significant decrement ($p<0.01$) table (1) for female and table (2) for male. The differentiation of white blood cell in female and male found that neutrophile, lymphocyte, monocyte, eosinophile and basophile mean count show significant increased ($p<0.01$) but in female eosinophile mean count show insignificant increase ($p>0.01$) as shown in table (1) for female and table(2) for male.

Table 1 The value of white blood cell and platelet× 10^3 (cell/ml) and differentiated×10^3 (cell/ml) count in rheumatoid arthritis patients and healthy control in female.

	GROUPS	No.	Mean± Std. Deviation	P value
Neutrophile ×10^3 (cell/ml)	patient	100	6.0054±2.44579	**<0.01****
	control	52	3.4865±0.91565	
Lymphocyte ×10^3 (cell/ml)	patient	100	2.5125±0.80977	**<0.01****
	control	52	2.0944±0.49977	
Monocyte ×10^3 (cell/ml)	patient	100	0.8156±0.29691	**<0.01****
	control	52	0.6392±0.27842	
Eosinophile ×10^3 (cell/ml)	patient	100	0.4258±1.48328	**>0.2*****
	control	52	0.1846±0.10281	
Basophile ×10^3 (cell/ml)	patient	100	.0754±0.03729	**<0.01****
	control	52	0.0281±0.02197	
WBC ×10^3 (cell/ml)	patient	100	9.7302±3.04487	**<0.01****
	control	52	6.7467±1.28822	
Platelet× 10^3(cell/ml)	patient	30	348.0000±109.20560	**<0.01****
	control	18	186.0000±19.54181	

****High significance level (p <0.01), *** No significant different(p>0.05).**

Table 2 The value of white blood cell and platelet $\times 10^3$ (cell/ml) and differentiated $\times 10^3$ (cell/ml) in rheumatoid arthritis patients and healthy control in female

	GROUPS	No.	Mean±Std. Deviation	P value
Neutrophile$\times 10^3$ (cell/ml)	Patient	30	6.6307±1.97888	**<0.01****
	control	18	3.3644±1.05446	
Lymphcyte $\times 10^3$ (cell/ml)	patient	30	2.5117±0.88925	**<0.01***
	control	18	2.1044±0.42007	
Monocyte $\times 10^3$ (cell/ml)	patient	30	0.8807±0.30727	**<0.01****
	control	18	0.5633±0.20309	
Eosinophil $\times 10^3$ (cell/ml)	patient	30	0.3043±0.17986	**<0.01****
	control	18	0.1861±0.07188	
Basophile $\times 10^3$ (cell/ml)	Patient	30	0.0937±0.05041	**<0.01****
	control	18	0.0261±0.01754	
WBC $\times 10^3$ (cell/ml)	Patient	30	10.5367±2.59196	**<0.01****
	control	18	6.7894±1.28983	
Platelet$\times 10^3$ (cell/ml)	patient	30	348.0000±109.20560	**<0.01****
	control	18	186.0000±19.54181	

****High significance level (p <0.01)**

Biochemical result when measurement the value of serum intreleukin1-B, tumer necrotic factor and serotonin for female and male showed high significantly increased (p<0.01) when comparison with healthy control female table(3) and male table(4).

Table 3 Differences between patients with Rheumatoid Arthritis and healthy controls to interlukin1-B (pg/ml), tumour necrotic factor(pg/ml) and serotonin(ng/ml)in both sex.

Variable	Groups	No.	Mean±Std.Deviation	P value
Interlukin1B(pg/ml) for female	**Patient**	**100**	**9.0737±3.63374**	**<0.01****
	control	**52**	**2.7503±0.43326**	
Interlukin1-B(pg/ml) for male	**Patient**	**30**	**8.4177±2.17734**	**<0.01****
	control	**18**	**2.8982±0.100.44196**	
Tumour necrotic factor (pg/ml)for femal	**Patient**	**100**	**24.6442±4.99846**	**<0.01****
	control	**52**	**12.2321±1.01342**	
Tumour necrotic factor (pg/ml) for male	**Patient**	**30**	**21.9796±3.35395**	**<0.01****
	control	**18**	**12.1853±1.18672**	
Serotonin (ng/ml) for female	**Patient**	**100**	**199.7494±158.80407**	**<0.01****
	control	**52**	**94.1039±152.22977**	
Serotonin (ng/ml) for male	**Patient**	**30**	**204.8087±107.98279**	**<0.01****
	control	**18**	**58.6913±12.93605**	

****High significance level (p <0.01)**

Relation between Serum Serotonin and TMJ tenderness

The highly elevation of serum serotonin in patients the RA leading to increase of TMJ tenderness there is highly significant relationship between serum serotonin and tenderness (p<0.01) as seen in Table(5).

Table 5 Relation between serum serotonin and TMJ tenderness

Variable	Serotonin		$\chi 2$	df	P values
	Normal (%)	Abnormal (%)			
Joint tenderness					
Painless	**2 (4.2)**	**65 (55.6)**	**37.653**		**< 0.01****
Pain (intermittent	**11 (22.9)**	**10 (8.5)**		**2**	
palpitation)	**35 (72.9)**	**42 (35.9)**			
Pain (lateral palpitation)					

****High significance level (p <0.01).**

Discussion

The result of study found female more effected by male it is about 4/1 distribution depend on sex for rheumatoid patients. The cause is that estradiol act as immune stimulus effecting to increased incidents with RA or using contraceptives Doran *et al*[2]The result of patient age majority of ages of the effected patients with rheumatoid arthritis are within the age group 50-59 years old is about 38.5% this agrees with Lawrence *et al* [17]and major duration of RA from 1-10 years.

The result of physical and clinical examination of rheumatoid patient suffer with tenderness with or without palpation in TMJ in female about 60% and in male about 68% the percentage result these disagree with Gleissner *et al* [5] Many causes of tenderness one cause the platelet count increased due to inflammation that associated with increase secretion serum serotonin, leading to increase pain and tenderness in TMJ (table 5: relation between serum serotonin and TMJ tenderness) this agree with Alstergren [18], radiographic examination of condyle show flattened condyle that causes pain TMJ during maximum mouth opening.

The result of study the limitation of Mouth Opening show about 66.4% in female and in male 73.5% that agree with Helenius *et al* [20] . The TMJ sound (clicking) is 62% in female and 68% in male these result agree with Ozcan *et al*[6] on clinical examination after CT scan found clicking was associated with perforation of the disc, narrowing of joint space of the temporal surface in TMJ, these result accepted Greenberg and Glick [13].

The computer tomography is used to detect change of TMJ in RA This result agree with Helenius *et al* and Voog *et al* [7,11] who provide the CT radiographic signs of TMJ involvement included erosion, flattening and sclerosis that explain all clinical finding.

The Hematology (white blood cell and platelet)a statistically significant was increase in RA patient with RA that reason return to chronic inflammation is present in all joints, which agree Yu H-T*et al* [3]this disagree with Mehta &Hoffbrand [21]. After differentiated WBC found that the neutrophile, lymphocyte, monocyte, eosinophil and basophil count shows significant increase the and neutrophilia and eosinophilia may result from inflammatory process, active infection or due to drug effect Yu H-T*et al* [3]. The platelet value is highly increased when compared with healthy control as an indicator for thrombocytosis. Platelet count elevation in RA can occur as a result of inflammation that lead to increase production of platelet activating factor and increase platelet count Mehta &Hoffbrand [21].

The immunological results (serum Interluikin1-B (IL-1B), Tumor

Necrotic Factor(TNF- α) and Serotonin).

The pro-inflammatory cytokine IL-1B is highly increased in rheumatoid patients when compared with healthy once this result is accepted with Choy *et al* [22]. The elevation value of serum IL-1B of RA patients was associated with clinical sign of TMJ bone destrtuction and less degree of anterior open bite Alstergren *et al* [8].

The pro-inflammatory cytokine (TNF-α) it is highly increased in rheumatoid patients to compared with healthy once this result agree with Voog *et al* [11]. Also this elevation in TNF-α causes an increase in pain in joints including TMJ, this reason explans for occurrence TMJ symptom and radiograph change of TMJ. Patients with pain on maximum mouth opening had higher levels of serum TNF-α Nordahl *et al* [10].

The serotonin act as mediator of pain in TMJ, it increased in RA by over production from platelets, this arises of serotonin leading to increased in tenderness in TMJ, resembling Alstergren [18] the elevation of serum level of serotonin was found to be associated with pain during mandibular movements in RA patients, and increase bone resorption Voog *et al* [11].

Conclusion

1.The patients had more debilitating symptoms and functional disabilities, and thus need to be referred to TMJ clinics promptly and managed more actively. The most of the RA patients received treatment from rheumatologists rather than dentists, this study attempted to analyze the link between markers of RA severity and tempromandibular disorder in order to provide a useful guide for rheumatologists in predicting the probability of severe TMJ involvement in their patients.

2.The computer tomography CT analysis can be an excellent tool for identifying the TMJ abnormality, and develope a three-dimensional (3D) imaging analysis by contributing to exam facial symmetry or asymmetry could be measured accurately.

3.The measurement of serum TNF- α, IL-1B serotonin and high elevation if compared with healthy control that give results of radiographic signs of joint tissue destruction in patient with clinical TMJ involvement by RA.

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