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Comparative effects of intra-articular hyaluronic acid and corticosteroids combined with physiotherapy on knee osteoarthritis: A quantitative study at Mitiga Military Hospital

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Abstract: Knee osteoarthritis is a prevalent degenerative joint disorder that significantly impairs mobility and quality of life. Intra-articular injections, such as those containing corticosteroids and hyaluronic acid, are commonly used for symptom relief, often in conjunction with physical therapy. However, comparative data on their combined efficacy in clinical practice remain limited. This study aimed to evaluate and compare the clinical effectiveness of intra-articular corticosteroids and hyaluronic acid, each combined with physiotherapy, in reducing pain and improving range of motion in patients with knee osteoarthritis. A total of 60 Libyan patients with knee osteoarthritis treated at Mitiga Military Hospital were randomly assigned to three groups (n=20 each): Group A: received corticosteroid injections plus physiotherapy, Group B: received hyaluronic acid injections plus physiotherapy, and Group C: received physiotherapy alone. Pain intensity was assessed using the visual analog scale, and joint function was measured using active and passive range of motion assessments. Evaluations were conducted at baseline and four weeks post-treatment. Data were analyzed using a paired *t*-test and ANOVA. All groups demonstrated significant reductions in visual analog scale scores and improvements in range of motion post-treatment ($p<0.001$). Group A exhibited the greatest pain reduction (6.15±1.42 to 2.00±1.17), while Group B showed superior improvement in range of motion (passive: 101.20°±11.45° to 122.45°±8.69°). Group C demonstrated moderate but statistically significant improvement in both parameters. Corticosteroid and hyaluronic acid injections, when combined with physiotherapy, significantly improve pain and joint function in knee osteoarthritis patients. Corticosteroids may offer faster pain relief, while hyaluronic acid appears more effective in enhancing joint mobility. These findings support the use of tailored treatment approaches based on individual patient needs and therapeutic goals.

Introduction

Knee osteoarthritis (OA) is one of the most prevalent chronic joint disorders worldwide, significantly affecting mobility and quality of life, particularly among middle-aged and elderly populations. It is characterized by cartilage degradation, synovial inflammation, and joint dysfunction, posing a considerable burden on individuals and healthcare systems [1-3]. As the disease progresses, effective management strategies are essential to alleviate symptoms and improve functional outcomes. Intra-articular (IA) injections, such as corticosteroids (CS),

hyaluronic acid (HA), and platelet-rich plasma (PRP), have gained traction for their ability to alleviate pain and inflammation associated with knee OA. CS injections are effective for short-term pain relief, while HA and PRP have demonstrated potential for long-term benefits, including enhanced joint lubrication and cartilage regeneration [4-6]. A systematic review by Bannuru and others [7] emphasized that IA injections provide pain relief comparable to oral medications but with fewer systemic side effects.

Physiotherapy remains a cornerstone in the conservative management of knee OA, focusing on joint mobility, muscle strengthening, and functional rehabilitation. Previous studies have shown that structured exercise therapy significantly affects the efficacy of physiotherapy, which is influenced by the severity of joint degeneration and patient adherence [1]. Other studies have explored the combined use of IA injections and physiotherapy, proposing that IA injections alleviate pain and inflammation, thereby enhancing participation in and outcomes of physiotherapy [8]. Research has shown that IA HA combined with exercise yielded superior results in all outcomes compared to exercise with saline over eight weeks [9] and exercise alone over 12 months [10]. Additionally, one study reported that IA HA combined with exercise was more effective than HA alone in reducing self-reported pain [11]. However, other studies found no additional benefit of IA CS injections before initiating exercise interventions. Despite these findings, there is a lack of clinical guidance regarding a multimodal approach to knee OA management, particularly the concurrent use of IA injections and physiotherapy. This represents a significant gap, as both treatments are feasible and complementary. For instance, physicians could administer an IA CO injection to alleviate immediate pain and inflammation, followed by supervised exercise therapy to maximize functional recovery. However, many healthcare professionals remain uncertain about the unique benefits of combining these interventions [12]. This uncertainty is especially relevant in contexts where IA injections may not be as readily accessible as physiotherapy. By comparing combined therapy to physiotherapy alone, this study seeks to provide a comprehensive understanding of their synergistic effects. Also, it addresses a critical evidence gap, particularly in Libya, where data on the combined use of IA injections and physiotherapy in knee OA management is limited. Through this investigation, we aim to contribute valuable insights into optimizing treatment strategies for knee OA, ultimately improving patient outcomes and quality of life.

Materials and methods

This study employed a comparative quantitative research design, conducted between January and May 2023 at Mitiga Military Hospital, Tripoli, Libya, to evaluate the effects of IA HA and CS on knee OA outcomes when combined with physiotherapy. Before commencement, approval for conducting the research was obtained from the Department of Physiotherapy at the Faculty of Medical Technology, University of Tripoli, as well as approval from the Mitiga Hospital administration. The study was carried out entirely within the hospital on patients regularly attending the physiotherapy department for the treatment of knee OA, following the hospital's standard therapeutic protocol, with no additional interventions from the research team. All data were collected and analyzed in a manner that fully respected participants' privacy and confidentiality. Participation was entirely voluntary, with all patients informed about the nature and objectives of the study, and their consent obtained after explaining all relevant details.

A total of 40 participants were divided into three groups based on the treatment they were receiving: Group A (HA, n=15) included patients receiving IA HA injections (120 mg) combined with physiotherapy; Group B (CS, n=15) consisted of patients receiving intra-articular corticosteroid injections (40 mg/mL) with physiotherapy; and Group C (control, n=10) involved patients undergoing physiotherapy alone. The physiotherapy plan was consistent across all groups and included 18 sessions over 45 days, comprising ultrasound therapy (1.0 MHz, 1.5/cm^2, 10 min, 100% duty cycle), transcutaneous electrical nerve stimulation (TENS) for 10 min, and isometric

quadriceps strengthening exercises. Data collection involved a questionnaire capturing demographic information (gender, age, body mass index) and knee OA severity assessed through X-ray imaging graded by the Kellgren-Lawrence scale. Outcome measures included range of motion (ROM), assessed using a goniometer, and pain severity, evaluated using the visual analogue scale (VAS). The study included male and female participants aged 45-75 years diagnosed with grade II-III knee OA. Exclusion criteria comprised a history of prior IA treatment, use of nonsteroidal anti-inflammatory drugs (NSAIDs), and pregnancy. Additionally, individuals with knee pain due to causes other than OA, recent fractures, limb surgeries, vitamin or calcium deficiencies, or any metabolic or neoplastic disorders associated with bone pain were excluded from the study.

Statistical analysis: The analysis was performed using SPSS Version 27. Descriptive statistics were calculated, and group differences were assessed using a *t*-test and one-way ANOVA. Post-intervention comparisons of VAS and ROM among the three groups were conducted using the Least Significant Difference (LSD) test. A p-value less than 0.05 is considered significant.

Results

The demographic characteristics of the study participants are summarized in **Table 1**. The sample consisted of 40 individuals, with 26 females (65.0%) and 14 males (35.0%). Participants were categorized into three age groups: five individuals (12.5%) were aged 45-54 years, 19 individuals (47.5%) were aged 55-64 years, and 16 individuals (40.0%) were aged 65-75 years. In terms of body mass index (BMI), 11 participants (27.5%) had a BMI between 18 and 25, while 29 participants (72.5%) had a BMI between 25 and 30. Regarding the severity of knee OA, as classified by the Kellgren-Lawrence grading system, 28 participants (70.0%) were diagnosed with grade II OA, while 12 participants (30.0%) had grade III OA.

Table 1: Demographic characteristics of the study participants

Demographic information		Frequency	Percentage
Gender	Female	26	65.0%
	Male	14	35.0%
Age	45-54	05	12.5%
	55-64	19	47.5%
	65-75	16	40.0%
BMI	25-18	11	27.5%
	30-25	29	72.5%
	30		
Kellen Lawrence grade	II	28	70.0%
	III	12	30.0%

Sample equivalence: After dividing the participants into three groups, an equivalence test was conducted to ensure no significant differences in baseline characteristics, including age, BMI, Kellgren-Lawrence Grade, and pre-test measurements of ROM and VAS. One-way ANOVA was performed to assess group comparability. The results presented in **Table 2** indicate no significant differences among the three groups in terms of age ($F=0.622$, $p=0.542$), BMI ($F=2.151$, $p=0.131$), and Kellgren-Lawrence grade ($F=1.595$, $p=0.217$). Similarly, for pre-test measurements of VAS and ROM, no significant differences were observed among the HA, CS, and control groups. The analysis revealed that baseline VAS ($F=3.147$, $p=0.065$) and ROM ($F=1.711$, $p=0.195$) values were comparable across groups, with $p>0.05$. These findings confirm that the groups were statistically equivalent in terms of pain perception and joint mobility before treatment, reinforcing the validity of the study design.

Table 2: Analysis of age, body mass index\Kellen Lawrence grade, and pre-measurements of ROM & VAS

Variables	Groups	Sum of squares	df	Mean square	F	P
Age	Between	0.533	02	0.267	0.622	0.542
	Within	15.867	37	0.429		
	Total	16.400	39			
BMI	Between	0.667	02	0.333	2.151	0.131
	Within	5.733	37	0.155		
	Total	6.400	39			
Kellgren Lawernce grade	Between	0.667	02	0.333	1.595	0.217
	Within	7.733	37	0.209		
	Total	8.400	39			
VAS	Between	15.467	02	7.733	3.147	0.065
	Within	90.933	37	2.458		
	Total	106.400	39			
ROM	Between	350.608	02	175.304	1.711	0.195
	Within	3790.367	37	102.442		
	Total	4140.975	39			

To evaluate the impact of HA injections on pain reduction and joint mobility, a paired-sample *t*-test was conducted to compare pre-test and post-test measurements of VAS scores and ROM within the HA group. The results, presented in **Table 4**, indicate a significant improvement in both parameters following treatment. The mean pre-test VAS score was 5.73±2.017, which decreased to 1.80±1.320 post-test, while the mean ROM improved from 107.33°±11.629° to 119.33°±10.328°. The paired *t*-test results revealed statistically significant differences in VAS (t=14.750, p<0.001) and ROM (t = -12.616, p<0.001), favoring the post-test measurements. These findings confirm the efficacy of HA injections in alleviating pain and enhancing joint mobility in patients with knee OA.

Table 4: Analysis of the pre-test and post-test measurements of ROM & VAS in the HA group

Hyaluronic acid dose			Paired differences				t	df	P
			Mean	SD	95% CI				
					Lower	Upper			
VAS	Pre-measurement	Post-measurement	3.93	1.033	3.36	4.51	14.750	14	0.000
	5.73	1.80							
RoM	Pre-measurement	Post-measurement	12.00	3.684	-14.04	-9.96	-12.616	14	0.000
	107.33	119.33							

Corticosteroid group: To evaluate the effectiveness of CS injections in improving pain and joint mobility, a paired-sample t-test was conducted on pre-test and post-test measurements of VAS scores and ROM within the CS dose group. The results, presented in **Table 5**, indicate a significant reduction in pain and an improvement in joint mobility. The mean pre-test VAS score was 5.20±1.37, which decreased to 2.00±1.31 post-test, while the mean ROM improved from 111.73°±7.94° to 121.33°±5.50°. The paired *t*-test results showed a statistically significant difference in VAS (t=18.330, p<0.001) and ROM (t=-6.994, p<0.001), favoring the post-test measurements. These findings support the effectiveness of CS injections in reducing pain and enhancing joint function in patients with knee OA.

Table 5: Analysis between the pre-test and post-test measurements (RoM &VAS) for the cortisone group

Corticosteroid dose			Paired difference				t	df	P
			Mean	SD	95% CI				
					Lower	Upper			
VAS	Pre-measurement	Post-measurement	3.20	0.676	2.83	3.57	18.330	14	0.000
	5.20	2.00							
ROM	Pre-measurement	Post-measurement	-9.60	5.316	-12.54	-6.66	-6.994	14	0.000
	111.73	121.33							

Control group: To assess the effectiveness of physiotherapy alone in improving pain and joint mobility, a paired-sample *t*-test was conducted on pre-test and post-test measurements of VAS scores and ROM within the control group. The results, presented in **Table 6**, indicate a reduction in pain and an improvement in joint mobility. The mean pre-test VAS score was 6.80±0.919, which decreased to 4.60±1.647 post-test, while the mean ROM improved from 104.30°±10.615° to 111.50°±9.443°. The paired t-test results showed a statistically significant difference in VAS ($t=7.571$, $p<0.001$) and ROM ($t=-5.014$, $p=0.001$), favoring the post-test measurements. These findings suggest that physiotherapy alone contributed to pain reduction and increased joint mobility, though to a lesser extent compared to intra-articular injection groups.

Table 6: Descriptive analysis between the pre-test and post-test measurements (RoM & VAS) for the control group

Control group			Paired differences				t	df	p
			Mean	SD	95% CI				
					Lower	Upper			
VAS	Pre-measurement	Post-measurement	2.20	0.919	1.54263	2.85737	7.571	9	0.000
	6.80	4.60							
RoM	Pre-measurement	Post-measurement	-7.20	4.541	-10.44856	-3.95144	-5.014	9	0.001
	104.30	111.50							

Table 7 presents the post-test comparisons of VAS and ROM among the three study groups using the LSD test. For post-test VAS measurements, the HA group demonstrated the most significant improvement compared to the control group, with a mean difference of -2.80 ($p<0.05$), favoring the HA group. Similarly, the CS group showed a statistically significant improvement over the control group, with a mean difference of -2.60 ($p<0.05$), in favor of the CS group. However, the difference between the HA group and the CS group was minimal (-0.20) and not statistically significant ($p=0.698$), despite a slight preference for the HA group. Regarding post-test ROM measurements, the CS group exhibited the highest improvement compared to the control group, with a mean difference of 9.83 ($p=0.008$), favoring the CS group. The HA group also showed significant improvement over the control group, with a mean difference of 7.83 ($p=0.031$), in favor of the HA group. However, the difference between the HA group and the CS group was -2.00 ($p=0.527$), which was not statistically significant, although the results slightly favored the CS group.

Table 7: LSD for the post-measurements of VAS & ROM among the three groups

Multiple Comparisons						
LSD						
Dependent variable	(I) Groups	(J) Groups	Mean Difference (I-J)	P	95% CI	
					Lower Bound	Upper Bound
Post-VAS	Hyaluronic acid dose	Corticosteroid dose	-0.20	0.698	-1.2378	0.8378
		Control group	-2.80	0.000	-3.9603	-1.6397
	Corticosteroid dose	Control group	-2.60	0.000	-3.7603	-1.4397
Post-RoM	Hyaluronic acid dose	Corticosteroid dose	-2.00	0.527	-8.3426	4.3426
		Control group	7.83	0.031	0.7421	14.9246
	Corticosteroid dose	Control group	9.83	0.008	2.7421	16.9246

Discussion

This study aimed to evaluate the efficacy of IA injections of HA and CS in conjunction with a physiotherapy protocol for Libyan patients with knee OA at Mitiga Military Hospital. A total of 40 participants were assigned to three groups: the HA group (n=15), the CS group (n=15), and a control group (n=10). Statistical analyses were conducted to assess improvements in pain relief and ROM across the groups. The demographic analysis revealed no statistically significant differences among the study groups, as confirmed by ANOVA. This homogeneity ensures that the observed treatment effects are attributable to the interventions rather than baseline differences. The findings of this study demonstrated significant improvements in pain and ROM across all groups, with the IA HA and CS injection groups showing superior outcomes compared to the physiotherapy-only group. These results align with international guidelines, which emphasize a multimodal approach to knee OA management that combines pharmacological and non-pharmacological strategies [4]. For instance, the European Alliance of Associations for Rheumatology (EULAR) recommends a comprehensive treatment plan that includes patient education, individualized exercise programs, and weight management, along with supportive measures such as walking aids and appropriate footwear to alleviate pain and improve function [13]. Additionally, the Osteoarthritis Research Society International (OARSI) advises the use of NSAIDs as a first-line pharmacological therapy, with IA CO injections recommended for short-term pain relief in patients experiencing moderate to severe symptoms [4]. The enhanced outcomes observed in the HA and CS groups in this study further support the potential benefits of integrating IA injections with physiotherapy as part of a holistic knee OA management strategy. HA injections have been shown to not only alleviate symptoms but also enhance joint lubrication, restore the viscosity of synovial fluid, normalize hyaluronan synthesis, and inhibit proteoglycan degradation. Furthermore, HA possesses analgesic and anti-inflammatory properties and is associated with a longer duration of therapeutic effect compared to CS [14, 15]. In contrast, CS injections are widely utilized for their rapid and effective short-term symptom relief, typically lasting between one and four weeks. However, repeated or prolonged use of CS has been linked to adverse effects, including joint degeneration and soft tissue atrophy [16]. These findings highlight the necessity of individualized treatment planning that carefully weighs the immediate benefits of CS against the sustained therapeutic advantages of HA, particularly when used in conjunction with physiotherapy.

Discrepancies between the present results and the previous studies reporting limited benefits of IA CS injections [12] may be due to variations in physiotherapy protocols. Earlier studies primarily utilized cycling and circuit training, focusing on strength and coordination, whereas the protocol at Mitiga Military Hospital incorporated therapeutic ultrasound (TUS), transcutaneous electrical nerve stimulation (TENS), and isometric quadriceps

strengthening exercises [17-20]. The integration of these additional physiotherapy modalities may have contributed to the enhanced efficacy of IA CS injections observed in this study, resulting in greater pain relief and improved functional outcomes. These findings highlight the potential role of adjunct physiotherapy techniques in optimizing the therapeutic effects of IA interventions for knee OA. Previous research has yielded mixed findings regarding the efficacy of HA injections combined with exercise. Some studies have reported no additional benefits of HA when combined with exercise over three months [21] or six months [22]. Conversely, other studies have found HA plus exercise to be superior in all outcome measures compared to exercise with saline [9] and to exercise alone over 12 months [10]. Additionally, some evidence suggests that HA combined with exercise is more effective than HA alone in reducing pain [11]. The variations in study protocols may account for these conflicting results, underscoring the need for further investigation into optimal treatment strategies. A direct comparison between HA and CS revealed minimal differences in efficacy. The HA group showed improvements in VAS scores (from 5.73 to 1.80) and ROM (from 107.33° to 119.33°), while the CS group exhibited similar reductions in VAS scores (from 5.20 to 2.00) and ROM improvements (from 111.73° to 121.33°). These differences were not statistically significant. However, the CS group demonstrated greater short-term improvements in pain relief and ROM compared to the HA and control groups. This finding aligns with the research of Khan and others [23], which concluded that HA and CS are effective treatments for knee OA, each with distinct mechanisms and timelines for achieving therapeutic benefits. The research team observed that CS injections provide rapid pain relief and are effective for short-term symptom management, whereas HA injections require a longer period, approximately four to five weeks, to exert their full therapeutic effect. Although these observations are supported by previous studies, no intermediate outcome measurements were taken during the treatment period in the present study to monitor the progression of improvement over time. Future research should incorporate periodic assessments, such as weekly evaluations, to better understand the progression of functional and symptomatic changes [24]. This study provides evidence supporting the integration of IA HA, and CS injections with structured physiotherapy as an effective approach for managing knee OA. While HA and CS demonstrated clinical benefits, their distinct therapeutic timelines and mechanisms highlight the importance of individualized treatment planning. The inclusion of adjunct physiotherapeutic modalities may further enhance clinical outcomes, particularly in terms of pain reduction and functional improvement. These findings reinforce the growing consensus that a comprehensive, multimodal management strategy offers superior therapeutic benefits for patients with knee OA. The absence of intermediate evaluations during the treatment period restricts insights into the progression of symptomatic improvement over time is to be considered.

Conclusion: The combined use of intra-articular hyaluronic acid and corticosteroid injections with a structured physiotherapy regimen appears to be an effective strategy for alleviating pain and improving joint function in patients with knee osteoarthritis. The findings support the importance of a personalized, multimodal treatment approach and emphasize the potential value of incorporating physiotherapy modalities to optimize clinical outcomes.

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التأثيرات المقارنة لحمض الهيالورونيك داخل المفصل والكورتيكوستيرويدات مع العلاج الطبيعي على خشونة الركبة: دراسة كمية في مستشفى معيتيقة العسكري

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ملخص: يُعدّ فصال الركبة اضطرابًا تنكسيًا شائعًا في المفاصل، يُؤثر سلبًا على الحركة ونوعية الحياة. تُستخدم الحقن داخل المفصل، مثل تلك التي تحتوي على الكورتيكوستيرويدات وحمض الهيالورونيك، بشكل شائع لتخفيف الأعراض، وغالبًا ما يكون ذلك بالتزامن مع العلاج الطبيعي. ومع ذلك، لا تزال البيانات المقارنة حول فعاليتها مجتمعةً في الممارسة السريرية محدودة. هدفت هذه الدراسة إلى تقييم ومقارنة الفعالية السريرية للكورتيكوستيرويدات داخل المفصل وحمض الهيالورونيك، كلٌّ منهما مع العلاج الطبيعي، في تقليل الألم وتحسين مدى الحركة لدى مرضى فصال الركبة. قُسّم ما مجموعه 60 مريضًا ليبياً مصابًا بفصال الركبة، والذين عولجوا في مستشفى معيتيقة العسكري، عشوائيًا إلى ثلاث مجموعات (عدد المرضى في كل مجموعة 20): المجموعة أ: تلقت حقن الكورتيكوستيرويد بالإضافة إلى العلاج الطبيعي، المجموعة ب: تلقت حقن حمض الهيالورونيك بالإضافة إلى العلاج الطبيعي، والمجموعة ج: تلقت العلاج الطبيعي وحده. تم تقييم شدة الألم باستخدام مقياس التناظر البصري، وقيست وظيفة المفصل باستخدام تقييمات مدى الحركة النشطة والسلبية. أُجريت التقييمات في بداية العلاج وبعد أربعة أسابيع من العلاج. تم تحليل البيانات باستخدام اختبار t المقترن وتحليل التباين (ANOVA). أظهرت جميع المجموعات انخفاضًا ملحوظًا في درجات مقياس التناظر البصري وتحسنًا في مدى الحركة بعد العلاج ($p<0.001$). أظهرت المجموعة (أ) أكبر انخفاض في الألم (6.15±1.42 إلى 2.00±1.17)، بينما أظهرت المجموعة (ب) تحسنًا أكبر في مدى الحركة (سلبي: 101.20°±11.45° إلى 122.45°±8.69°). أظهرت المجموعة (ج) تحسنًا متوسطًا ولكنه ذو دلالة إحصائية في كلا المعيارين. عند دمج حقن الكورتيكوستيرويد وحمض الهيالورونيك مع العلاج الطبيعي، يُحسّن الألم ووظيفة المفاصل بشكل ملحوظ لدى مرضى هشاشة العظام في الركبة. قد يُخفف الكورتيكوستيرويد الألم بشكل أسرع، بينما يبدو حمض الهيالورونيك أكثر فعالية في تحسين حركة المفاصل. تدعم هذه النتائج استخدام أساليب علاجية مُصممة خصيصًا بناءً على احتياجات كل مريض وأهدافه العلاجية.