

# Clinical Assessment of the Use of Sodium Hyaluronate in the Treatment of Chondromalacia Patellae

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## الخلاصة

**الخلفية :** من خلال مراجعة الدراسات المتعلقة بموضوع استعمال عقار (sodium hyaluronate) في علاج (تلين غضروف الرضفة chondromalacia patellae ) لم نجد سوى دراسة واحدة خاصة بنفس الموضوع. sodium hyaluronate ويسمى ايضا(hyaluronic acid (HA او hyaluronan ، وهو مادة ذات سيولة مطاطية موجودة في السائل الزلوي طبيعيا وله اهمية في ترطيب وحماية وتغذية الغضروف المفصلي.

**الاهداف :** ان الهدف من هذه الدراسة هو بيان دور sodium hyaluronate في علاج تلين غضروف الرضفة .  
**طريقة البحث:** هذه دراسة عشوائية مسيطر عليها اجريت على عينة من 30 مريض مصابين ب(تلين غضروف الرضفة) تم اختيارهم عشوائيا للفترة من نيسان 2008 ولغاية كانون اول 2011، تم توزيع الحالات الى : 1. عينة الدراسة 15 حالة اعطية العلاج (2 مل من مادة sodium hyaluronate السائل تم حقنها في مفصل الركبة مرة واحدة اسبوعيا لثلاث اسابيع متتالية ) مع تمارين تقوية العضلة الرباعية . 2.عينة المقارنة: 15 حالة تم فيها استخدام التمرين فقط . تمت متابعه الحالات دوريا كل 6 اشهر ولغية سنتين، اختبرت النتائج باستخدام اختبار Fisher's exact لدرجة ثقة 95%.

## النتائج :

اظهرت النتائج بعد 6 اشهر فيما يخص عينة الدراسة ان 33,3% من المجموع الكلي لديهم استجابة ممتازة للعلاج ،33,3% عندهم استجابة جيدة للعلاج ، بينما اظهرت نتائج عينة المقارنة ان 10% فقط من المجموع الكلي لديهم استجابة معتدلة للعلاج.

بعد سنة من الدراسة كانت النتائج نفسها فيما يخص عينة الدراسة بينما6,67% من المجموع الكلي لعينة المقارنة لديهم استجابة جيدة للعلاج،33,3%استجابته معتدله.

بعد سنة ونصف من الدراسة وفيما يخص عينة العلاج ،26,6% كان لديهم استجابة ممتازة للعلاج،33,3% لديهم استجابة جيدة ،33,3% لديهم استجابة معتدله،فيما يخص عينة المقارنة 6,67% لديهم استجابته جيده،3% لديهم استجابة معتدلة. بعد سنتين من العلاج،كانت النتائج نفسها فيما يخص العينة التي استلمت العلاج بينما 3,33% من عينة التمرين كان عندهم استجابته جيده ،33,3% عندهم استجابته معتدله . وتم استخدام نسبه الاراحيه بحدود ثقه مقدارها 95%.

**الاستنتاجات:** من الممكن استعمال (sodium hyaluronate) في علاج تلين غضروف الرضفه.

## Abstract

**Background :** Review of the literatures reveals that some of them advised to use hyaluronic acid (HA) as a treatment for chondromalasia patellae [CMP] depending on very few clinical studies, hyaluronic acid (HA) or Sodium hyaluronate, also referred to as or hyaluronan, is a viscoelastic substance that occurs naturally in synovial fluid and is thought to play an important role in lubricating, protecting, and maintaining nutrition of the articular cartilage.

**Objectives:** To answer the following question: is there a role for (HA) in the treatment of [CMP]?

**Methods:** A randomized controlled trial study was carried out among 30 patients (15 patients as study group, 15 patients as control group )with [CMP] from April 2008 to December 2011.

For the study group: intraarticular injection of 2 mL sodium hyaluronate solution, once per week, for 3 weeks + quadriceps strengthening exercises.

For the control group: quadriceps strengthening exercises only.

Follow-up for both groups was done every 6 months until 2 years and results regarding improvement were evaluated by Fisher's exact test, the corresponding 95% of confidence interval (95% C.I) was used.

**Results:** At the follow up visits, the studied group had improvement from baseline after the use of sodium hyaluronate solution at any time point. According to response to treatment after 6 months for the studied group, 33.3% had excellent response, 3.33% had good response, no patient had fair response, and 13.33% had no response. While the controlled group had no excellent or good improvement after the use of exercises, only 10% had fair response. This difference is statistically significant (95%CI, p-value< 0.05). After 1 year, the studied group had the same response to treatment, While 6.67% of the controlled group had good response, 13.33% had fair response, and 30% had no response. This difference is statistically significant (95%CI, p-value< 0.05). After 1.5 years, 26.6% of the studied group had excellent response to treatment, 3.33% had good response, 3.33% had fair response, 13.33% had no response and 3.33% had recurrence. While no one in the controlled group had excellent response, 6.67% had good response, 13.33% had fair response, 30% had no response and no one had recurrence. This difference is statistically significant (95%CI, p-value< 0.05). After 2 years, the studied group had the same response, 3.33% of the controlled group had good response, 13.33% had fair response, 30% had no response and 3.33% had recurrence. This difference is statistically significant (95%CI, p-value< 0.05).

**Conclusions:** Sodium hyaluronate can be used successfully in the treatment of chondromalacia patellae as about (73.26%) of the studied group had a response to treatment. Follow up for 2 years showed that (66.66%) had a response to treatment. The drug can be indicated for patients who cannot take NSAID and those who are unwilling to or not cooperative to perform the advisable exercises.

Keywords: Chondromalacia patella, Sodium hyaluronate.

## Introduction

chondromalasia patella is softening and fibrillation in the cartilage of the articular surface of patella [ 1,2,13 ].

Causes: [1,2,3,13]

- Excessive torsional deformity of the tibia;
- High or lateral position of the patella.
- Shallow femoral trochlea.
- Atrophy of vastus medialis muscle.
- Increased quadriceps angle (often in those with wide hips).
- Over-development of the vastus lateralis muscles.
- Flat feet.

- Excessive pronation of the feet (feet turn up to the side) [2].

Symptoms: [1, 2, 3]

- A grinding or clicking feeling when straightening the knee (known as crepitus).
- Pain at the front of the knee.
- Pain which is often worse when walking downstairs.
- Pressing down on the knee cap when the knee is straight may be painful.
- Pain when standing after extended periods of sitting (known as movie-goers knee or the theatre sign).
- Minor swelling may be present.
- History: Individuals may complain of knee pain with walking, running, squatting, and ascending or descending stairs. However, knee pain is not always present, and is not an indicator of the severity of chondromalacia patella. The individual may report a feeling of grating, catching, or locking of the knee with motion. Some individuals have a sensation that the knee is giving out. Many individuals report pain after sitting with the knee bent for long periods (e.g., during movies, car rides, plane trips) [2, 3].
- Physical exam: Chondromalacia patella may be evaluated by placing manual pressure on the patella while the individual contracts the quadriceps muscle. Pain during this maneuver is suggestive of chondromalacia patella. A crackling sound in the knee (crepitus) is often noticeable with passive range of motion. Active range of motion against resistance is usually painful. Alignment of the patella may be evaluated by measuring the quadriceps angle (Q-angle) although this is difficult to interpret because of the malposition of the x tube and the position of the overlap of the anatomical structures.
  - Tests: Routine knee x-rays will include special views of the patella (Merchant view) to evaluate its position in the femoral groove. MRI or CT scans can be used to evaluate the articular surface [3], and arthroscopy to confirm diagnosis and to evaluate the degree of articular cartilage involvement.

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Treatment:

Temporarily resting the knee and taking non steroidal anti-inflammatory drugs (NSAIDs) may help relieve pain. Physical therapy, especially quadriceps strengthening and hamstring stretching, may be helpful. If the pain does not improve and there are signs of arthritis developing around the kneecap ; surgery may be an option .

Surgery:

1. Re alignment of quadriceps pulling mechanism "e.g. medial release and lateral reefing"
2. Elevation of the quadriceps insertion.
3. Arthroscopy by drilling and shaving of the cartilage involved

### Hyaluronic Acid

Hyaline cartilage is the most abundant cartilage in the body. It serves to add structure and flexible support. The proteoglycans [Glycosaminoglycans are linear, unbranched, high molecular weight polysaccharides containing a repeating disaccharide unit (D-glucuronic acid and N-acetyl glucosamine) + a core of protein], within the hyaline cartilage are shaped like a bottle brush, with hyaluronic acid making up the backbone of the brush. Without the strength of the backbone, the proteoglycan falls apart, leaving the cartilage to deteriorate [4, 6]. Hyaluronic acid in its natural state, weights anywhere from 1.2 to 1.5 million daltons. Its weight lends itself to high viscosity and excellent lubrication within the body [5, 6]. At low load speeds it act as a lubricant and during faster movements as a shock absorber. [11, 12]

The cartilage is a vascular, as it contains no blood vessels. It must be fed by the synovial fluid [7]. Without the appropriate levels of hyaluronic acid, the synovial fluid loses its ability to perform, thereby leaving the joints unprotected and the cartilage undernourished [8, 9].

The American College of Rheumatology recommends hyaluronic acid injections and suggests they may have disease-modifying benefits, making them superior to NSAIDs [6,7] while the American academy of orthopedic surgeons neither recommends nor denies the use of HA ,waiting for more results. [12]

Its success has been attributed to its natural viscosity and ability to penetrate the extracellular matrix of the joint connective tissue [9].

## **Materials and Methods:**

This is a randomized control trial study carried out among 30 patients with [CMP] from April 2008 to December 2011. Sample size taken was 15 in each group. For study group: 1. An intra articular injection with 2 mL sodium hyaluronate solution [the knee At 90 degrees flexion ,lateral to patellar tendon] once per week, for 3 weeks. 2. Quadriceps strengthening exercises for six weeks.

For the controlled group, the treatment will be exercises only for six weeks.

Follow up for both groups was done every 6 months until 2 years and results regarding improvement were evaluated according to the following criteria:

Excellent: Knee movement (flexion >130, extension= 0), no pain, squatting for 1 hour, positive tolerance to work.

Good: Knee movement (flexion 110-130, extension= 0), no pain, squatting for 45 minutes, positive tolerance to work.

Fair: Knee movement (flexion 90, extension= 0), occasional pain, squatting for 30 minutes, some pain during work.

Bad: Knee movement (flexion < 90, extension=10), pain present, squatting for 15 minutes, no tolerance to work, need NSAID to relief pain.

Exercises:

Exercises involve strengthening-stretching of the quadriceps muscle. All strengthening of the quadriceps muscle should be done within the range that keeps pressure on the kneecap low. This range is between full extension (the knee is completely straight) to approximately 45 degrees of bending of the knee. The exercises should be done with lightweight [3kg] and high repetition in three sets of 30. There should be no pain during the exercises. After the exercise program ice should be applied to the front part of the knee for approximately 5 minutes.

Statistics: Fisher's exact test was used to compare between studied and controlled groups. The corresponding 95% of confidence interval (95% C.I) were used.

## Results

For the studied group 33.3% showed excellent response to treatment, 3.33 showed good responses, no patient with fair response, 13.33% showed no response to treatment. For the controlled group, no patient showed excellent or good responses, 10% with fair response, 40% showed no response to treatment. This result showed statistical significant difference (p- value < 0.05).

The two-tailed 2x4 Fisher's exact test demonstrates that the difference between studied and controlled group is statistically significant: P=0.0001.

Table 1 shows distribution of the studied and controlled groups according to response to treatment after 6 months.

Group	Response to treatment	Total
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	Excellent	Good	Fair	No response	
Studied	10 33.3%	1 3.33%	0 0%	4 13.33%	15 50%
Controlled	0 0 %	0 0 %	3 10%	12 40 %	15 50%
Total	10 33.3%	1 3.33%	3 10%	16 53.33%	30 100%

For the studied group 33.3% showed excellent response to treatment, 3.33 showed good responses, no patient with fair response, 13.33% showed no response to treatment. For the controlled group, no patient showed excellent response to treatment, 6.67% showed good response, 13.33% with fair response, 30% showed no response to treatment. This result showed statistical significant difference (p- value < 0.05). The two-tailed 2x4 Fisher's exact test demonstrates that the difference between studied and controlled group is statistically significant: P=0.0002.

Table 2: Distribution Of the studied and controlled groups according to response to treatment after 1 year.

Group	Response to treatment				Total
	Excellent	Good	Fair	No response	
Studied	10 33.3%	1 3.33%	0 0%	4 13.33%	15 50%
Controlled	0 0	2 6.67%	4 13.33%	9 30%	15 50%
Total	10 33.3%	3 10%	4 13.33%	13 43.33%	30 100%

For the studied group 26.67% showed excellent response to treatment, 3.33% showed good response, 3.33% showed fair response, 13.33% showed no response to treatment, 3.33% showed recurrence. For the controlled group, no patient showed excellent response to treatment, 6.67% showed good response, 13.33% with fair response, 30% showed no response to treatment and no patient showed recurrence. This result showed statistical significant difference (p- value < 0.05) The two-tailed 2x5 Fisher's exact test demonstrates that the difference between studied and controlled group is statistically significant: P=0.003

Table 3 shows distribution of the studied and controlled groups according to response to treatment after 1.5 year.

' Group	Response to treatment					Total
	Excellent	Good	Fair	No response	Recurrence	
Studied	8 26.67%	1 3.33%	1 3.33%	4 13.33%	1 3.33%	15 50%
Controlled	0 0%	2 6.67%	4 13.33%	9 30%	0 0%	15 50%

Total	8 26.67%	3 10 %	5 16.67%	13 43.33%	1 3.33%	30 100%
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For the studied group 26.67% showed excellent response to treatment, 3.33% showed good response, 3.33% showed fair response, 13.33% showed no response to treatment, 3.33% showed recurrence. For the controlled group, no patient showed excellent response to treatment, 3.33% showed good response, 13.33% with fair response, 30% showed no response to treatment and 3.33% showed recurrence. This result showed statistical significant difference (p- value < 0.05). The two-tailed 2x5 Fisher's exact test demonstrates that the difference between studied and controlled group is statistically significant: P=0.004. Table 4 shows distribution Of the studied and controlled groups according to response to treatment after 2 years.

Group	Response to treatment					Total
	Excellent	Good	Fair	No response	Recurrence	
Studied	8 26.67%	1 3.33%	1 3.33%	4 13.33%	1 3.33%	15 50%
Controlled	0	1 3.33%	4 13.33%	9 30%	1 3.33%	15 50%
Total	8 26.67%	2 6.67%	5 16.67%	13 43.33%	2 6.67%	30 100%

## Discussion

Review of the literatures showed one study by Jiang et al. (2007) [10], regarding the use of sodium hyaluronate for treatment of chondromalacia patella. This study was insufficient to conclude that sodium hyaluronate is effective for treatment of CMP for the following reasons:

1. There is no control group to compare with the studied group.
2. The follow up period is short (only 5 weeks).

So we conducted this randomized controlled trial study with a follow up period for 2 years.

In this study, follow up after 6 months showed that for the studied group 66.6% of the 15 patients had excellent response to treatment, 6.66% of the ISpatients of studied group showed good response, so (73.26%) had excellent and good response to treatment, no patient with fair response, and 26.66% showed no response to treatment. For the control group no patient showed excellent response to treatment, or good response, 20% with fair response, 80% showed no response to treatment. This result showed statistical significant difference (p- value < 0.05).

Jiang et al. (2007) [10], reported that after 5-week treatment, the rate of excellent and good curative effects was 91.1 % ( cohort uncontrolled study).

Follow up after 1 year showed that the result for the 15 studied group was the same as that after 6 months (73.26% had excellent and good response to treatment). For the 15 patients of controlled group no patient showed excellent response to treatment, 13.33% showed good response.

Follow up after 1.5 year showed that 66.66% of the 15 patients of studied group had excellent and good response to treatment (53.34% for excellent, 6.66 for good, 6.66 for fair), while no patient from the controlled group showed excellent response to treatment, 13.33% showed good response to treatment.

Follow up after 2 years showed that the result for the 15 studied group was the same as that after 1, 5 year (66.66% had excellent and good response to treatment). While no patient from the controlled group showed excellent response to treatment, 3.33% showed good response to treatment.

The problems that interfere with this study are:

1. The drug is expensive.
2. The drug needs more evaluation regarding effect and side effect.
3. Patients need to visit clinics frequently. [ to overcome this problem ; phone calls and E mail massages used for uncooperative patients]
4. The method of introducing the drug (intra articular injection) is causing discomfort to the patient and not free from side effects as infection and pseudoseptic reaction. [12]

No patient included in the study suffers from major complications apart from pain during injections.

## **Conclusions and recommendations**

Sodium hyaluronate can be used successfully in the treatment of chondromalacia patellae as about (73.26%) of the studied group had a response to treatment. Follow- up for 2 years showed that (66.66%) had a response to treatment. The drug can be indicated for patients who cannot take NSAID.



## Transparency

1. This study was funded by the researcher only (the drug and the follow up visits).
2. All patients had been informed thoroughly about the program of the treatment and the possible complications.

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