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The effect of hyaluronic acid injection on the outcome of flexor tendon repair in zone II of the hand

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Abstract

Background and objective: Flexor tendon injuries of the hand are common, especially in zone II. Various pharmacologic agents have been used to improve the outcome of primary tendon repair. One must select an option that accomplishes an excellent total active movement of the repaired tendon. This study aimed to find out the effect of hyaluronic acid injections in the restoration of normal gliding and power of the repaired tendon.

Methods: An interventional study of 47 cases of zone II flexor tendon injury managed from May 2017 to May 2018. The data were assembled in a questionnaire. Standardized photographs for pre-, intra-, and postoperative were taken. Hyaluronic acid injections were used in selected cases.

Results: Sharp injury (34 cases, equal to 72%) was found to be the commonest mechanism of flexor tendon injury. Male predominance was noticed (38 cases out of 47) due to their working nature. The hyaluronic acid injection was delivered to selected cases (10 cases, equal to 21%) based on preoperative evaluation. Eighty percent of repairs regained total active movement uneventfully. Few complications happened which responded to conservative management. The *P* value of total active movement in relation to hyaluronic acid injection was 0.036, which is considered statistically significant.

Conclusion: This study shows that intraoperative injection of high molecular weight of hyaluronic acid improves the outcome of flexor tendon repair, presumably by decreasing the chance of adhesion.

Keywords: Flexor tendon injury; Hyaluronic acid; Adhesion.

Introduction

One of the most challenging problems that have been considered for surgeons was flexor tendon injuries. Poor results of flexor tendon repair made one hand surgeon, Boyes to state that two flexor tendons in a small area passing through tight sheath and pulley system, in which repair of one or both of tendons will lead to thickening at the repair site, that makes normal gliding and movement to be impossible.[1] The most common zone of injury is zone II, especially in young- workers involving one or both tendons, which are flexor digitorum superfiscialis and flexor digitorum profundus. Zone II flexor tendon injuries are the most challenging area to repair because of the pulley system, and coursing of the flexor digitorum profundus through the chiasm of the flexor digitorum superfiscialis. Furthermore, Bunnell coined the term "no man's land" to emphasize the difficulties associated with this area of the digital sheath.[2] Zone II of the hand has a complex anatomy, which made of five annular pulleys, three cruciate pulleys, and two flexor tendons, as shown in Figure 1. Because of various causes beginning from edema, hematoma, re-rupture, to resulting in adhesion between any of the mentioned structures; Good outcome is difficult to achieve in repairing one or both tendons. Even though surgical technique and improved postoperative rehabilitation

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programs had its breakthrough, after primary repair of the tendons, still adhesions seem to be a problem for surgeons. Various pharmacologic agents have been used to reduce peritendinous adhesions after flexor tendon surgery.[3] Some of them have been found to cause a severe inflammatory response and impairment of the tendon healing process. Various pharmacologic agents such as indomethacin and ibuprofen have been proposed.[4] Steroids and antihistamines had promising experimental results, but it is not possible to use clinically because of toxicity or impairment of wound healing.[5] Hyaluronic acid is one of these agents, which is a high molecular weight polysaccharide, mostly found in the extracellular matrix where it functions variously in different organisms. The half-life of hyaluronic acid in the circulation is only three to five minutes, whereas a day in a tissue, and one to three weeks in cartilage. It can be divided into three groups based on their molecular weight as low, medium, and high molecular weight.[6,7] It promotes the healing process through regeneration and growth rather than scarring and fibrosis.[8] Depending on concentration and molecular weight, the effect of hyaluronic acid varies. It is believed that low molecular weight and concentration stimulates granulocyte function. However, high molecular weight and concentration hyaluronic acid inhibit the movements and phagocytosis of granulocytes. It was found that for inhibition of granulocyte function, a molecular weight of 10^5 to 10^6 Daltons is needed.[9,10] After tendon repair in zone II, finger motion can be impaired due to various causes such as edema, and later by excessive scar formation, and/or by adhesions between the tendon and sheath or other tissues. To overcome these unwanted outcomes, proper balance between stabilization and mobilization must be done in order to promote adequate healing of the tendon. Also, nowadays hyaluronic acid has been used widely in the surgical repair of the tendons.[11,12] Previous studies explained the effect of hyaluronic acid by the fact that it creates a scaffold around the tenorrhaphy site because of its high viscoelastic property, which would prevent adhesions to the surrounding tissue. The other analysis is that it serves as an effective soft tissue lubricant, might decline the new extracellular matrix formation due to the inhibition of mononuclear phagocytes and lymphocytes.[13,14] The aim of this study is to investigate the outcome of hyaluronic acid injections versus the controlled group that was not injected with any substance over a period of three months to determine the effect of the substance on the outcome of flexor tendon repair in zone II. The objective is to show the role of hyaluronic acid in the management of the flexor tendon injuries in zone II in increasing the chance of normal function of the repaired tendon in the matter of resorting the normal gliding and power; Thus, decreasing the chance of tendon adhesion formation after surgical repair.

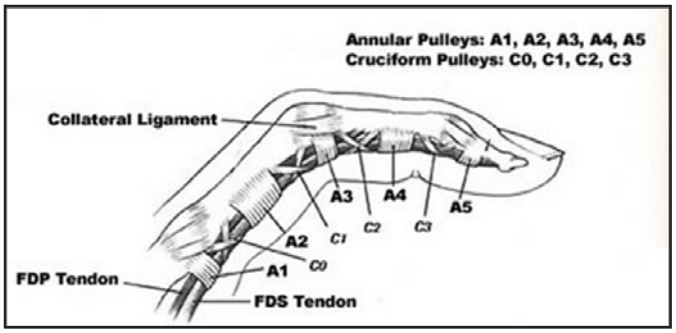

Figure 1: Complex anatomy of flexor tendons through zone II of the hand. Consisting of five annular pulleys, four cruciform pulleys, collateral ligament and two tendons.[15]

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Methods

An interventional study was conducted on 47 patients, aged 15-50 years, who had a surgical repair for flexor tendon injuries from May 2017 to May 2018 in Rozhawa Emergency Hospital in Erbil. The median age of the patients was 29. The actual work was done on 50 fingers from these patients. Our inclusion criteria were flexor tendon injury in zone II of the hand either partial or complete cut of the flexor digitorum profundus with or without flexor digitorum superfiscialis. The criteria of exclusion were those with associated injuries to the same finger such as skin loss or fracture within the same digit or any other digits of the same hand, those with congenital hand deformities, mentally disturbed, and those who cannot follow the treatment protocol. Through the random number table, ten patients out of 47 were prospectively and randomly selected to receive hyaluronic acid injections. The remaining 37 patients were only received repair of their injured tendons without the administration of any kind of drug. All patients participated by their own will. A detailed explanation of their surgery was discussed with them with the discretion of their true identity in the research was promised. The study was approved by the Research Ethics Committee at the College of Medicine, Hawler Medical University. Both groups were agreed on participation in the study after signing an informed consent agreeing on the surgery and its possible results that might occur. The questionnaire was filled with details such as age, gender, profession, fingers involved, and mechanism of injury. All operations were performed under general anesthesia with tourniquet control within the first 24 hours of injury. Tendons were approached by various methods per the site and type of the injury; for example, transverse laceration through skin crease at finger was followed by two incisions to make like one z-plasty, or another approach was used like zig-zag method. Only flexor digitorum profundus was repaired with polyproline suture (4.0 prolene) using four core suture technique, followed by an epi-tendinous running suture (6.0 prolene). During all tendon repairs, both A2 and A4 were preserved. Before closing the wound, 1 ml of high molecular weight hyaluronic acid was injected into the site of the tendon repair in high concentrations (20mg/ml). In the controlled group, no substances were injected. The same reconstructive options were done to all the patients apart from Hyaluronic acid injections to (10 cases), which involved (12 fingers), as two cases had more than one finger involvement. The other (37 cases) were treated like the other group apart from the hyaluronic acid injection, as shown in Figures 2 and 3. After surgery, the wrist was held in approximately 30 degrees' palmar flexion, the metacarpophalangeal joints flexed in 40 degrees, and another 30 degrees for the Proximal interphalangeal and distal interphalangeal joints. The same postoperative care and physiotherapy protocol were applied to the groups (Early active movement) using Kleinert splint. Both groups were followed up on a weekly basis for one month, then twice a month for another two months to evaluate the outcome of their tendon repair using standard flexor tendon evaluation. Our evaluation was done3-month post-surgery, which was determined on the gliding of the injured tendon(s) through the pulley system and their peritendinous sheath, range of total active motion (TAM) of each tendon at all the joints that were involved, and lastly, physical examination of the wound to see any swelling or mass formation. All the patients after being evaluated were categorized per their finding into 4 groups, which are excellent that its TAM was equal to normal finger, good if its TAM >75%, fair if TAM>50% and poor outcome if TAM<50%. Statistical analysis was done by the statistical package for the social sciences (version 23). Measurement data were recorded as median and frequencies, whereas count data were expressed as

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ratios. The Chi-square test was used to compare proportions between groups, with $P \leq 0.05$ was considered statistically significant.

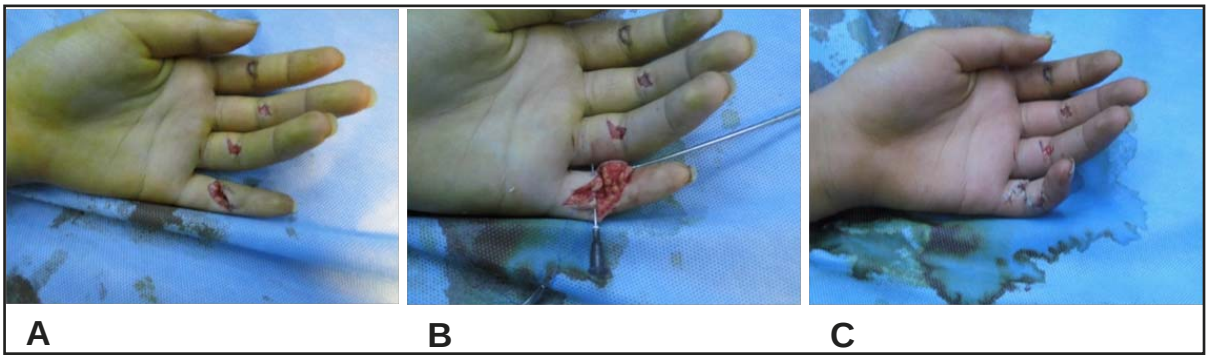

Figure 2: Flexor tendon injury repair in zone II of the little finger. (A) preoperative evaluation (B) Intra-operative tendon identifying (C) postoperative repair and restoration of the normal cascade.

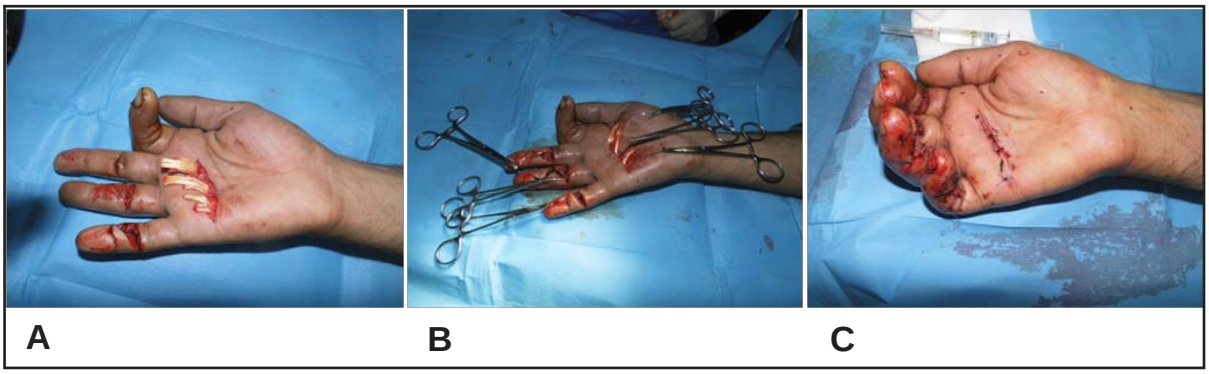

Figure 3: Flexor tendon injury in the little, ring, and middle finger (multiple fingers). (A) Preoperative evaluation and identifying the injured tendons. (B) Intra-operative, Using NG-tube for insertion of the tendon through its sheath. (C) Postoperative closure of wound after injection of hyaluronic acid injection.

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Results

The mean age of participants was 30 years with male predominance. Most of the male patients were unskilled manual workers. Sharp injury (34 cases) was more than crush injury (13 cases) in the mechanism of injury, which all are shown in Table 1. The commonest finger to be involved with the injury of the flexor tendon in zone II was isolated index finger, whereas multiple finger involvement of the same hand was the least (two cases). These, along with the frequency of other fingers, are shown in Table 2. Eighty percent of cases with hyaluronic acid injections healed uneventfully. Two cases suffered from complications that managed conservatively. However, in the controlled group, apart from 14 cases that completed their treatment without complications, the rest suffered complications that were also managed in a conservative fashion, as shown in Table 3.

Table 1: Frequency of mechanism of injury according to the gender of patients.

Gender	Sharp mechanism		Crush mechanism		Total		*P value*
	No.	(%)	No.	(%)	No.	(%)	
Male	27	(71.0)	11	(29.0)	38	(100.0)	0.68
Female	7	(77.0)	2	(23.0)	9	(100.0)	
Total	34	(72.0)	13	(28.0)	47	(100.0)	

Table 2: Frequency of the finger involved.

Finger	Frequency	%
Thumb	11	23.4
Index	14	29.8
Middle	7	14.9
Ring	5	10.6
Little	8	17.0
Multiple digits	2	4.3
Total	47	100.0

Table 3: Postoperative complications.

Hyaluronic acid injection	Complications						Total No. (%)
	Tendon rupture No. (%)	Tendon adhesion No. (%)	Infection No. (%)	No complications No. (%)	Joint stiffness No. (%)	Others No. (%)	
Yes	0 (0)	1(10)	0 (0)	8 (80)	1 (10)	0 (0)	10(100)
No	4 (11)	11 (30)	1 (3)	14 (38)	2 (5)	5(13)	37 (100)
Total	4 (8)	12 (26)	1 (2)	22 (47)	3 (6)	5 (11)	47 (100)
P value	0.08						

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All patients whom hyaluronic acid was used in their operation were satisfied with the end result, and the surgeon's satisfaction was in the majority of cases, comparing these results with the controlled group are shown in Table 4. Half of the cases that were injected with hyaluronic acid were ended with total active movement of excellent, while only four cases out of 37 cases of the controlled group were stated as excellent. All results of both groups regarding restoration of function are shown in Table 5.

Discussion

Zone II comprise the most common zones of flexor tendon injury. The male predominance is noted due to increased exposure and occupational hazards. The majority of males were house building workers, unskilled manuals, or agricultural. Sharp injury (34 cases) was seen to be the commonest cause of injury, this agrees with the study done by Ozgenel and Etoz in Bursa who found that sharp injury was the commonest cause of injury.[16] The main problem after flexor tendon injury in zone II is adhesion formation between the tendon and surrounding tissue, which restricts the normal gliding of the tendon through its sheath. Many pharmacological agents and interpositional materials have been described to overcome this problem, both synthetic and biologic.[17] Hyaluronic acid is one of these pharmacologic agents that has been an agent of interest, which exists in synovial fluid and connective tissue of the human body, richly in the extracellular matrix.[18] In this study, Viscoplus was used. The molecular weight and concentration of hyaluronan in Viscoplus were about 2.5 Million Daltons and 10 mg/ml. Many experimental studies have revealed that exogenously administered sodium hyaluronate helps healing of flexor tendon repair in zone II without the formation of postoperative adhesion.[19] The first prospective study about the hyaluronic acid effect on the prevention of adhesion by Hagberg, did not demonstrate any significant benefit of a single dose.[20] We believe this is because of low concentration and molecular weight with the rapid elimination of hyaluronic acid effect around the sites of repair. However, another study by Ozgenel and Etoz on hyaluronic acid effect, they preferred three injections of hyaluronic acid.[16] The first

Table 4: The patient's satisfaction and Surgeon's satisfaction.

Hyaluronic acid injection	Patient's satisfaction		Surgeon's satisfaction	
	Yes No. (%)	No No. (%)	Yes No. (%)	No No. (%)
Yes	10 (100)	0 (0)	8 (80)	2 (20)
No	31 (84)	6 (16)	25 (68)	12 (32)
P Value	0.04		0.07	

Table 5: Total active movement in each group.

Hyaluronic acid injection	Total active movement							
	Excellent		Good		Fair		Poor	
	No.	%	No.	%	No.	%	No.	%
Yes	5	50	3	30	2	20	0	0
No	4	11	16	43	11	30	6	16
P Value	0.036							

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injection was given at the time of surgery, and the other two were given at a week interval. Their results show significant benefits in the long-term and at three months, not before that. In order to limit the number of injections and overcome the results of the study done by Hagberg, we preferred to use a single injection in high molecular weight and low concentration.[16] This study compared the effect of hyaluronic acid injection to not injecting it or any other pharmacologic agent in the outcome of the repair of flexor tendon injury in zone II. In this study, a single high molecular weight was used, unlike the previous two studies which used single molecular weight injection or repetitive (three) injections of low molecular weight. Despite the fear of inhibition of phagocytosis of granulocytes and its movement. As its new line of management of tendon repair in order to reduce adhesions, only 10 cases were selected randomly to be injected out 47 cases that were collected. In a few of our cases, we came across a tense inflammatory response in the first postoperative week, which none of the previous studies have faced it. We believe because we injected a high concentration of hyaluronic acid; in contrast to the other two studies where they used low molecular weight. Fortunately, the inflammatory response subsided quickly within a matter of two weeks in the majority of the cases. The effects on the outcome were beneficial, as out of 10 cases injected with hyaluronic acid, only one case suffered from adhesion. Unlike the study by Hagberg, which also used a single injection but did not reveal any statistical difference, we believe that is because of the concentration and molecular weight of the injected hyaluronic acid. There are many methods of postoperative rehabilitation that influence the clinical result of flexor tendon repair by decreasing adhesion and giving more tensile strength by promoting nutrition to the tendon and intrinsic healing of it. However, early active mobilization may elongate the repair site and increase the rupture rate. However, we used the four-core suturing technique to overcome this problem with peripheral suturing placing it superficially for good alignment. That is because studies have demonstrated that the number of strands increases the resistance and strength of the suture to prevent gap formation or rupture. Although, it may increase adhesions and damage to the nutrition of the tendon.[21,22] The most widely used classification for evaluation of flexor tendon repair, especially in zone II is Strickland classification.[23] In this study, functional status for evaluation was labeled as excellent, good, fair, and poor. The fingers which were treated with hyaluronic acid showed 50% excellent, 30% good, and 20% fair results, whereas fingers treated without it showed 11% excellent, 43% good, 30% fair, and 16% poor results. As a result, Hyaluronic acid treated fingers showed superior outcome compared to non-hyaluronic acid treated fingers regarding total active movement and restoration of normal function after three months of surgery, as shown in Figure 4. Confirmed by statistical analysis, which chi -square test was performed using the likelihood ratio due to 5 cell violations, our *P* value was 0.036, which was considered statistically significant.

Conclusion

This study shows that single high molecular weight hyaluronic acid injections reduce the formation of adhesions. Hence, better restoration of normal function in matter of tendon gliding and power than those without hyaluronic acid injection. However, further studies needed to support the results of the study and whether molecular weight and concentration are the best to use along with single or multiple injections.

Competing interests

The authors declare no competing interests.

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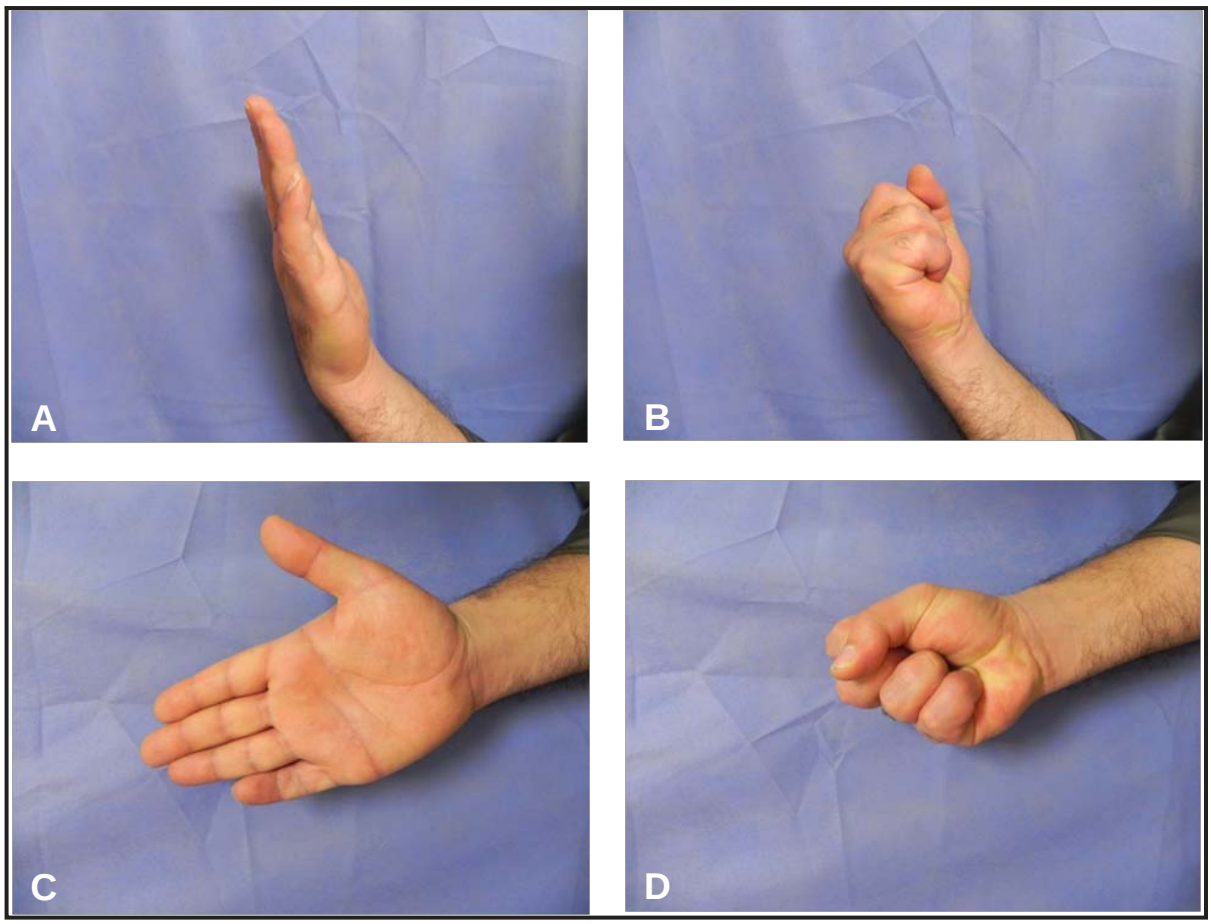

Figure 4: Three-month postoperative TAM of the little finger (A) Full extension, lateral view. (B) Full flexion, lateral view. (C) Full extension, anterior view. (D) Full flexion, anterior view

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