

# Comparison between Hyalgan and Indomethacin in the treatment of osteoarthritis

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## Abstract

**Aim & purposes:** Osteoarthritis (OA) is a disease with significant morbidity in patients. Knee joint is commonly involved in the OA. There is several treatment modalities, such as medical and surgical treatment. Many of patients interested to medical treatment and avoid surgical procedure. One of this treatment, treatment via indomethacin and hyaluronic preparation. This study was carried out in order to evaluate effect of hyalgan and indomethacin in the treatment of OA. **Patients and methods:** Patients with advanced grade of OA were included in this study. For this purpose, every patients with severe knee pain, limited range of motion, cryptation, joint stiffness, and difficulty in daily activity, were selected. Upright knee x-ray (AP, Lat) were obtained and radiologic changes were recorded. Before treatment, all cases were asked about pain, joint stiffness, knee cryptation, and other and were recorded. All patients received recommendation about activity modification and physiotherapy for quadriceps muscle. Then this patients were divided in two Hyalgan and Indomethacin groups. This study was conducted in the orthopedy clinic of Imam Khomeini Hospital, Ahwaz, Iran. Patients in Hyalgan groups, were received intra-articular injection 20mg weekly for 5 weeks. Patients in indomethacin group, were treated with dosage 25mg three times daily. All patients were evaluated post treatment. **Results:** in this study 39 patients (60 joints, 32 right and 28 left) underwent hyalgan and 27 patients (50 joints, 25 right and 25 left) treated by indomethacin. From Hyalgan group 54 knee joint had grade IV and 6 have grade III radiology of OA. In the indomethacin group, 43 knee joints had grade IV and 7 joints had grade III. There is significant difference between two group for post treatment score (HA: 38.45±57.77 vs Indomethacin: 32.16±67.29,  $P=0.00007$ ). In the patients treated with HA, 56.67%, and 28.33% had excellent and good prognosis respectively. In indomethacin group 24.00%, and 34.00% had excellent and good prognosis respectively. Patients treated with HA had better outcome than patients treated with indomethacin ( $P\text{-value}=0.001475$ ). In HA group, satisfaction about treatment was significantly higher than indomethacin group ( $P\text{-value}=0.003045$ ). Pain in resting, morning stiffness, limitation in range of motion, and crypation was significantly lower in patients treated with HA compared to another ( $P<0.05$ ). Pain at activity was significantly lower in indomethacin group ( $p<.05$ ) **Conclusion:** this study showed significant effect of HA compared to indomethacin in reducing morning stiffness, pain during resting, limitation in ROM. This study support early administration of HA for treatment of OA.

## INTRODUCTION AND AIM

Osteoarthritis (OA) is a disease with significant morbidity in the patients due its clinical manifestation and limited range of motion.<sup>1</sup> Knee joint is one of the joint which is commonly involved. In the Framingham study, OA prevalence was reported 6% in the adults aged >30yrs. About half of the people aged >65 had evidence of OA.<sup>2</sup> In addition to age, sex can also incidence and prevalence of OA. In the aged<50, OA predominately seen in male. After that, incidence and prevalence of OA was higher in female.<sup>3</sup> Many patients are interested to non surgical treatment. There are several non surgical treatment modalities for treatment of OA. These treatments include lifestyle modification, NSAIDs, intraarticular injection of corticosteroid, and intra-

articular hyalgan.<sup>4</sup> Hyalgan has less adverse effect than intra-articular injection of corticosteroid.<sup>5</sup> Hyalgan is a poly saccharide chain which seen in connective tissue in high quantity and prevents chondral damage.<sup>6</sup> In OA, concentration and molecular weight of hyaluronate was reduced as 33-50%.<sup>7</sup> The aim of this study was to compare of indomethacin and hyaluronic acid preparation for treatment of OA.

## PATIENTS AND METHODS

Patients with advanced grade of OA were included in this study. For this purpose, every patients with severe knee pain, limited range of motion, cryptation, joint stiffness, and difficulty in daily activity, were selected. Upright knee x-ray

(AP, Lat) were obtained and radiologic changes were recorded. Before treatment, all cases were asked about pain, joint stiffness, knee cryptation, and other and were recorded. All patients received recommendation about activity modification and physiotherapy for quadriceps muscle. Then this patients were divided in two Hyalgan and Indomethacin groups. In the Hyalgan group, 6 joint has grade III OA and 54 had grade IV OA. In the indomethacin group, 7 joints had grade III, and 43 joints had grade IV. This study was conducted in the orthopedy clinic of Imam Khomeini Hospital, Ahwaz, Iran. Patients in Hyalgan groups, were received intra-articular injection with dosage 20mg weekly for 5 weeks. Patients in indomethacin group, were treated with dosage 25mg three times daily. All patients were evaluated post treatment. Thirty- nine patients were treated with Hyalgan. These patients had 60 joints involved with osteoarthritis. Twenty-seven cases were treated with indomethacin, and these cases had 50 knee joints involved with osteoarthritis. We evaluated effect of HA and indomethacin by using this proposed criteria. The criteria were as follows:

**Figure 1**

<b>1- Sensation of sound or audible sounds in the knee joint( Cryptation)</b>		
Never		5
Rarely	Mild	4
Sometimes		3
Often	Moderate	2
Always	Severe	1
<b>2- Sensation of stiffness in the knee joint ( after morning waking)</b>		
Never		5
Mild		4
Moderate		3
Severe		2
Extremely severe		1
<b>3- Joint pain during resting</b>		
Never		5
Mild		4
Moderate		3
Severe		2
Extremely severe		1
<b>4- Joint pain during activity</b>		
Never		5
Mild		4
Moderate		3
Severe		2
Extremely severe		1
<b>5- Acceptable distance walking</b>		
100 meters		1
200 meters		2
300 meters		3
400 meters		4
500 meters		5
<b>6- Rate of ability for physical activity</b>		
Daily activity without problem		5
Indoor activity without problem		4
Personal activity without problem		3
Personal activity with problem		2
Unable to personal activity without help		1
<b>7- Walking</b>		
Without help		2
With device		0
<b>8- Knee joint range of motion</b>		
>120 (NO)		5
90-120 (Mild limitation)		4
75-89 (Moderate limitation)		3
50-74 (Severe limitation)		2
<50 (Extremely severe limitation)		1
<b>9-rate of flexion deformity of knee joint</b>		
25		1
20		2
15		3
10		4
<10		5
<b>10- Ability of physical activity</b>		
Down and upward of stir without problem		2
Down and upward of stir with problem		0
<b>11-toilet usage (Iranian)</b>		
Yes		2
Unable		0
<b>12-occupational activity</b>		
Without problem		2
With problem		0
<b>13- Praying (Islamic)</b>		
Standing		2
Sitting		0
Maximum of score is 50 and minimum is 8. According to score we classify the results as follows:		
Response to therapy	Score	
Excellent	40-50	
Good	30-40	
Fair	20-30	
Poor	<20	

If patient has score 30-50, there is satisfactory from treatment. If patients score was less than 30, there is unsatisfactory treatment. We compared two groups of patients for cryptation, limitation in range of motion, pain at activity, resting pain, satisfaction during treatment, total outcome, total score, and morning stiffness after treatment. Spss and Epiinfo ver 6.0 were used for analysis. We define

the criteria for evaluation these patients.

## RESULTS

In this study 39 patients (60 joints, 32 right and 28 left) underwent hyalgan and 27 patients (50 joints, 25 right and 25 left) treated by indomethacin. From Hyalgan group 54 knee joint had grade IV and 6 have grade III radiology of OA. In the indomethacin group, 43 knee joints had grade IV and 7 joints had grade III. There is significant difference between two group for post treatment score (HA: 38.45±57.77 vs Indomethacin:32.16±67.29,  $P=0.00007$ ). Total outcome between two groups were shown in Table-I.

**Figure 2**

Table- I: Comparison between outcome among two groups of patients ( $P$ -value:0.001475)

Outcome	Hyalgan	Indomethacin
Excellent	34(56.67%)	12(24.00%)
Good	17(28.33%)	17(34.00%)
Fair	8(13.33%)	15(30.00%)
Poor	1(1.67%)	6(12.00%)

Results of satisfaction of treatment, were shown in table-II

**Figure 3**

Table- II: Post treatment satisfaction among patients underwent treatment with HA and indomethacin ( $P$ -value :0.003045)

Satisfaction		Hyalgan	Indomethacin
Satisfy	Right	29	15
	Left	22	15
	Total	51	30
Unsatisfy	Right	3	10
	Left	6	10
	Total	9	20

Comparison between effect of HA and Indomethacin on the Pain at rest, pain at activity, and morning stiffness was shown in table-III

**Figure 4**

Table-III: Pain at rest, pain at activity, and morning stiffness in patients underwent treatment with indomethacin and HA.

Severity	Pain at rest		Pain at activity		Morning stiffness	
	Ind	HA	Ind	HA	Ind	HA
No	1(2.00%)	32(53.33%)	15(30.00%)	13(21.66%)	2(4.00%)	28(46.66%)
Mild	16(32.00%)	14(23.33%)	24(48.96%)	23(38.34%)	18(36.00%)	18(30.00%)
Moderate	12(24.00%)	10(16.67%)	11(22.00%)	15(25.00%)	23(46.00%)	9(15.00%)
Severe	21(42.00%)	4(6.66%)	0(0%)	9(15.00%)	7(14.00%)	5(8.33%)
	$P$ -value=0.0, $\chi^2=40.42$		$P$ -value=0.03, $\chi^2=8.94$		$P$ -value=0.00003, $\chi^2=28.32$	

Pain at rest and Morning stiffness was significantly lower in

HA group ( $P<0.05$ ) and Pain at activity was significantly lower in Indomethacin group ( $P<0.05$ ). Limitation in ROM and Cryptation has significantly lower in patients treated with HA (Table-IV)

Table-IV: Comparison between indomethacin and HA on the cryptation and limitation in ROM. ( $P$ -value  $<0.05$ )

## DISCUSSION

In the current study, good effect of Hyalgan in the management of osteoarthritis was shown. Pain at rest, morning stiffness was significantly lower in HA group. Satisfaction from treatment was significantly higher in the patients treated with HA. Pain at activity was significantly better in the patients treated with indomethacin. Cohen MM et al showed that sodium hyaluronate may be a safe and effective option for pain associated with ankle OA<sub>8</sub>. Turajane T et al showed beneficial effect of intra-articular sodium hyaluronate in the management of OA<sub>9</sub>. Turajane also concluded IA-HA should be considered as a medical intervention before surgical procedures in knee OA patients who failed conservative treatments. Even though the cost of IA-HA treatment would increase the total costs of treatment and some patients might fail, it was only 6.44% of the total costs. On the other hand, if patients responded to IA-HA treatment, then the surgical procedures were not required. This treatment could save the cost from cancellation or delayed surgical procedures at 63.26%<sub>10</sub>. In the study conducted by Lundsgaard et al, intra-articular hyaluronate did not significantly reduce pain compared with physiological saline placebo in patients with OA of the knee<sub>11</sub>. In the study done in Poland, marked improvement was observed in patients with low or medium degree of degenerative changes<sub>12</sub>. There are also several reports supporting efficacy of repeated intraarticular injection of Hyalgan for treatment of OA<sub>13,14,15</sub>. In the study done in animal model, hyalgan therapy was beneficial<sub>16,17</sub>. Bagga et al. showed that 6 months after 3 consecutive period of HA injection, HA concentration was high and suggested that HA injection may stimulate production of endogenous HA and modifying disease progression<sub>18</sub>. Growing evidence supports the notion that, in addition to relieving the symptoms of OA, HA also modify the structure of the diseased joint and the rate of disease progression, at least early in the evolution of disease process<sub>19</sub>. Hyalgan seems to be safe and good efficacy in the treatment of OA even in the earlier phase of disease. Earlier use of Hyalgan was recommended according to published works.

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