Outcomes of Intra-Articular Injection of Sodium Hyaluronate for the Treatment of Osteoarthritis of the Knee

Thana Turajane MD*, Aree Tanavaree MD**,
Viroj Labpiboonpong MD*, Samart Maungsiri MD*

** Department of Orthopedics, Police General Hospital, Affiliated with Srinakarinwirot University*
*** Department of Orthopedics, Faculty of Medicine, Chulalongkorn University*

Background: *Intra-articular injection of hyaluronic acid has become an intervention step between conservative and operative treatment of knee osteoarthritis. This is recommended by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). However, the expected outcomes and the selection criteria are undetermined and controversial. A few articles have mentioned the long-term result of Sodium Hyaluronate in failed conservative treatment.*

Objective: *Determine the clinical outcomes of treatment with three intra-articular Sodium Hyaluronate injections (500-730 kilodalton (KDA), Hyalgan®) in knee-osteoarthritis patients who failed conservative treatment.*

Material and Method: *This was an uncontrolled, retrospective-cohort study with at least a 24- month follow-up period. The outcomes of the treatment were evaluated by questionnaires and telephone calls. The primary efficacy parameter was the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score and the secondary efficacy parameter was delay or cancellation of any surgical treatments during the follow-up period. Patients who had undergone surgical treatments were placed in the non-response group. The response group has repeated treatment every year.*

Results: *One hundred and eighty-three patients (208 knees) treated with intra-articular Sodium Hyaluronate were classified into three groups according to radiographic assessment. In group 1, narrowing joint space (Ahlback grade 1-2), WOMAC score improved from 70.46 to 26.55 ($p < 0.0001$), 41 in 46 patients (44/49 knees) did not require any surgical treatments. In group 2, bony attrition (Ahlback grade 3-4), WOMAC score improved from 70.19 to 40.38 ($p < 0.0001$), 47 in 70 patients (51/78 knees) did not require surgical treatment. In group 3, lateral subluxation (Ahlback grade5) WOMAC score improved from 64.71 to 32.67 ($p < 0.0001$), 58 in 67 patients (69/81knees) did not require surgical treatment. The result from WOMAC subscale analysis revealed an improvement in pain, stiffness, and function in all groups ($p < 0.0001$), but did not improve in ambulatory status.*

Conclusion: *Intra-articular Sodium Hyaluronate injection, used in knee-osteoarthritis patients who failed conservative treatment, was effective in visible cartilage patients (Ahlback grade1, 2) without mechanical problems involved. In severe osteoarthritis patients (Ahlback grade 3, 4, 5), this treatment was of less benefit if those patients were young, active, and expected independent ambulation. Surgical treatment may be a procedure of choice to meet patient expectation in improving function and ambulatory status. On the other hand, if patients were old and inactive with household ambulation, using intra-articular Sodium Hyaluronate was beneficial in improving pain, stiffness, and function but not ambulation level with 86.56% of excellent or good in overall satisfaction level. Thus, the radiographic evaluation, age, ambulatory status, and patient expectation may be the key factors to determine successful outcomes.*

Keywords: *Hyaluronic acid, Failed Conservative Treatment, Knee Osteoarthritis*

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Correspondence to : Turajane T, Department of Orthopaedics, Police General Hospital, 492/1 Rama I Rd, Pathumwan, Bangkok 10400, Thailand. Phone & Fax: 0-2253-5836, E-mail:thanaturajane@yahoo.com

Sodium Hyaluronate (500-730 kilodalton) has played a role in knee osteoarthritis treatment in Europe since 1987 and in USA since 1997. It has been recommended by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) since 2001[1]. However, this treatment remains unpopular. The efficacy of Sodium Hyaluronate treatment remains in controversy, some articles mentioned the positive effects, some showed undifferentiated results from placebo[2]. Moreover, conclusions from meta-analysis published during 2004-2005 were still debatable[3]. In 2004-2005, the incidence of cardiovascular and renal risk in the elderly using selective COX-2 inhibitors has increased. As a result, the European Medicine Agency suggested to limit this anti-inflammatory drugs group for a short period and as small a dose as possible to decrease long-term complication[4]. Adjuvant therapy, intra-articular Sodium Hyaluronate, have been addressed to decrease pain, improve quality of life, and possibly delay surgery up to the appropriate time. A number of clinical trials of Sodium Hyaluronate treatment have been compared with conservative treatment, including oral medication, or intra-articular steroid injection. However, few studies mentioned the long-term results of intra-articular Sodium Hyaluronate in knee-osteoarthritis patients who failed conservative treatment[5,6]. The purpose of the present study was to evaluate the results of intra-articular Sodium Hyaluronate treatment in knee-osteoarthritis patients who failed conservative treatment in term of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and its efficacy to delay or cancel from any surgical treatments during the follow-up period.

Material and Method

One hundred and ninety-five knee-osteoarthritis patients (220 knees) were enrolled during March 2001 and March 2004. Twelve patients were excluded because of death (3 patients) or loss of follow-up (9 patients; 3 patients in each group). One hundred and eighty-three patients (208 knees) were in the present study. There were 46 males and 137 females with an average age of 68.74 years (range, 50-84 years). Of 208 knees, 103 were left and 105 were right knees. The patients were followed-up for at least 24 months (range between 24 - 48 months). The inclusion criteria were primary osteoarthritis of the knee as defined by the ACR, failed to conservative treatment more than 6 months (all these patients had been treated with anti-inflammatory drugs and others, physical therapy and bracing with unsatisfactory improvement), and no contraindication for surgery. The exclusion criteria were other degenerative arthritis or other diseases unrelated to arthritis such as Pigmented villonodular synovitis (PVS) and Paget's disease, history of previous surgery, allergic to avian protein or Sodium Hyaluronate, and using any intra-articular treatment within 6 months. Patients were divided into three groups according to radiographic evaluation, group1- Ahlback grade 1 (joint spaces lost less than 5 mm) and grade 2 (joint spaces lost more than 5 mm), group 2 - Ahlback grade 3 (minor bone attrition) and grade 4 (major bone attrition), group 3 - Ahlback grade 5 (lateral subluxation). Baseline patient characteristics are summarized in Table 1. Primary efficacy outcomes were considered by WOMAC score with subscale analysis (pain, stiffness, function) and ambulatory function in each group. The secondary efficacy outcomes were the delay or cancellation of any surgical treatments during the follow-up period. Complications after surgeries were considered for the safety of intra-articular Sodium Hyaluronate injection giving beforehand. Patients who had undergone any surgical treatments afterwards were considered as a failure group.

Study design

All knee osteoarthritis patients treated with intra-articular Sodium Hyaluronate and followed-up at Orthopedic Clinic in Police General Hospital during March 2001 and March 2004 were enrolled for the present study. This study was a retrospective-cohort study and approved by the ethical committee. Patients were asked to provide informed consent before enrollment. The recording data included the primary efficacy parameters i.e.: WOMAC pain subscale recorded on 0-100 mm visual analogue scale (VAS; where 0 = no pain, 100 = extreme pain), the WOMAC stiffness subscale, the WOMAC physical function subscale, the patient satisfaction level (excellent, good, fair, poor) and the changes of ambulatory status (dependent, independent, household ambulatory), the secondary parameters were the delay or cancellation of any surgical treatments during the follow-up period.

All patients received at least a single course of three intra-articular injections of 20 mg Sodium Hyaluronate given at weekly intervals injected through anteromedial and anterolateral of the knee in the sitting position. All patients continued the home program of physical therapy by fixed arch quadriceps exercise, and received selective COX-2 inhibitor as a rescue medication. In the response group, the patients continued

Table 1. Baseline characteristics of patients

Characteristic	Group 1	Group 2	Group 3	Total
Ahlback Classification	grade 1-2	grade 3-4	grade 5	
Number of patients (Male:Female)	46 (18:28)	70 (20:50)	67 (8:59)	183 (46:137)
Mean (range) age (years)	64.85 (50-82)	68.57 (50-83)	71.6 (62-84)	68.74 (50-84)
Mean (range) bodyweight(kg)	67.24 (58-85)	67.4 (58-106)	64.5 (58-80)	67.0 (58-106)
Mean height(cm)	162.8	163	164.2	163
Mean body mass index (kg/m2)	25.36	25.36	23.92	25.21
Number of knees (Right:Left)	49 (32:17)	78 (35:43)	81 (38:43)	208 (105:103)
Bilateral Knee(s)	3	8	14	25
Mean (range) TF angle* (degree)	6.9 (2-10)	10.7 (6-15)	10.5 (2-18)	9.87 (2-18)
Household ambulation (patients)	6	29	41	76
Independent ambulation without walking aid gait (patients)	36	28	18	82
Independent ambulation with walking aid gait (patients)	4	13	8	25

* TF angle: Tibiofemoral angle

Table 2. Primary efficacy outcome: mean (range) WOMAC score

WOMAC	Group 1		Group 2		Group 3	
	pre	post	pre	post	pre	post
Pain	76.75 (68-84.6)	26.04* (20-56)	78.81 (54-84.8)	32.60* (10-56.8)	70.44 (36-86.2)	27.65* (10-53)
Stiffness	75.53 (20-85.5)	29.25* (10-82.5)	73.27 (45-83)	41.01* (10-82.5)	65.91 (20-90)	29.60* (10-83)
Function	59.11 (39.4-71.8)	24.37* (13.8-58.2)	58.50 (38.2-85.9)	47.52* (8.2-85.9)	57.77 (31.2-85.9)	40.77* (14.1-69.4)
Average	70.46 (45.5-77.6)	26.55* (18.2-61)	70.19 (55.7-82.7)	40.38* (94-72.6)	64.71 (30.7-80.3)	32.67* (12.5-59.1)

* Significant improvement ($p < 0.0001$)

to repeat the course of three intra-articular injections every 12 months. In the failure group, which was classified by lack of unimprovement of pain and knee functions after completion of the first course of three injections, the surgery would be scheduled within 3-4 weeks after the last injection.

Statistical analysis

T-test: Paired two samples for means was used for comparison of total WOMAC scores and WOMAC subscales of patients in each group (two-tailed test, type 1 error 5%).

Chi-square test was used to evaluate the relationship between patient satisfaction and ambulatory status or age in each group. A p-value of less than 0.05 was considered statistically significant.

Results

WOMAC subscale analysis

Patients in group 1, 2, and 3 had significant ($p < 0.0001$) improvement in pain, stiffness, and function with mean WOMAC from 70.46 to 26.55, 70.19 to 40.38 and 64.71 to 32.67, respectively (Table 2).

Table 3. Overall patient satisfaction level

Satisfaction level	Group 1 (n = 46)	Group 2 (n = 70)	Group 3 (n = 67)
Excellent	21	25	30
Good	20	26	28
Fair	2	10	3
Poor	3	9	6

Patients in group 2 and 3 had no improvement in ambulatory status. Patient satisfaction level are mentioned in Table 3.

Surgical treatment

In group 1 (Ahlback grade1-2), 41 patients (44 knees) were considered clinical improvement and did not need any surgical treatments during the follow-up period (Table 4). Five patients (5 knees) needed surgical treatments: three patients had undergone arthroscopic surgery, and two patients had undergone unicompartmental knee arthroplasty (UKA) (Table 5).

Table 4. Patients who delayed or cancelled surgical treatments

Data	Group 1	Group 2	Group 3	Total
Ahlback Classification	grade1-2	grade 3-4	grade 5	
No. of patient (%)	41 (89.1)	47 (67.1)	58 (86.5)	146 (79.8)
No. of knee (%)	44 (89.7)	51 (65.4)	69 (85.1)	164 (78.9)

Table 5. Patients who have undergone surgical treatments

Data	Group 1	Group 2	Group 3	Total
Ahlback Classification	grade1-2	grade 3-4	grade 5	
No.of patient (%)	5 (10.9)	23 (32.9)	9 (13.4)	37 (20.2)
No.of knee (%)	5 (10.2)	27 (34.6)	12 (14.8)	44 (21.1)
Procedure (knee)	3 Arthroscopy 2 UKA	27 TKA (4 bilateral TKA)* (19 unilateral TKA)	12 TKA (3 bilateral TKA)* (6 unilateral TKA)	
Complication after surgery	none	1 (Skin infection)	none	

* Simultaneous bilateral knee within 6-10 weeks

Table 6. Patient satisfaction level (in term of pain improvement) related to ambulatory status

	Group 1		Group 2		Group 3	
	excellent/good	fair/poor	excellent/good	fair/poor	excellent/good	fair/poor
Ambulatory status (n)						
Household	6	0	28	1	39	2
Independent	31	5	11	17	8	10
Aided gait	1	3	8	5	7	1
Total	38	8	47	23	54	13

Table 7. Patient satisfaction level (in term of pain improvement) related to age

	Group 1		Group 2		Group 3	
	excellent/good	fair/poor	excellent/good	fair/poor	excellent/good	fair/poor
Age(n)						
< 70 years	31	4	14	20	8	7
≥ 70 years	10	1	33	3	50	2
Total	41	5	47	23	58	9

In group 2 (Ahlback grade 3-4) 47 patients (51 knees) were considered clinical improvement and did not need any surgical treatment during the follow-up period (Table 4). Twenty-three patients (27 knees) needed surgical treatment; all patients had undergone total knee arthroplasty (TKA) (Table 5).

In group 3 (Ahlback grade 5) 58 patients (69 knees) were considered clinical improvement and did not need any surgical treatment during the follow-up period (Table 4). Nine (12 knees) needed surgical treatments, all patients had undergone TKA (Table 5).

Patient satisfaction level

In group 1 there was a significant relationship between satisfaction level (in pain improvement) and ambulatory status ($p < 0.01$) but there was no significant relationship between satisfaction level and age. Group 2 and 3 show a significant relationship ($p < 0.0001$) between satisfaction levels and age, and satisfaction levels and ambulatory status (Table 6, 7).

Discussion

Modern concepts regarding the etiology of osteoarthritis are based on both biological and biomechanical problems. There is no clear-cut demarcation between biology and biomechanics. Although conservative treatments are still effective, prolonged NSAID's consumption increased risks of gastrointestinal side-effects and selective COX-2 inhibitors consumption also increased risks of cardiovascular effect[4]. These side-effects gradually increased as they related to dosage and duration[4]. Although surgical treatment is a standard treatment for patients who failed by conservative treatment, the results are varied according to the surgical procedures that have been done. The percentage of patients with clinical improvement after various surgical treatments is different as follows: 50-75% for arthroscopic surgery, 70-90% for post high tibial osteotomy (HTO), 75-92% for UKA and 80-90% for TKA[7]. The anterior knee pain after TKA is about 8-12%. The risk of complications varies from 5-10% and early revisions need to be considered. Some studies have revealed outcome of TKA were evaluated at 70%[8-10] among patients. Decision making for surgery depends on the severity evaluated by clinical and radiographic evaluation. Most common indications for surgery are to relieve severe pain in patients who did not respond to conservative treatment and to improve quality of life.

Intra-articular Sodium Hyaluronate is also considered one of the treatments for osteoarthritis because of many supporting evidences. Some studies showed that treatment of intra-articular Sodium Hyaluronate provided benefit of cartilage preservation[11,12]. Another study revealed the efficacy of intra-articular Sodium Hyaluronate, which was not only in controlling pain in a selective group of elderly with household ambulatory status regarding appropriate demand-match, but also significant decreasing selective COX-2 inhibitor consumption by 50-75% in responding patients[13]. Altman et al showed the benefit of intra-articular Sodium Hyaluronate compared with Naproxen treatment for 6 months[14,15]. Pietrogrande et al compared intra-articular Sodium Hyaluronate with intra-articular steroid and found that the injection of Hyaluronic acid showed similar pain relief within one month, but after that, the hyaluronic acid seemed to have more benefit[16]. Many studies demonstrated the benefit of the hyaluronic acid that could last long varied from 6 to 12 months[17,18]. Intra-articular Sodium Hyaluronate is also recommended by ACR, EULAR for osteoarthritis treatment. The benefit of intra-articular Sodium Hyaluronate can be explained by its pharmacologic properties that it provided not only visco-supplement effect but also anti-inflammatory and chondro-protective effect[19]. Although meta-analysis in Cochrane Review demonstrated that efficacy of intra-articular Sodium Hyaluronate was superior to placebo in improving pain, function and global patient assessment, different products provided different efficacy[20]. In knee-osteoarthritis patients with visible joint space (Ahlback grade 1, and 2) who failed conservative treatment, the standard treatment is either arthroscopic debridement or high tibial osteotomy. The curative result of arthroscopic debridement is about 50-80%. There are controversies about the benefit of arthroscopic debridement in osteoarthritis knee[21]. From the above reasons, the hypothesis of this study is, if the cartilage evaluated by radiography still exists, patients will respond to intra-articular Sodium Hyaluronate. From the present study in group 1, 41 patients (44 knees) were considered to have attained clinical improvement on the WOMAC scale (pain, stiffness, function), satisfaction levels were excellent or good, 89.1%. Most failed cases in the present study were misdiagnosis of meniscal pathology, which can be investigated by MRI. All patients who responded to the intra-articular Sodium Hyaluronate treatment did not need any surgical treatments during the follow-up period. This was pre-dictable as were many observations and articles which supported this result[22]. According to the present study, the incidence of arthroscopic surgery decreased significantly resulting from

benefits of Sodium Hyaluronate. Using intra-articular Sodium Hyaluronate will save cost and decrease risk of surgery in Ahlback grade 1, and 2 patients without mechanical symptoms involved. Cost-effectiveness of this treatment should be further investigated. Pharmacologic effects of intra-articular Sodium Hyaluronate are improving cartilage metabolism, improving synoviocyte function for hyaluronic acid production and stabilizing macrophage. These effects are related to molecular weight and concentration of each product. Patients in group 2 (Ahlback grade 3-4) and group 3 (Ahlback grade 5) who failed conservative treatment, the standard treatment are HTO or TKA which depends on the patients' criteria and radiographic evaluations. Even though surgery outcomes are highly successful and there is no age-limitation for undergoing surgery, risks from anesthetic and surgical procedures still exist. Some studies showed benefit from treatment with intra-articular Sodium Hyaluronate in reduction of surgical treatment. Nevertheless, other efficacy outcomes were not mentioned[6]. The results from the present study showed that WOMAC subscale analysis for pain, stiffness, and function were significantly reduced ($p < 0.0001$) in patients group 1 and 2, but did not improve their ambulatory status. Most patients had high satisfaction level and significant reduction in surgical treatments. In group 2, most patients were active and in the expected independent ambulation level, only pain and stiffness improvement might not be enough to improve their quality of life and surgical treatment might be their choice. The role of intra-articular Sodium Hyaluronate in this group is considered for the patients who were not ready for surgical treatment with any reasons to extend schedule for surgery at appropriate times. In group 3 (Ahlback grade 5) it showed significant improvement in pain, stiffness and function but not ambulatory status which was the same result as patients in group 2. However, data revealed high satisfaction level and significant reduction in surgical treatment different from group 2 patients. The characteristic of patients in group 3 were old and inactive with household ambulation, so they did not have high expectation. Controlling pain and decreasing NSAID's or selective COX-2 consumption in order to avoid GI and CV risks were enough to fulfill their expectation. Patients who failed conservative treatment more than 6 months that have the following criteria: first; visible joint space without mechanical problems such as loose bodies, plica, meniscus tear, second; non-visible joint spaces in the elderly (age > 70 years) with household ambulation are suggested to use intra-articular Sodium hyaluronate. On the other hand, in young active patients (aged 60-70 years) with high expectation, intra-articular Sodium Hyaluronate treatment may not achieve patient satisfaction regarding the results. Moreover, future studies in the aspect of cost-effectiveness and medico-economic should be performed.

Conclusion

Intra-articular injection of Sodium Hyaluronate for knee-osteoarthritis patients who failed conservative treatment was safe and effective especially in cartilage sparing patients (Ahlback grade1, and 2) if mechanical symptoms have been excluded. In severe osteoarthritis patients (Ahlback grade 3, 4, and 5), the benefit of intra-articular Sodium Hyaluronate was inferior in young, active patients who expected independent ambulation. Thus, surgical treatment may be a procedure of choice to meet patient expectation in improving function and ambulatory status. On the other hand, in the same group (Ahlback grade 3, 4,and 5) if the patients were old and expected household ambulation, using intra-articular Sodium Hyaluronate was beneficial in improving pain, stiffness and function, but not for ambulatory status. Repeated course of intra-articular Sodium Hyaluronate injection was recommended to preserve cartilage till the appropriate time for surgery. The radiographic evaluation, age, ambulatory status, and patients' expectation may be the key factors to determine successful outcomes.

References

1. Mazieres B, Bannwarth B, Dougados M, Lequesne M. EULAR recommendations for the management of knee osteoarthritis. Report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials. Joint Bone Spine 2001; 68: 231-40.
2. Lo GH, LaValley M, McAlindon T, Felson DT. Intra-articular hyaluronic acid in treatment of knee osteoarthritis: a meta-analysis. JAMA 2003; 290: 3115-21.
3. Wang CT, Lin J, Chang CJ, Lin YT, Hou SM. Therapeutic effects of hyaluronic acid on osteoarthritis of the knee. A meta-analysis of randomized controlled trials. J Bone Joint Surg Am 2004; 86-A: 538-45.
4. Solomon SD, McMurray JJ, Pfeffer MA, Wittes J, Fowler R, Finn P, et al. Cardiovascular risk associated with celecoxib in a clinical trial for colorectal adenoma prevention. N Engl J Med 2005; 352:

1071-80.
5. Scali JJ. Intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee: a long term study. Eur J Rheumatol. Inflamm 1995; 15: 57-62.
6. Barrett JP, Siviero P. Retrospective study of outcomes in Hyalgan® treated patients with osteoarthritis of the knee. Clin Drug Invest 2002; 22: 87-97.
7. Garvin KL, Tria AJ, Pellicci PM. Long term results of total knee replacement. In: Pellicci PM, Tria AJ, Garvin KL, editors. Orthopaedic knowledge update: hip and knee reconstruction 2. Rosemont, IL: AAOS; 2000: 301-17.
8. Berger RA, Lyon JH, Jacobs JJ, Barden RM, Berkson EM, Sheinkop MB, et al. Problems with cementless total knee arthroplasty at 11 years followup. Clin Orthop Relat Res 2001; 392: 196-207.
9. Rand JA, Trousdale RT, Ilstrup DM, Harmsen WS. Factors affecting the durability of primary total knee prostheses. J Bone Joint Surg Am 2003; 85-A: 259-65.
10. Froimson MI. Knee reconstruction and replacement. In: Vaccaro AR, editor. Orthopaedic knowledge update 8. Rosemont, IL: AAOS; 2005: 457-67.
11. Listrat V, Ayral X, Patarnello F, Bonvarlet JP, Simonnet J, Amor B, et al. Arthroscopic evaluation of potential structure modifying activity of hyaluronan (Hyalgan) in osteoarthritis of the knee. Osteoarthritis Cartilage 1997; 5: 153-60.
12. Frizziero L, Govoni E, Bacchini P. Intra-articular hyaluronic acid in the treatment of osteoarthritis of the knee: clinical and morphological study. Clin Exp Rheumatol 1998; 16: 441-9.
13. Turajane T. Therapeutic effects of intra-articular hyaluronic acid on failed conservative treatment of knee osteoarthritis with minimum 2 years follow-up. Thai J Orthop Surg 2003; 3: 215-22.
14. Altman R, Brandt K, Hochberg M, Moskowitz R, Bellamy N, Bloch DA, et al. Design and conduct of clinical trials in patients with osteoarthritis: recommendations from a task force of the Osteoarthritis Research Society. Results from a workshop. Osteoarthritis Cartilage 1996; 4: 217-43.
15. Altman RD, Moskowitz R. Intraarticular sodium hyaluronate (Hyalgan) in the treatment of patients with osteoarthritis of the knee: a randomized clinical trial. Hyalgan Study Group. J Rheumatol 1998; 25: 2203-12.
16. Pietrogrande V, Melanotte PL, Agnolo D. Hyaluronic acid versus methylprednisolone intra-articularly injected for treatment of osteoarthritis of the knee. Curr Ther Res 1991; 50: 691-701.
17. Bunyaratavej N, Chan KM, Subramanian N. Treatment of painful osteoarthritis of the knee with hyaluronic acid. Results of a multicenter Asian study. J Med Assoc Thai 2001; 84(Suppl 2): S576-81.
18. Maheu E, Ayral X, Dougados M. A hyaluronan preparation (500-730 kDa) in the treatment of osteoarthritis: a review of clinical trials with Hyalgan. Int J Clin Pract 2002; 56: 804-13.
19. Jubb RW, Piva S, Beinat L, Dacre J, Gishen P. A one-year, randomised, placebo (saline) controlled clinical trial of 500-730 kDa sodium hyaluronate (Hyalgan) on the radiological change in osteoarthritis of the knee. Int J Clin Pract 2003; 57: 467-74.
20. Bellamy N, Campbell J, Robinson V, Gee T, Bourne R, Wells G. Viscosupplementation for the treatment of osteoarthritis of the knee. Cochrane Database Syst Rev 2006; CD005321.
21. Moseley JB, O'Malley K, Petersen NJ, Menke TJ, Brody BA, Kuykendall DH, et al. A controlled trial of arthroscopic surgery for osteoarthritis of the knee. N Engl J Med 2002; 347: 81-8.
22. Wai EK, Kreder HJ, Williams JI. Arthroscopic debridement of the knee for osteoarthritis in patients fifty years of age or older: utilization and outcomes in the Province of Ontario. J Bone Joint Surg Am 2002; 84-A: 17-22.

ผลการรักษาของ โซเดียม ไฮยาลูโรเนต (500-730 กิโลดาลตัน, ยัลแกน) ฉีดเข้าข้อในผู้ป่วยข้อเข่าเสื่อม

ธนา ธุระเจน, อารี ตนาวลี, วิโรจน์ ลาภไพบูลย์พงศ์, สามารถ ม่วงศิริ

ภูมิหลัง: *การรักษาผู้ป่วยข้อเข่าเสื่อมโดยการใช้ โซเดียม ไฮยาลูโรเนต ฉีดเข้าข้อ เป็นหนึ่งในขั้นตอนการรักษาที่ the American College of Rheumatology (ACR) และ the European League Against Rheumatism (EULAR) แนะนำให้ใช้ในผู้ที่ผ่านการรักษาด้วยวิธีการรักษาแบบดั้งเดิม (Conservative treatment) ก่อนที่จะได้รับการรักษาโดยวิธีการผ่าตัด อย่างไรก็ตาม ยังไม่มีบทสรุปที่แน่ชัดของผลการรักษาและวิธีการคัดเลือกผู้ป่วย นอกจากนี้ การศึกษาผลของการใช้ยาดังกล่าวในผู้ป่วยที่รักษาด้วยวิธีการรักษาแบบดั้งเดิมไม่ได้ผลยังมีไม่มากนัก*

วัตถุประสงค์: *เพื่อศึกษาผลทางคลินิกของการใช้ โซเดียม ไฮยาลูโรเนต ฉีดเข้าข้อสัปดาห์ละ 1 เข็ม ติดต่อกัน 3 สัปดาห์ ในผู้ป่วยข่อเข่าเสื่อมที่รักษาด้วยวิธีการรักษาแบบดั้งเดิมไม่ได้ผล*

วัสดุและวิธีการ: *การศึกษานี้เป็นการติดตามผลการรักษาแบบต่อเนื่องเป็นระยะเวลาอย่างน้อย 24 เดือน ผลการรักษาได้จากการสอบถามผู้ป่วยโดยใช้แบบสอบถามประเมินอาการและการโทรศัพท์สอบถามอาการ โดยตัวชี้วัดปฐมภูมิได้แก่ โวแมคสกอร์ (the Western Ontario and McMaster Universities Osteoarthritis Index; WOMAC score) และตัวชี้วัดทุติยภูมิ ได้แก่ การชะลอหรือยกเลิกการรักษาด้วยวิธีการผ่าตัด*

ผลการศึกษา: *มีผู้ป่วยข้อเข่าเสื่อมที่รักษาด้วยวิธีการรักษาแบบดั้งเดิมไม่ได้ผลเข้าร่วมโครงการทั้งสิ้น จำนวน 183 ราย (208 เข่า) โดยแบ่งผู้ป่วยเป็น 3 กลุ่มตามความรุนแรงของภาวะข้อเข่าเสื่อมโดยพิจารณาจากภาพถ่ายทางรังสี ผลการรักษามีดังนี้ กลุ่มที่หนึ่ง: ภาพรังสีมีการแคบของช่องข้อเข่า (Ahlback grade 1-2) มีการเปลี่ยนแปลงของโวแม็คสกอร์ดีขึ้นอย่างมีนัยสำคัญ ($p < 0.0001$) จาก 70.46 เป็น 26.55 และผู้ป่วย 41 ใน 46 ราย (44 ใน 49 เข่า) ไม่ต้องการการผ่าตัด กลุ่มที่สอง: ภาพรังสีมีกระดูกติดกันของข้อเข่า (Ahlback grade 3-4) มีการเปลี่ยนแปลงของโวแม็คสกอร์ดีขึ้นอย่างมีนัยสำคัญ ($p < 0.0001$) จาก 70.19 เป็น 40.38 ผู้ป่วย 47 ใน 70 ราย (51 ใน 78 เข่า) ไม่ต้องการการผ่าตัด กลุ่มที่สาม: ภาพรังสีมีการเคลื่อนของกระดูกทางด้านนอกของข้อเข่า (Ahlback grade 5) มีการเปลี่ยนแปลงของ โวแม็คสกอร์ดีขึ้นเช่นกัน ($p < 0.0001$) จาก 64.71 เป็น 32.67 และผู้ป่วย 58 ใน 67 ราย (69 ใน 81 เข่า) ไม่ต้องการการผ่าตัด โดยผู้ป่วยทุกกลุ่มมีอาการปวดลดลง อาการติดขัดของข้อลดลง และสามารถดำเนินกิจวัตรประจำวันได้ดีขึ้นอย่างมีนัยสำคัญ ($p < 0.0001$) แต่อย่างไรก็ตามความสามารถในการเคลื่อนไหวของผู้ป่วยยังคงไม่แตกต่างไปจากเดิม*

สรุป: *การใช้ โซเดียม ไฮยาลูโรเนต ฉีดเข้าข้อ สำหรับผู้ป่วยข้อเข่าเสื่อมที่รักษาด้วยวิธีการรักษาแบบดั้งเดิมไม่ได้ผล ให้ประสิทธิภาพดีในกลุ่มผู้ป่วยที่มีภาพถ่ายรังสีที่สามารถมองเห็นกระดูกอ่อนผิวข้อ (Alhback grade 1-2) และไม่มีอาการผิดปกติของข้อจากสาเหตุเชิงกลร่วมด้วย ในกลุ่มที่มีข้อเสื่อมมาก (Alhback grade 3, 4, 5) ถ้าผู้ป่วยอายุน้อยและมีความคาดหวังต่อผลการรักษาสูง เช่น ต้องการหายเป็นปกติและสามารถเดินได้ด้วยตนเอง การรักษาด้วยการผ่าตัดอาจเป็นวิธีที่เหมาะสมมากกว่าการใช้ยา แต่ในผู้ป่วยอายุมากที่ไม่มีกิจวัตรมากนัก การใช้ยาดังกล่าวสามารถสร้างความพึงพอใจให้แก่ผู้ป่วย โดยยามีผลลดอาการปวด อาการติดขัดของข้อ ซึ่ง 85.56 เปอร์เซ็นต์ของผู้ป่วยดังกล่าว มีความพึงพอใจในระดับดีและดีมาก ดังนั้น ภาพรังสีวินิจฉัย อายุ ความสามารถในการเคลื่อนไหว และความคาดหวังของผู้ป่วย อาจจะเป็นปัจจัยสำคัญต่อผลสำเร็จของการรักษา*