



Efficacy of Intra-Articular Triamcinolone Acetonide Injections for Wrist Pain in Rheumatoid Arthritis Patients: A Retrospective Study

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Abstract: *Background:* Synovectomy, arthroplasty, and other surgical procedures are generally used to correct wrist joint destruction in patients with rheumatoid arthritis (RA). *Methodology:* We unilaterally injected 20 mg of triamcinolone acetonide and 5 mL of 1% lidocaine hydrochloride of RA patients with joints pain who refused surgery. We then evaluated the clinical benefit and safety of intra-articular triamcinolone acetonide by analyzing data on (1) the number of injections with Larsen's grade and whether a biologic was used or not, (2) decrease in visual analog scale pain, (3) changes in carpal height ratio, radio carpal distance ratio and radial rotation angle in dorso-palmar plain X-ray imaging, and (4) the side effects of triamcinolone acetonide injection into the joints. *Results:* The mean number of injections per patient was less than 5 times, and sufficiently reduced or eliminated joints pain. X-ray evaluation did not reveal progress of joint destruction due to triamcinolone acetonide. No side effects of injection did not occur. *Conclusions:* It was found that joint injection of triamcinolone acetonide can reduce joint pain and suppress joint destruction, and it is possible that surgery will not be necessary in the future.

Keywords: RA, Wrist, Joint Pain, Steroid Injection

1. Introduction

Synovectomy, arthroplasty, and similar surgical procedures are generally used to correct wrist joints destruction in patients with rheumatoid arthritis. We unilaterally injected 20 mg of triamcinolone acetonide and 5 mL of 1% lidocaine hydrochloride to wrist joints of rheumatoid arthritis patients with joints pain who refused surgery. We then evaluated the clinical benefit and safety of intra-articular triamcinolone acetonide by analyzing data on.

(1) Number of injections in each grade and those in patients with or without the use of biologics, (2) decrease in pain, as measured on a visual analog scale (VAS) 1 month after injection, in each grade in patients with or without the use of biologics, (3) the side effects of triamcinolone acetonide injection into the joints, and (4) plain wrist joint X-ray front images were compared changes in carpal height

ratio (CHR), radio carpal distance ratio (RCDR), and radial rotation angle (RRA).

In a previous report, intra articular injection of triamcinolone acetonide reduce wrist joint pain and there was no change in carpal height ratio, radio carpal distance ratio, and radial rotation angle, although it was as short as 3 years and 8 months. This time we followed for 5 years and 9 months to check if the previous results changed, depending on the presence or absence of triamcinolone acetonide injection and biologic.

2. Materials and Methods

2.1. Methodology

The study included patients with RA who experienced wrist joint pain but refused surgery from November 2009 to

December 2017. All received unilateral injections of triamcinolone acetonide (20 mg) and 1% lidocaine hydrochloride (5 mL) into the dorsum of the distal radio-ulnar joint without fail using a 23-gauge needle. The follow-up period was 6 months to 8 years 1 month (mean 5.9 years).

2.2. Number of Injections

Of the 162 patients receiving injections during the period, 118 patients were able to be followed up after exclusion of those who did not visit hospitals or underwent surgery.

One-hundred eighteen patients (104 women and 14 men) were enrolled in the study. The duration of the disease ranged from 2 to 20 years (mean 8.9 years), age at the time of injection was 27 to 85 years (mean 64 years). Out of 118 patients, a total of 49 wrists of 32 patients were grade I on the Larsen scoring system [1], 44 wrists of 30 patients were grade II, 50 wrists of 33 patients were grade III and 36 wrists of 23 patients were grade IV.

During the same period, another 23 patients (20 females and 3 males: grade III and IV patients, age at the time of injection was 22 to 83 years; mean 62 years) who took anti-rheumatic drugs but did not use triamcinolone acetonide and biologic were checked the changes in CHR, RCDR and RRA as a control group by X-ray examination of the wrist joint. No patients had complication of diabetes mellitus or glaucoma.

2.3. Use of Biologics

Of the 42 patients treated with a biologic, 19 received etanercept (Grade I: 3 cases, Grade II: 6 cases, Grade III: 7 cases, Grade IV: 4 cases), 7 received infliximab (Grade I: 2 cases, Grade II: 1 case, Grade III: 2 cases, Grade IV: 2 cases), 3 received adalimumab (Grade I: 1 case, Grade III: 1 case, Grade IV: 1 case), 6 received abatacept (Grade I: 1 case, Grade II: 2 cases, Grade IV: 3 cases), 5 received tocilizumab (Grade II: 1 case, Grade III: 3 cases, Grade IV: 1 case), 4 received golimumab (Grade I: 2 cases, Grade III: 1 case, Grade IV: 1 case) and 1 received certolizumab in Grade III. Some of the patients used more than 1 biologic (Figures 1-4).

2.4. Decrease in Pain

The following endpoints were recorded and analyzed for each patient: (1) number of injections in each grade and those in patients with or without the use of biologics (statistically analyzed using paired Student's *t*-test); (2) decrease in pain, as measured on a VAS 1 month after injection, in each grade in patients with or without the use of biologics (statistically analyzed using paired Student's *t*-test).

2.5. Adverse Effects of Intra-articular Triamcinolone Acetonide

Any adverse effects on the subcutaneous tissue and extensor tendons of triamcinolone acetonide injection into the joints were checked.

No.	age	sex	Biologi	site	grade	injection time
1	64	F		L	I	3
2	46	F		L	I	1
3	76	F		R	I	1
4	36	F		R	I	1
5	65	F		L	I	1
6	60	F		L	I	1
7	54	F		R	I	1
8	42	F		R	I	1
9	80	F		L	I	1
10	69	F		R	I	3
11	64	F		R	I	3
12	41	F		L	I	2
13	78	F	Etanercept	R	I	1
14	51	F		R	I	1
				L	I	2
15	61	F		R	I	14
				L	I	11
16	72	F		R	I	5
				L	I	3
17	83	F		R	I	6
				L	I	6
18	47	F		R	I	5
				L	I	3
19	60	F		R	I	1
				L	I	1
20	59	F		R	I	4
				L	I	2
21	64	F		R	I	2
				L	I	3
22	57	F		R	I	2
				L	II	2
23	66	F	Etanercept	R		0
				L	I	3
24	43	F	Tofacitinib	R	I	5
				L	I	6
25	42	F	Infliximab	R	I	7
				L	I	7
26	50	F	Adalimumab	R	I	2
				L	I	2
27	77	M	Golimumab	R	I	3
				L	I	2
28	69	F	Etanercept	R	I	3
				L	I	2
29	78	F	Abatacept	R	I	5
				L	I	7
30	48	F	Golimumab	R	I	4
				L	I	6
31	65	M	Etanercept	R		0
				L	I	2
32	40	F	Infliximab	R	I	7
				L	I	1

Figure 1. Number of injections in grade I patients.

No.	age	sex	Biologi	site	grade	injection time
1	72	F		L	II	1
2	72	F		L	II	1
3	70	F		L	II	5
4	71	F		L	II	1
5	37	F		R	II	2
6	92	M		R	II	1
7	60	F		R	II	2
8	59	F		L	II	2
9	55	F		L	II	1
10	72	F		L	II	1
11	66	F		R	II	8
12	71	F	Abatacept	R	II	1
13	66	M	Infliximab	L	II	2
14	60	F	Abatacept	L	II	2
15	65	M		R	II	1
				L	II	1
16	64	F		R	II	8
				L	II	6
17	58	M		R	II	6
				L	II	5
19	72	F		R	II	4
				L	II	2
20	61	F		R	II	1
				L	II	1
21	60	F		R	II	1
				L	II	1
22	69	F		R	II	2
				L	III	1
23	46	F		R	II	10
				L	II	11
24	65	M		R	II	16
				L	II	16
18	56	F	Etanercept	R	II	1
				L	II	1
25	75	F	Etanercept	R	II	3
				L	II	10
26	62	F	Etanercept	R	II	13
				L	II	16
27	87	F	Etanercept	R	II	1
				L	II	7
28	59	F	Tocilizumab	R	II	1
				L	II	2
29	75	F	Etanercept	R	II	4
			Iguratimod	L	II	4
30	81	F	Etanercept	R	II	3
				L	II	2

Figure 2. Number of injections in grade II patients.

No.	age	sex	Biologi	site	grade	合計
1	67	F		L	III	1
2	59	F		L	III	1
3	62	M		R	III	1
4	59	F		R	III	2
5	37	M		R	III	3
6	54	M		L	III	6
7	54	F		L	III	2
8	57	F	Infliximab	L	III	3
9	84	F	certolizumab	R	III	2
10	65	F	Etanercept	R	III	1
11	71	F	Etanercept	R	III	1
12	77	F	Etanercept, Tocilizumab	R	III	1
13	75	F		R	III	2
				L	III	1
14	43	F		R		0
				L	III	2
15	66	F		R	III	1
				L	III	1
16	64	F		R	III	2
				L		0
17	79	F		R		0
				L	III	2
18	59	F		R	III	11
				L		0
19	66	F		R	III	2
				L	III	4
20	73	F		R	III	2
				L	III	2
21	84	F		R	III	1
				L	III	1
22	38	F		R	III	6
				L	III	3
23	62	F		R	III	4
				L	III	4
24	77	F		R	III	4
				L	III	8
25	33	F		R	III	7
				L	III	2
26	62	F		R	III	1
				L	III	1
27	64	F		R	III	1
				L	III	1
28	59	F	Etanercept	R	III	1
				L	III	1
29	69	F	Etanercept	R	III	15
				L	III	11
30	65	M	Etanercept Golimumab	R	III	6
				L	III	1
31	75	F	Etanercept Tocilizumab	R	III	8
				L	III	2
32	75	F	Adalimumab	R	III	2
				L	III	1
33	65	F	Infliximab Tocilizumab	R	III	3
				L	III	2

Figure 3. Number of injections in grade III patients.

No.	age	sex	Biologi	site	grade	合計
1	78	F		R	IV	2
2	80	F		L	IV	1
3	75	F		R	IV	2
4	50	F		L	IV	2
5	71	F		R	IV	1
6	68	F		L	IV	2
7	79	F	Tocilizumab	L	IV	2
8	56	F	Infliximab	L	IV	2
9	70	F	Etanercept Abatacept	R	IV	2
10	45	F		R	IV	13
				L	IV	19
11	58	F		R	IV	6
				L	IV	5
12	62	F		R	IV	3
				L	IV	4
13	83	F		R	IV	11
				L	IV	9
14	75	M		R	IV	2
				L	IV	5
15	70	M		R	IV	2
				L	IV	1
16	60	F		R	IV	1
				L	IV	1
17	80	F	Golimumab	R	IV	2
			L	IV	1	
18	63	F	Etanercept	R	IV	2
			L		0	
19	49	F	Adalimumab	R	IV	2
			L	II	1	
20	84	F	Etanercept	R	IV	1
			L	IV	1	
21	47	F	Infliximab	R	IV	12
			L	IV	12	
22	71	F	Abatacept	R	IV	2
			L	IV	2	
23	63	M	Etanercept Abatacept	R	IV	5
			L	IV	5	

Figure 4. Number of injections in grade IV patients.

2.6. Changes in Carpal Height Ratio, Radio Carpal Distance Ratio and Radial Rotation Angle with and Without Injection of Triamcinolone Acetonide

Plain wrist joint X-ray front images captured at baseline and at the end of December 2017 (at the time of this investigation) were compared. The follow-up period ranged from 3 years and 3 months to 8 years (mean, 5.9 years). Patients with advanced wrist joint destruction (Larsen grades III and IV) were classified into the following three treatment regimens:

(A) 23 patients (46 wrists) who did not receive triamcinolone acetonide and biologics as a control group. (B)

35 patients (53 wrists) who received triamcinolone acetonide injection without biologics, and (C) 21 patients (33 wrists) who received triamcinolone acetonide with biologics. These groups were statistically analyzed using paired Student's *t*-test.

For these cases, carpal height ratio (b/a), radial carpal distance ratio (c/a) and radial rotation angle (α) were measured by dorso-palmar X-ray imaging (a: length of the third metacarpus, b: carpal height, c: radial carpal distance, lined: surface of distal joint of the radius, line e: radial margin of the second metacarpus, α : radial rotation angle) [2] (Figure 5). Unpaired student's *t*-test was used for statistical analyses.

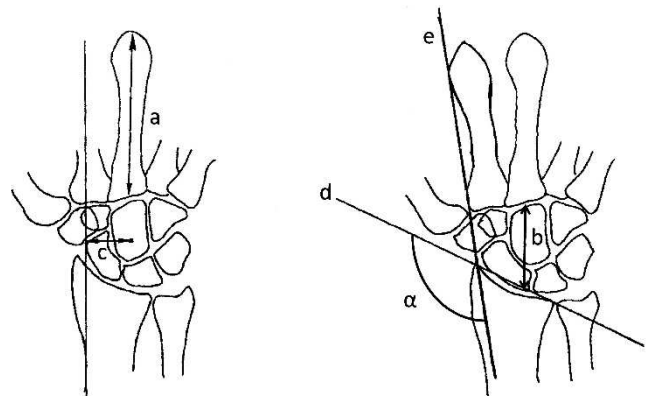


Figure 5. Methods of measuring carpal height, radio-carpal distance and radial rotation angle of the carpus (a: length of the third metacarpus, b: carpal height, c: radial carpal distance, line d: surface of distal joint of the radius, line e: radial margin of the second metacarpus, α : radial rotation angle).

3. Results

3.1. Number of Injections in Each Grade and in Patients with or Without the Use of Biologics

There were a total of 394 injections in 116 wrist joints in patients with the use of biologic and 259 in 69 wrist joints in patients without the use of biologics. The average number of injections was 3.07 ± 3.00 and 3.94 ± 2.34 for grade I patients with and without the use of biologics, respectively, and 4.07 ± 4.44 and 4.29 ± 4.55 for grade II patients with and without the use of biologics, respectively. No statistically significant differences in the number of injections were observed between the patients who received and those who did not receive biologics. The average number of injections was 2.49 ± 2.42 and 3.59 ± 4.01 for grade III patients with and without the use of biologics, respectively, which was statistically different ($P < 0.05$). The average number of injections was 4.6 ± 4.86 and 3.18 ± 3.56 for grade IV patients with and without the use of biologics, respectively, which was statistically different ($P < 0.05$) (Figure 6).

	Bio. (+)			Bio. (-)			P value
	no. of wrist	total number of injection	average number of injection	no. of wrist	total number of injection	average number of injection	
Grade I	30	92	3.07 ± 3.00	18	71	3.94 ± 2.34	ns
Grade II	29	118	4.07 ± 4.44	17	73	4.29 ± 4.55	ns
Grade III	37	92	2.49 ± 2.42	17	61	3.59 ± 4.01	P<0.05
Grade IV	20	92	4.6 ± 4.86	17	54	3.18 ± 3.56	P<0.05
Total	116	394		69	259		

Figure 6. Number of injections in each grade and in patients with or without the use of biologics.

3.2. Decrease in Pain

Mean VAS improved from 81.29±19.28 mm at baseline to 8.39±9.34 mm post-injection in Grade I. Mean VAS improved from 72.90±19.53 mm to 11.61±16.14 mm in Grade II, 71.00±24.12 mm to 15.33±16.13 mm in Grade III, and from 71.90±20.15 mm to 7.14±10.56 mm in Grade IV. Statistical analysis showed significant in all grade ($P < 0.001$).

3.3. Adverse Effects of Intra-articular Triamcinolone Acetonide

No abnormality was observed subcutaneously.

3.4. Changes in Carpal Height Ratio, Radio Carpal Distance Ratio and Radial Rotation Angle with and Without Injection of Triamcinolone Acetonide

A total of 79 patients (132 wrists) in Larsen classification III and IV in which joint destruction progressed were traceable.

(A) 23 patients (46 wrists) who did not receive triamcinolone acetonide and biologics as a control group: In

the grade III and IV groups, there were no significant differences in CHR (baseline: 0.440±0.079; post-injection: 0.443±0.07), RCDR (baseline: 0.354±0.066; post-injection: 0.358±0.04, and RRA (baseline: 109.76±10.42; post-injection: 136.2±159.2).

(B) 35 patients (53 wrists) who received triamcinolone acetonide injection without biologics: In grade III and grade IV, CHR changed from 0.423±0.07 at baseline to 0.413±0.09 post-injection, and RCDR changed from 0.356±0.06 to 0.355±0.07, with no significant difference observed in ulnar deviation. Finally, RRA changed from 111.9±10.58 to 107.51±9.25, and only a one-side test showed a significant difference ($P<0.05$) indicating progression in the radial rotation of the carpal bones, but no significant differences were observed a two-side test.

(C) 21 patients (33 wrists) who received triamcinolone acetonide with biologics: There were no significant differences in CHR (baseline: 0.413±0.083; post-injection: 0.41±0.08), RCDR (baseline: 0.359±0.034; post-injection: 0.364±0.04), and RRA (baseline: 107.9±7.76; post-injection: 136.2±169.2 (Figure 7).

(A) Triamcinolone Acetonide (-), Bio (-)					
(Grade III + IV, N = 23 patients, 46 wrists)		pre-inj.	post-inj.	S.D. two-side	S.D. one-side
Carpal height ration (CHR)		0.440 ± 0.079	0.433 ± 0.07	ns	ns
Radiocarpal distance ratio (RCDR)		0.354 ± 0.066	0.358 ± 0.04	ns	ns
Radial rotation angle (RRA)		109.76 ± 10.42	136.2 ± 159.2	ns	ns
(B) Triamcinolone Acetonide (+), Bio (-)					
(Grade III + IV, N = 35 patients, 53 wrists)		pre-inj.	post-inj.	S.D. two-side	S.D. one-side
Carpal height ration (CHR)		0.423 ± 0.07	0.413 ± 0.09	ns	ns
Radiocarpal distance ratio (RCDR)		0.356 ± 0.06	0.355 ± 0.07	ns	ns
Radial rotation angle (RRA)		111.9 ± 10.58	107.51 ± 9.25	ns	P<0.05
(C) Triamcinolone Acetonide (+), Bio (+)					
(Grade III + IV, N = 21 patients, 33 wrists)		pre-inj.	post-inj.	S.D. two-side	S.D. one-side
Carpal height ration (CHR)		0.413 ± 0.083	0.41 ± 0.08	ns	ns
Radiocarpal distance ratio (RCDR)		0.359 ± 0.034	0.364 ± 0.04	ns	ns
Radial rotation angle (RRA)		107.9 ± 7.76	136.2 ± 10.06	ns	ns

Figure 7. Changes in carpal height ratio, radio carpal distance ratio, and radial rotation angle in dorso-palmar plain X-ray imaging.

4. Discussion

Biologic agents are recently used for successful control of RA. Nevertheless, many RA patients complain of wrist pain despite receiving biologic therapy. In this study 20 mg of triamcinolone acetonide was unilaterally injected to reduce persistent wrist pain in RA patients who refused surgery. The distal radio-ulnar joint was selected as the injection site because surgical experience indicates that many patients have extensive synovial proliferation of the distal radio-ulnar joint and triangular fibro-cartilage Complex (TFCC) ruptures. The anatomy and function of the TFCC of the wrist was reported that the TFCC was found to be perforated in 53% of specimens dissected [3].

Prior to conducting this study, the modified Sauvé-Kapandji method was performed for wrist pain and its usefulness was reported [4]. After that, triamcinolone acetonide was first injected for all wrist pain. The reason is that we thought it would reduce synovial proliferation and wrist pain.

The number of injections in grade III was statistically lower in biologics use cases than in non-use cases, while in grade IV, biologics use cases were statistically higher than in non-use cases. But the average number of injections was less than 5 times / year and the effect of injection were demonstrated. The reason for this is that in the case of Grade III, IV biological drug administration is suppressed proliferation of synovium but pain due to joint destruction remains, so joint injection of triamcinolone acetonide is necessary to suppress this pain.

VAS score was observed at 1 month after injection, and the number of injections was less compared with the mean number of injections in patients with longer duration of effect.

Reduction in the radial rotation (RRA) of the carpal bones were observed in patients receiving triamcinolone acetonide injection without the use of biologics ($P < 0.05$ only by unpaired one-sided test). No significant differences were observed in patients without joint injection of triamcinolone acetonide and without biologic administration and no significant differences were observed in patients with joint injection of triamcinolone acetonide with biologic administration.

There have been many reports that intra-articular injection of steroids can suppress joint pain and not promote joint destruction. Subsequent loading of the knee conferred an excessive burden on the knees, resulting in joint damage [5-7]. Ostergaard *et al.* [8] noting that intra-articular triamcinolone acetonide confers a longer response than other corticosteroids, recommend up to 3 to 4 injections per year with a 6-week dosing interval. The Western literature contains many reports of wrist injections of corticosteroids for treating RA patients [9-12]. It has been reported that injection of steroid into the trigger finger caused tendon rupture [13].

Due to the above reasons, intra-articular corticosteroid injection is not generally done, and literature discusses no long-term follow-up investigation of patients receiving

intra-articular corticosteroid injections for joints pain. Previously we injected triamcinolone acetonide into the wrist within average 5 times during a year and followed until 3 years and 8 months period, then reported its usefulness [14]. This time, we investigated about 5 years and 9 months using the X-ray changes with and without intra-articular injection of triamcinolone acetonide and with or without biologics. As a result it is difficult to determine whether the joint change is due to progression of RA or side effects of triamcinolone acetonide. However, the lack of any acute joint destruction following injection suggests that triamcinolone acetonide was not responsible.

Many patients achieved a long-term response with just single injection during the treatment period. No skin atrophy or extensor tendon rupture was occurred because the drugs were properly injected into the joints. We believe that joint prolapse does not precede in triamcinolone acetonide injection cases because the triamcinolone acetonide injection effect suppresses synovial proliferation.

In recent years it has been reported that sustained-release-triamcinolone acetonide improved pain relief effect predominantly than the currently used immediate-release triamcinolone acetonide are doing [15-17]. It has also been reported that RA can be controlled more by the intra-articular injection of triamcinolone acetonide and the simultaneous use of biologics [18-20]. In this survey, of joint pain despite using biologic. As a result of injecting triamcinolone acetonide within 5 times a year into these cases, a decrease in joint pain was observed with or without biologic.

Recently, it has been said that the evaluation of RA differs between doctors and patients because doctors evaluate joint swelling and patients mainly evaluate joint pain to understand the state of RA. Therefore, it is said that shared decision making is necessary [21].

In 2020 EULAR recommends careful intra-articular injection of steroid into joints first [22]. Intra-articular triamcinolone acetonide does not stop RA progression but relieve joint pain.

5. Conclusion

It was found that joint injection of triamcinolone acetonide less than 5 times a year can reduce joint pain and suppress joint destruction and no abnormality was observed. It is possible that surgery will not be necessary in the future.

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