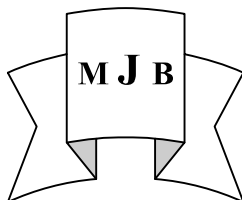


Glucosamine and Chondroitin Sulfate in Knee Osteoarthritis

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Abstract

Osteoarthritis common disease of knee joint , due to aging specially after age of 40 , it disorder of synovial joint .the glucosamine and chondrotin provide much of the resistance to compression and its used now for the treatment .the aim of this study to show the effect of this dietary supplement in knee osteoarthritis ,between 2006 &2008 in merjan teaching hospital 120 patients was selected according to ACR criteria & divided in two groups 60 for each ,they examined and follow-up regularly for six months ,group [1] given the dietary supplement ,the other given NSIAD [meloxicam],the knee joints of both groups examined at regular interval to show the response according to different parameter ,the functional score show improvement 31 while group [2] show 26 and the visual analogue score was more improved in group [1] than in group [2] and the radiological score show no difference

In this study the dietary supplement show rapid improvement with maximum at 4 months while other group show improvement at 2 months with no more improvement , the side effect in group [1] were less in group [2].

The glucosamine and chondrotin should be uswd as alternative drugs tn NSAIDs because less side effect and better response in different functional score.

عقار كلوكوزامين والكوندروتين في التهاب المفصل الضموري للركبة

الخلاصة

التهاب المفصل الضموري مرض شائع يصيب الركبتين نتيجة تقدم العمر وخصوصا بعد العقد الرابع من العمر، وهو مرض يصيب المفاصل الزلالية .الكلوكزامين والكوندروتين تزود القسم الأكبر من المقاومة للانضغاط . وهو يستخدم حاليا في علاج هذه الحالة .إن الهدف من هذه الدراسة هو لدراسة تأثير هذه المكملات الغذائية في علاج التهاب المفصل الضموري للركبة وقد أجريت بين عامي 2006 و2008 في مستشفى مرجان التعليمي في بابل، 120 مريضا تم اختيارهم حسب المعايير الخاصة لكلية المفاصل الأمريكية وتم فصلهم الى مجموعتين 60 مريضا لكل مجموعة ،المجموعة الأولى عولجت بعقار الكلوكوزامين والكوندروتين والأخرى عولجت بعقار الملبكسوكام . وتم فحص مفاصل الركبتين لكلتا المجموعتين في فترات محددة لغرض قياس الاستجابة اعتمادا على قياسات مختلفة .وكانت النتيجة الوظيفية ومقدار النتيجة البصرية للألم للمجموعة الأولى أفضل من المجموعة الثانية ولكن النتيجة الإشعاعية لم يتغير طول فترة الدراسة

في هذه الدراسة دلت على ان المكملات الغذائية أدت إلى تحسن أسرع يصل إلى الحد الأعلى في فترة 4 أشهر لكن العلاج الآخر تبدأ الاستجابة في شهرين مع عدم تغير في معدل الاستجابة مع استمرار فترة الدراسة كما إن المضاعفات الدوائية اقل في المجموعة الأولى إن عقار الكلوكوزامين والكوندروتين يفضل ان يكون بديلا للأدوية لا ستيرويديه كونها اقل من ناحية المضاعفات الدوائية وتظهر استجابة أسرع في النتيجة الوظيفية والبصرية

Introduction

Osteoarthritis is most common form of joint disease , its disease of aging

, 90% of all people have Radiographic features of Osteoarthritis in weight bearing joints by age of 40, symptomatic

disease also increase with age. the most important clinical aspect in this disease is pain and impairment of movement

This arthropathy is characterized by degeneration of cartilage and hypertrophy of bone at the articular margins , inflammation usually minimal, Hereditary and mechanical factors may involved in Pathogenesis[1].

Osteoarthritis is a disorder of Synovial Joints . The most frequently affected sites are apophyseal joints of the cervical and lumbar spine & knee & hip , unlike inflammatory arthropathies , it does not always affect whole joint . e.g is effect medical tibiofemorel & lat Pattallofemorel compartment of the knee [2]

Chondroitin Sulfate is an important structural component of Cartilage and provides much of its resistance to compression , along with glucosamine , chondroitin Sulfate has become a widely used dietary supplement for treatment of Osteoarthritis[3] .

They are major component of extracellular matrix & important in maintaining the structural integrity of the tissue. Both found in dietary supplements used as an alternative medicine to treat Osteoarthritis & also approved and regulated as a symptomatic slow acting drug for this disease.

The benefit from them are likely the result of a number of effects including its anti inflammatory activity, the stimulation of. the synthesis of proteoglycans and Hyaluronic acid, inhibiting the synthesis of proteolytic enzymes [4], nitric oxide and substances that contribute to damage cartilage matrix and cause death of articular choudrocytes[5].

Aims of Studies

The study is aimed to show the effect chondroitin- glucosamine – dietary supplement benefit in the treatment of OA knee patients & compare with other drug to treat patient & improve functionally disability of knee joints in Iraqi patients.

Patients and Methods

Study was done in Hilla in privet clinic. Between 2006-2008 / Babylon Province. Patients were selected according to these criteria :

Patient al either sex more than 50 years & they fulfilling the American collage of Rhenmatology (ACR) criteria of clinical, laboratory and radiographic findings[6], those patients were diagnosed with primary osteoarthritis with lequesns score in the range of (10-18) [7]& those patients can come for regular visit. 150 patient were included in the study ,30 patients were excluded because either they had arthritis due to other cause like Rheumatoid arthritis or have renal or hepatic dysfunction or other serious medical illness (Sever Ischemic heart Disease. Or heart failure.

The first screening visit , Patient medical history was taken & clinical assessment was done . The knee its were examined by local examination & specific parameter for assessing the severity subjectivity as well as objectivity.

All patients were asked to guard the severity of pain based on visual analogue scale (VAS) ranging from no pain at bottom of the scale to unbearable pain at the top of 100 mm colored scale. The other variable in the scale were mild , modrate and sever pain separated by 20 mm. [8] , lequesnes index (Table 1)

Table 1 Lequesne's index (Functional Index for OA of Knee).

Pain or Discomfort	Index[†]
<u>During Nocturnal Bed rest:</u>	
None or insignificant	0
Only on movement or in certain positions	1
With no movement	2
<u>Morning Stiffness Or Regressive Pain After Rising:</u>	
1 minute or less	0
More than 1 but less than 15 minutes	1
15 minutes or more	2
<u>After Standing For 30 Minutes</u>	0 to 1
<u>While Ambulating:</u>	
None	0
Only after ambulating some distance	1
After initial ambulation and increasing with continued ambulation	2
After initial ambulation, not increasing with continued ambulation	1
<u>While Getting Up From Sitting Without The Help Of Arms</u>	0 to 1
<u>Maximum Distance Walked (may walk with pain):</u>	
Unlimited	0
More than 1 km, but limited	1
About a km in about 15 min	2
From 500 to 900 m about 15 min	3
From 300 to 500 m	4
From 100 to 300 m	5
Less than 100m	6
With one walking stick or crutch	1
With two walking sticks or crutches	2
<u>Activities Of Daily Living:</u>	
Able to climb up a standard flight of stairs	0 to 2
Able to climb down a standard flight of stairs	0 to 2
Able to squat or bend on the knees	0 to 2
Able to walk on uneven ground	0 to 2

[†] Without Difficulty: 0; With Small Difficulty: 0.5; Moderate: 1; Important Difficulty: 1.5; Unable: 2.

which is functional scoring system was measured accordingly[8].

The objective assessment of the knee joint was done by noting the presence or absence of swelling , deformities , tenderness, warmth, crepitus, joint effusion – and muscle atrophy & the joint mobility was assess by patients. Global assessment done by all these parameter measured by physican & patients, recorded very poor , poor, good, very good[9].

Laboratory assessment such complete blood picture (CBP), Random Blood Sugar (RBS) and electro Cardiogram, and Liver and Renal Function Test for inclusion and exclusion of patient first assessment of patients also done at end of the study .

Knee joints X Ray were done for each patients , for each follow up ((at 2 months interval)) , The wave graded by a scoring system of 1-4 by the radiologist (Table 2)[10].

Table 2. Radiological scoring for Knee osteoarthritis

Radiological scoring	X-ray finding
0	Normal
1	Doubtful narrowing of joint space/possible osteophytes lipping
2	Definite osteophytes/absent or questionable narrowing of joint space
3	Moderate multiple osteophytes, definite narrowing of joint space, some sclerosis, possible joint deformity of bone ends
4	Large osteophytes, marked narrowing of joint space, severe sclerosis, definitive joint deformity of bone ends and subchondral cysts may be present.

120 patient were included , divided into: two groups for period of 6 months follow for each patient with regular visit at 2 months interval between.

The Group (1) 60 patients were give combinations of 500 ghecosamine sulphate& 400 Chondnotion sulphate. 2 tablet per day.

The Other Group (2) 60 patients were give Meloxicam 15 mg / Day.

All Patient to instructed not take any analgesic except paracetamol (only if needed during the study period . The Except no more 1000 mg / day and they asked at each visit how much they have taken of the drug .

Patients were follow up 0- 2 – 4 – 6 – months :

The knee joints were examined on each visit according to above parameter . The Patient compliance was considered good if the patient takes 75% of drug which prescribed . All Patients were advised about knee exercise at home .

Results

This study was design as compared study between [two] groups group one and two both include 60 patients for

each ,the mean age of group [1] was 57 years and group [2] was 58 years.

Sex ratio ,group [1],51 female and 9 male and group [2] 50 female and 10 male table [1].

The functional score was recorded for both groups from the start of the study and at 2 months interval to the end of the study ,in group [1] the improvement was 30-/+ 5 while group [2] was 25-/+5 at the end of the study table [2].

The visual analogue scale for both groups were recorded at the start and 2 months interval to the end of the study ,the improvement from 70-/+6 to 35 in group [1] where the improvement in group [2] was from 72 to 50 table [3]

The radiological score ,there was no difference between both groups during the study period and no difference in progress of osteoarthritis radiological features. table[4].

To compare the use of additive drug [paracetamol] by the numbers of the tablets [more than 10 tablets] per week ,in group one 41 patients had recorded to use the drug while group [2] 38 patients were use the drug. table[5] .

The patient and physician assessment during the study the difference was more

in patients self assessment than physician assessment .,58% of group [1] patients showing improvement at the end of the study while group [2] only 45% show improvement ,the physician assessment show that group [1] 55% of

patients and group [2] only 52% at end of the study ,table[6]

The hematological and biochemical fallow up of both groups at the start of the study and end of the study showed in table[7].

Table I : group I & II

Group I	Group II
No = 60 patients	No = 60 patients
Sex F 51[85%] = M 9[15%]	Sex F 50[83%] = M 10[17%]
Mean age = 57 year	Mean age = 58
Duration clinical Symptom = 3-5 year	Duration clinical Symptom = 3-5 year

Table II : Functional scores

Group	0	2months	4months	6 months
G I	14 + 5	18	25 + 5	30 + 5
G II	15	16	18	22 + 5

Table III : Visual analogue score :

Group	0	2months	4months	6 months
G I	70 + 6	60	45	35
G II	72	55	50	48

Table IV Radiological score

Group	0	2months	4months	6months
G I	2.5	2.4	2.3	2.3
G I	2.5	2.4	2.4	2.4

Table V

Group	No of patients	%
I	41 patient	68.1%
II	38 patient	63.5%

Table VI Patient & physician assessment

Assessment	Group 1	Group 2
Patient	58%	42%
Physician	55%	52%

Table VII

Lab study	I		II	
	0	6 month	0	6 month
Hb %	11.5	11	11.7	10.5
WBC	6.3	6.5	5.7	6.5
ESR	35	30	30	30
Blood glucose	100	110	105	103
B urea	40	41	35	45
AST	27	29	26	35
ALT	25	28	27	32

Discussion

Osteoarthritis is a disease of progressive cartilage damage seen mostly after the age of 40s years ,

The pain may arise from synovial inflammation or periosteal nerve stimulation ,previously NSIADs widely used for relieving the pain in osteoarthritis but mostly there is good present of patients that stop drug because adverse effect that related to the therapy and the older people with multiple clinical problem that NSIADs lead to more adverse effect ,due to this fact there was new drugs emergence that would work to reduce patients symptoms ,and they act to regenerate cartilage and act as anti inflammatory with low risk for patients[11] this supported also by study of Alekseeva et al [12]

The glucosamine and chondrotin combination has been sued in all over the world for knee osteoarthritis and many studies work for that, it used as nutritional supplements for knee osteoarthritis[13].

In this study combination of glucosamine and chondrotin has work well as compare with treatment by melocexam drug ,the pain score was assessed by the visual scale ,this parameter showed progressive improvement over the period of drug therapy with maximum benefit at 4

months point while the other group show rapid improvement at 2 months point but then no more improvement after that point ,when compare with Bourgeois et al [14], 3 months trial of 1200 mg of both combination in single or divided doses its showed that decrease of lequense index and spontaneous joint pain score versus placebo [$p<0.1$]

The lequesne index that assess the functional score the functional mobility of the joints depending on the daily activity ,it showed mark improvement than the other group at 2-4 months and such result was documented in other studies e.g Muller et al [14] ,Noack et al[15] and they found that this index to be a sensitive indicator of the improvement, Muller and colleagues [16] in short term study [4 weeks] study to compare this drug versus ibuprofen showed that its effective like ibuprofen and better tolerated [$p<0.1$]

The radiological score change in this study show no difference between 2 groups during the this study period ,they not correlated with patients symptoms many patients show functional disability that not correlated with X ray finding . And only 6% show adverse effect while 35% eboburfen group show adverse effect mainly gastrointestinal, in our study CS group show 10% show adverse

effect and the other group 21% show adverse mainly gastrointestinal effect . Many study show and support the use of alternative drug to higher risk group patients of NSAID or cyclooxygenase 2 inhibitor for osteoarthritis

We used the combined medication from the same drug manufacture to avoid the difficulties that found with commixture of the medication that found by leeb et al whom performed a met analysis of 7 trials including 372 patients that cited the difference . While Richy et al study [17]that examined both the structural and symptomatic efficacy of the drug via radiological progression of the joint space narrowing ,the patients in this study which include 1975 patients show significant effect on the joint space narrowing but over 3 years period and the tolerance was equal to placebo ,we used the combined medication from the same drug company because in the market many trade manes from different companies to avoid the difficulty that found with mixtures of the medication that found by leeb et al [18]whom preformed a meta analysis of 7 trials including 372 patients that cited the difference

Conclusion

This drug is beneficial when it used in Iraqi patients with no adverse effect like NSAIDs specially gastrointestinal ,it lead to improve functional ability of the patients and decrease the pain but longer study to be performed to see the effect on the joint space narrowing and other studies to be done to see the effect on others joints

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