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Original article

Functional assessment in patients with knee osteoarthritis treated with glucosamine and a rehabilitation program

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SUMMARY. Osteoarthritis is the most frequent rheumatic disease seen in clinical practice. The purpose of this study is to assess the efficacy of a Rehabilitation program and glucosamine by means of a function assessment using the WOMAC scale. Two balanced, randomized groups were put together: Group A with glucosamine and Group B with placebo. Both implemented an exercise program. Subjects answered the functional WOMAC scale questionnaire in the beginning, at two months, and at the end of the study. The average age in Group A was 57.6 years and in Group B, 53.0 years (p = 0.02). Baseline values in both groups were the same for all 3 variants analyzed (pain, rigidity and difficulty) with a total p = 0.98. Three age subgroups were created for a better observation of the results. Both treatments are beneficial to handle knee osteoarthritis. Both groups showed functional improvement. Age subgroups showed that the older the age, the better the response to treatment with glucosamine as shown on a reduced WOMAC scale score.

Key words: osteoarthritis, glucosamine, rehabilitation, knee.

RESUMEN. La osteoartrosis es el padecimiento reumático más frecuentemente observado en la práctica clínica. El objetivo de este estudio es valorar la eficacia de un programa de Rehabilitación y la glucosamina haciendo una valoración funcional por medio de la escala de WOMAC. Se formaron 2 grupos balanceados aleatorizados, el grupo A con glucosamina y el grupo B con un placebo, a ambos se les implementó un programa de ejercicios. Contestaron la escala funcional de WOMAC al inicio, a los 2 meses y al final del estudio. El promedio de edad del grupo A fue de 57.6 años y del grupo B de 53.0 años (p = 0.02), los valores iniciales de ambos grupos fueron iguales en las 3 variantes analizadas (dolor, rigidez y dificultad) con un total de p = 0.98, para observar mejor los resultados se formaron tres subgrupos de edad. Ambos tratamientos son beneficiosos para el manejo de la osteoartrosis de rodilla, hubo mejoría funcional en ambos grupos. En los subgrupos de edad se observó que a mayor edad, mejor respuesta al tratamiento con glucosamina al disminuir los puntos de la escala de WOMAC.

Palabras clave: osteoartrosis, glucosamina, rehabilitación, rodilla.

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Abbreviations:

NSAIDS:	Non Steroid Anti-inflammatory Drugs
CNR:	National Rehabilitation Center
OA:	Osteoarthritis
WOMAC:	Western Ontario and McMaster Universities. Functionality osteoarthritis scale.

Introduction

Osteoarthritis (OA) or degenerative joint disease is the orthopedic condition most frequently seen in clinical practice and the second cause of disability among elderly people.[13,14] It has been estimated that between

15.8 and 50 million adult Americans are affected by OA. It is 5 times more prevalent among females than males. Thirty three per cent of adults aged 53 to 85 years show radiology evidence of knee OA. According to Pennix, the knee is the second most affected joint.[13,14] In Mexico, osteoarthritis ranks as the 4th cause of morbidity and the 2nd cause of disability. An estimated 12 to 45 million adults are suffering from osteoarthritis.[21]

OA frequency at the National Rehabilitation Center has increased over the years. In 2001, 727 new cases were diagnosed. Of these, a greater prevalence among women over men was confirmed.[41]

Patients with OA suffer from pain which typically worsens with overweight and activity while it improves with rest. They may suffer form morning stiffness and be accompanied by joint edema after inactive periods. On physical examination, one finds the joints soft, bone growth, crepitation with mobility and/or joint limitation.[1,7,12,19]

In addition to clinical diagnosis, diagnosis may be confirmed by laboratory testing, X rays using the Kellegren & Lawrence classification,[4] computerized tomography (CT), and magnetic resonance imaging (MRI).[1,4,18]

Although there is no known cure for OA, the treatment designated for each patient may reduce pain, maintain and/or improve joint mobility and reduce functional limitation. In 1995, the American College of Rheumatology published recommendations for the medical management of knee OA. These guidelines summarized the use of non pharmacological modes including patient education, physical and occupational therapy as a basis for treatment of individuals with OA, and the use of pharmacological agents in addition to specific recommendations for surgical management of OA.[8]

Quadriceps weakening is common among patients with knee OA. It is a manifestation of atrophy for disuse developed as a result of the painful limb not bearing weight. This weakness results in sensory dysfunction (reflected by a decreased proprioception). Traditionally, quadriceps strengthening has been emphasized as the most important element in training programs and conditioning designed to protect the knee.[22]

Drug therapy to handle pain is more effective when combined with non pharmacological strategies. Pain relief is the main indication for treating patients with OA. Virtually all non steroid anti-inflammatory agents marketed have been used for this purpose.[8,22]

Glucosamine sulfate has been characterized as a slow acting drug to treat osteoarthritis. Group studies[3,8,9,16,18,20] support the efficacy of glucosamine to relieve joint pain in patients with knee OA. Glucosamine is an amino monosaccharide which is a component in nearly every tissue, including cartilage.[2,18]

An exercise program for patients with knee osteoarthritis has been seen to improve functionality of patients by 40 to 60 per cent.[5,6,13] By using glucosamine, functional improvement by 20 to 25 per cent has been seen in patients. This functionality is measured using the WOMAC scale score.[15,16]

Considering the benefits of both treatments separately, this study aims at analyzing the effectiveness of the exercise program together with the administration of glucosamine sulfate.

Material and methods

A controlled, double blind clinical study was conducted with 2 balanced groups randomized under the following inclusion criteria–patients with primary knee osteoarthritis diagnosis, graded by X-ray as Grade III under Kellegren and Lawrence's classification, males and females. Ages ranged between 40 and 65 years. Patients not treated with glucosamine and physical therapy in other series. Patients signed an informed consent. Groups were organized as follows.

Group A: made by 15 patients given glucosamine and the CNR (Spanish acronym for National Rehabilitation Center) exercise program for patients with knee OA (Appendix I).

Group B: made by 15 patients given a placebo and the exercise program for patients with knee OA (Appendix I).

Group A was given glucosamine at 400 mg doses as an IM injection, twice a week for 4 weeks. After that, 1.5 glucosamine sulfate was given orally, Monday through Friday, for 8 weeks. The placebo was a harmless substance with the same physical characteristics and the same presentation.

Patients were given a presentation on the self-evaluation guidelines such as measuring at home and at work to decrease overload on the joint involved. In talks with patients the significance of reducing body weight was also discussed.

The rehabilitation program was divided into three phases, each one for 10 days, with institutional physical therapy.

The functional WOMAC scale questionnaire was given at the beginning, at 2 months, and at the end of the study.

Statistics

A chi^2 test was performed for age variants. Student's t test was used for independent analysis of variance (ANOVA) for the age subgroups.

Results

Group A (glucosamine) included 12 female and 3 male patients while Group B included 13 female and 2 male patients ($p = 0.50$). The average age in the first group was 57.6 years (SD = 5.1 years) and 53.0 years (SD = 5.8 years) in the second group ($p = 0.02$).

Tables 1 and *2* show the average changes from the first to the second and third pain, rigidity and difficulty assessments inside each study group.

The baseline values in both groups were the same for

all three variables analyzed (pain p = 0.98, rigidity p = 0.73 and difficulty p = 0.98, total p = 0.98). This assured the proper later comparability between both groups.

In comparing the averages of the second assessment (pain p = 0.67, rigidity p = 0.43, difficulty p = 0.81, total p = 0.83) and those of the third assessment (pain p = 0.70, rigidity p = 0.40, difficulty p = 0.32, total p = 0.50) no significant changes were shown favoring either treatment.

To control the age influence on the results, the univariant variance analysis was used with age as the covariable. For better result observation, three age sub-groups were created (*Table 3*).

About the pain in the first assessment, averages were seen to remain with no significant differences between glucosamine and placebo (p = 0.23). However, those averages changed significantly in the glucosamine group according to three age subgroups (p = 0.012) with the highest average for the oldest age subgroup. On the second and third assessment, pain average differences tended to cancel out among the age subgroups in the glucosamine group (p = 0.08 and 0.14 respectively) while comparison between both study groups continued with no significant differences (p = 0.26 for the second assessment and 0.28 for the third assessment).

Table 1. Changes in the pain, rigidity and difficulty averages. First to second assessments. Rehabilitation +.

	Glucosamine			Placebo		
Variable	Assessment 1	Assessment 2	P	Assessment 1	Assessment 2	P
Pain	10.2	6.6	0.005	10.4	7.2	0.001
Rigidity	4.1	2.5	0.006	4.0	2.8	0.010
Difficulty	35.2	24.4	0.006	36.0	23.6	0.005
Total	49.2	33.6	0.005	49.8	33.6	0.002

Table 2. Changes in pain, rigidity and difficulty averages. Second to third assessments. Rehabilitation +

	Glucosamine			Placebo		
Variable	Assessment 2	Assessment 3	P	Assessment 2	Assessment 3	P
Pain	6.6	5.4	0.16	7.2	6.0	0.010
Rigidity	2.5	2.0	0.26	2.8	1.6	0.113
Difficulty	24.4	15.9	0.009	23.6	19.2	0.004
Total	33.6	23.4	0.025	33.6	26.8	0.001

Table 3. Average assessments by study group and age subgroups. Age subgroups.

Variable	Group	46-52 years	53-59 years	60-65 years
Pain 1	Glucosamine	8.2	8.7	12.1
	Placebo	9.3	11.5	12.0
Pain 2	Glucosamine	6.0	5.7	7.5
	Placebo	6.3	7.2	9.3
Pain 3	Glucosamine	5.0	5.5	5.7
	Placebo	5.5	6.0	7.6
Rigidity 1	Glucosamine	3.0	3.7	5.0
	Placebo	3.5	4.5	4.6
Rigidity 2	Glucosamine	2.2	2.5	2.7
	Placebo	2.2	3.2	4.0
Rigidity 3	Glucosamine	2.0	1.0	2.7
	Placebo	1.7	0.7	2.3
Difficulty 1	Glucosamine	25.7	33.2	41.8
	Placebo	33.3	35.2	44.0
Difficulty 2	Glucosamine	22.2	19.7	28.4
	Placebo	21.3	24.5	28.6
Difficulty 3	Glucosamine	13.2	13.7	18.7
	Placebo	18.8	17.7	22.0

Discussion

From the results derived no significant differences were seen between the glucosamine group and the placebo group. It was seen that using both treatments is beneficial to handle patients with knee OA since both groups showed functional improvement. Notice that between the first and second assessment there were significant changes in all three variables (pain, rigidity and difficulty) for both groups. In contrast, changes were smaller from the second to the third assessment. In the glucosamine group pain and rigidity changes were not significant when comparing the third to the second assessment while in the placebo group change was not significant only for the rigidity variable. With regards to age subgroups, the older the age, the better response to treatment with glucosamine was seen since the WOMAC functional scale score decreased by several points.

Houp[9] conducted a research on the use of glucosamine salt for knee pain. The results suggest the need for a large group to determine the efficacy of this compound and that older individuals with knee OA improve with the use of glucosamine. Unlike that study, we combined glucosamine with an exercise program and they compared efficacy against a pain killer. Based on our results only, we confirmed the efficacy of an appropriate rehabilitation program.

Measuring physical capability and knee disability as well as muscle strengthening, aerobic work capacity and joint function are significant determinants of physical disability in people with knee OA. The relationship between muscle strength, joint pain and disability is complex as muscle weakness may result in an unstable joint; stress or an unstable joint may lead to innervated tissue stretching and produce pain and disability resulting, therefore, in disuse and more weakness thus creating a vicious circle[6]. Improving muscle strength in a 6 week program may probably be attributed to improved body coordination.[10,22] Observation studies suggest that regular physical exercise may be the most important preventive factors in setting off disabilities.

For this reason, the purpose of rehabilitating patients with knee OA should be aimed at reducing the inflammatory process, decreasing pain, preventing further joint damage, maintaining and restoring decreased muscle dysfunction, educating patients and family about the disease, and maintaining functional ability thus preserving their independence. Functional quality is the ability of performing tasks involving daily life activities such as getting dressed, walking and doing instrumental activities including eating, washing and cleaning, etc.), recreation, transportation and activities reflecting the patient's integration are also included as functional abilities. Functional disability causes alterations in the way a patient with OA performs. Pain uses more energy when conducting daily activities and doing work. Rehabilitation treatments are tailored to the needs of each patient. They should be practical, economical and really adapting to the purpose proposed for each patient. Furthermore, it needs to be started as soon as possible after the disease is diagnosed and at the time drug therapy begins.

APPENDIX 1

Rehabilitation program

Stage I

1. Hot moist packs for 15 minutes
2. Passive mobilization of the patella on its 2 axes and freely to hip and ankles
3. Isometric exercising of glutei, quadriceps (emphasis on oblique plane by contracting hip adductors) and hamstrings
4. Isotonic exercising of ankles on an open chain
5. Hip, quadriceps, hamstrings, and sural triceps flexor stretching
6. Proprioceptive training: biopodalic and tolerating monopodalic balance

Stage II

1. Hot moist packs for 15 minutes
2. Passive mobilization of the patella in its 2 axes and freely to hip and ankles
3. Closed chain exercising (not flexing the knees for more than:
   a) 3 minisquat series, 10 repetitions
   b) 3 step-up series, 8 repetitions
4. Isotonic ankle exercising
5. Hip, quadriceps, hamstrings, and sural triceps flexor stretching
6. Proprioceptive training: monopodalic balance

Stage III

1. Therapeutic tank for 15 minutes
2. Ergonometric bicycle for 5 minutes
3. Closed chain exercising (do not flex knees more than:
   a) Kinetron II:
      I. 50 cm/sec velocity, 2 minutes
      II. 30 cm/sec velocity, 1 minute
      III. 40 cm/sec velocity, 1 minute
   b) 3 step-down series, 8 repetitions
4. Hip, quadriceps, hamstrings, and sural triceps flexor stretching
5. Proprioceptive training: monopodalic support

Conclusion

From the results derived, we were able to confirm the benefits from setting an appropriate rehabilitation program for these patients. As for the study drug administration, we believe in the need for expanding the sample and assess the age group of people older than 60 years to check for the usefulness of glucosamine sulfate together with a rehabilitation program.

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