

Triamcinolone Acetonide, Biologics and Anti-rheumatic Drug Prevent Destruction of Larsen Grade III and IV Wrist Joint in Rheumatoid Arthritis Patients

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To cite this article:

Akihiro Fukui, Yamada Hideki. Triamcinolone Acetonide, Biologics and Anti-rheumatic Drug Prevent Destruction of Larsen Grade III and IV Wrist Joint in Rheumatoid Arthritis Patients. *American Journal of Internal Medicine*. Vol. 10, No. 4, 2022, pp. 86-91.

doi: 10.11648/j.ajim.20221004.13

Received: July 29, 2022; **Accepted:** August 12, 2022; **Published:** August 24, 2022

Abstract: *Objectives:* In Grade III and IV of advanced wrist joint destruction in RA patients, the combination of triamcinolone acetonide injection, biologics and anti-rheumatic drug use was investigated by X-ray examination to check if joint destruction progressed in an average of 5.9 years. *Methods:* We unilaterally injected 20 mg of triamcinolone acetonide and 5 mL of 1% lidocaine hydrochloride of RA patients. Changes in the X-ray image were compared between the time of the first visit and at the end of the investigation. Only triamcinolone acetonide injection patients were Group (A), and the number of patients was 35 patients and 53 wrists. Triamcinolone acetonide injection and biologics patients were Group (B), and the number of patients was 21 cases and 33 wrists. Group (C) was only taking anti-rheumatic drug cases in 23 patients and 33 wrists, and Group (D) was only biologics in 21 patients and 33 wrists. The total number of grade III and IV of Larsen classification were 100 patients and 152 wrists. *Results:* In Group (A), RRA changed only a one-side test, and showed a significant difference ($p < 0.05$) indicating progression, but no significant differences were observed a two-side test. There was no significant difference in Group (B), (C) and (D). *Conclusions:* It is thought that the slow progress of wrist joint destruction on X-rays is due to the fact that it is not a load joint. If wrist joint destruction did not progress, there was an opportunity to increase the number of injections, the degree of swelling and pain could be reduced.

Keywords: Rheumatoid Arthritis, Synovitis, Triamcinolone Acetonide, Wrist Joint

1. Introduction

For patients who complained of the wrist joint pain during the period from November 2009 to December 2017 but did not wish to undergo surgery, patients who had been infused with triamcinolone acetonide 20 mg and 1% lidocaine hydrochloride 5 ml for more than 6 months. Previously we reported the clinical benefit and safety of intra-articular triamcinolone acetonide by analyzing data on [1, 2].

In the previous report [2], combination of triamcinolone acetonide injection and the presence or absence of biologics was 118 patients. According to Larsen classification [3], grade III was 50 wrists of 33 patients, grade IV was 36 wrists of 23 patients.

Among them, triamcinolone acetonide injection patients were Group (A) and the number of patients was 53 wrists of

35 patients (grade III: 33 wrists of 22 patients, grade IV: 20 wrists of 13 patients).

Triamcinolone acetonide injection and biologics patients were Group (B), and the number of patients was 33 wrists of 21 patients. (grade III: 17 wrists of 11 patients, grade IV: 16 wrists of 10 patients).

Previous reports have investigated the effects of triamcinolone acetonide injection and biologics. However, there are many RA patients who use only taking anti-rheumatic drugs, which seems to be mild, or who cannot use taking anti-rheumatic drugs and shift to only biologics, and there are many patients where triamcinolone acetonide was not injected into the wrist joint. We investigated how the changes in the wrist joints in these cases progressed.

So, we added other patients of only taking anti-rheumatic drugs and patients of only biologics in grade III and IV, for

comparative study of the wrist joint destruction using X-ray images. Of these patients, Group (C) was only taking anti-rheumatic drug with grade III and IV in 23 patients and 33 wrists (grade III: 8 patients, 16 wrists, grade IV: 15 patients, 17 wrists), and Group (D) was only biologics with grade III and IV in 21 patients and 33 wrists (grade III: 6 patients, 12 wrists, grade IV: 15 patients, 21 wrists). The total number of grade III and IV of Larsen classification were 100 patients and 152 wrists. Changes in the X-ray image were compared between the time of the first visit and at the end of the investigation.

2. Materials and Methods

In previous report, total patient was 49 females and 7 males and grade III were 33 patients and 50 wrists and grade IV were 23 patients and 36 wrists (Tables 1, 2).

The time-dependent changes in the grade III and IV with advanced wrist joint destruction reported no remarkable change. [2].

I was interested in what kind of wrist joint changes would be shown in the only anti-rheumatic drugs or biologics treated patients. The time-related changes in the wrist joint treated with the same degree of progress were compared by X-ray. We added sixty-six wrists of 44 patients (grade III and IV only) who were treated only anti-rheumatic drugs or biologics. The breakdown of total patient was 36 females and 8 males. Grade III was 33 wrists of 23 patients, and grade IV was 33 wrists of 21 patients.

Finally, in this study, the total number of grade III and IV

patients was 100 patients 152 wrists. Total patient was 85 females and 15 males. Duration of illness in all patients was 2 to 23 years (mean 8.9 years), and the age at the time of injection was 27 to 88 years (mean 64 years).

There were no complications of diabetes or glaucoma in all cases.

Those patients were classified into the following groups (A) to (D).

Group (A). Triamcinolone acetonide was injected and no biologics. The number of patients was 53 wrists of 35 patients and Grade III was 24 wrists of 16 patients and grade IV was 7 wrists of 4 patients.

Group (B). Triamcinolone acetonide injected and biologics use. The number of patients was 33 wrists of 21 patients. Grade III was 12 wrists of 8 patients and grade IV was 15 wrists of 9 patients.

Group (C). Taking only anti-rheumatic drug. The number of patients were 33 wrists of 23 patients. Grade III was 16 wrists of 8 patients and grade IV was 17 wrists of 15 patients.

Group (D) Use of only biologics. The number of patients was 33 wrists of 21 patients. Grade III was 12 wrists of 6 patients and grade IV was 21 wrists of 15 patients.

Using Youm measurement method [4], plain wrist joint X-ray front images captured. the carpal height ratio (CHR) as an index of carpal bone destruction, the radio carpal distance ratio (RCDR) as an index of carpal deviation, and the radial rotation angle (RRA) as an index of the radial rotation of the bone was measured.

Table 1. Number of injections in grade III patients.

Grade III					
No.	age	sex	Biologics	site	injection time
1	67	F		L	1
2	59	F		L	1
3	59	M		R	1
4	50	F		R	2
5	37	M		R	3
6	54	M		L	6
7	54	F		L	2
8	56	F	Infliximab	L	3
9	54	F	Certolizumab	R	2
10	65	F	Etanercept	R	1
11	71	F	Etanercept	R	1
12	77	F	Etanercept, Tocilizumab	R	1
13	75	F		R	2
14	43	F		L	1
15	66	F		R	0
16	64	F		L	2
17	79	F		R	1
18	59	F		L	1
19	66	F		R	2
20	73	F		L	4
21	84	F		R	2
				L	1
				L	1

Grade III					
No.	age	sex	Biologics	site	injection time
22	38	F		R	6
				L	3
23	62	F		R	4
				L	4
24	77	F		R	4
				L	8
25	33	F		R	7
				L	2
26	62	F		R	1
				L	1
27	64	F		R	1
				L	1
28	59	F	Etanercept	R	1
				L	1
29	69	F	Etanercept	R	15
				L	11
30	65	M	Etanercept Golimumab	R	6
				L	1
31	75	F	Etanercept Tocilizumab	R	8
				L	2
32	75	F	Adalimumab	R	2
				L	1
33	65	F	Infliximab Tocilizumab	R	3
				L	2

Table 2. Number of injections in grade IV patients.

Grade IV					
No.	age	sex	Biologics	site	injection time
1	78	F		R	2
2	80	F		L	1
3	75	F		R	2
4	50	F		L	2
5	71	F		R	1
6	68	F		R	2
7	79	F	Tocilizumab	L	2
8	56	F	Infliximab	L	2
9	70	F	Etanercept Abatacept	R	2
10	45	F		R	13
				L	19
11	58	F		R	6
				L	5
12	62	F		R	3
				L	4
13	86	F		R	11
				L	9
14	75	M		R	2
				L	5
15	70	M		R	2
				L	1
16	60	F		R	1
				L	1
17	80	F	Golimumab	R	2
				L	1
18	63	F	Etanercept	R	2
				L	0
19	49	F	Adalimumab	R	2
				L	1
20	84	F	Etanercept	R	1
				L	1
21	47	F	Infliximab	R	12
				L	12
22	71	F	Abatacept	R	2
				L	2
23	63	M	Etanercept Abatacept	R	5
				L	5

3. Results

Group (A): Only triamcinolone acetonide injection: CHR, which is an index of carpal bone destruction changed from 0.4 ± 0.1 at baseline to 0.4 ± 0.1 post injection, and RCDR, which is an index of ulnar deviation changed from 0.4 ± 0.1 to 0.4 ± 0.1 , with no significant difference observed. RRA, which is an index of a radial rotation of the carpal bone changed from 111.9 ± 10.6 to 107.5 ± 9.3 , and only a one-sided 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-sided test.

Group (B): Triamcinolone acetonide injection and biologics use: There was no significant difference in CHR

(baseline 0.4 ± 0.1 ; post-injection 0.4 ± 0.1), RCDR (baseline 0.4 ± 0.1 ; post-injection 0.4 ± 0.1), and RRA baseline 107.9 ± 7.8 ; post-injection 136.2 ± 10.1).

Group (C): Only anti-rheumatic drugs alone: There was no significant difference in CHR (baseline 0.4 ± 0.1 ; post-injection 0.4 ± 0.1), RCDR (baseline 0.4 ± 0.1 ; post-injection 0.4 ± 0.1), and RRA baseline 109.8 ± 136.2 ; post-injection 136.2 ± 159.2).

Group (D): Only biologics use: There was no significant difference in CHR (baseline 0.4 ± 0.1 ; post-injection 0.4 ± 0.1), RCDR (baseline 0.4 ± 0.0 ; post-injection 0.4 ± 0.0), and RRA baseline 107.9 ± 7.8 ; post-injection 136.2 ± 169.0). (Table 3).

Table 3. Comparison of CHR, RCDR, and RRA as determined by dorso-palmar plain X-ray between with and without anti-rheumatic drug, triamcinolone acetonide and biologics in grade III/IV patients.

(A)	Triamcinolone acetonide (+)				
	Grade III & Grade IV (35 patients, 53 wrists)	Pre-injection	Post-injection	S.D. two-side	S.D. one-side
	Carpal height ration (CHS)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radiocarpal distance ratio (RCDR)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radial rotation angle (RRA)	111.9 ± 10.6	107.5 ± 9.3	NS	$p < 0.05$
(B)	Triamcinolone acetonide (+) Biologics (+)				
	Grade III & Grade IV (21 patients, 33 wrists)	Pre-injection	Post-injection	S.D. two-side	S.D. one-side
	Carpal height ration (CHS)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radiocarpal distance ratio (RCDR)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radial rotation angle (RRA)	107.9 ± 7.8	136.2 ± 10.1	NS	NS
(C)	Anti-rheumatic drugs only				
	Grade III & Grade IV (23 patients, 33 wrists)	Pre-injection	Post-injection	S.D. two-side	S.D. one-side
	Carpal height ration (CHS)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radiocarpal distance ratio (RCDR)	0.4 ± 0.1	0.4 ± 0.0	NS	NS
	Radial rotation angle (RRA)	109.8 ± 136.2	136.2 ± 159.2	NS	NS
(D)	Biologics (+) only				
	Grade III & Grade IV (21 patients, 33 wrists)	Pre-injection	Post-injection	S.D. two-side	S.D. one-side
	Carpal height ration (CHS)	0.4 ± 0.1	0.4 ± 0.1	NS	NS
	Radiocarpal distance ratio (RCDR)	0.4 ± 0.0	0.4 ± 0.0	NS	NS
	Radial rotation angle (RRA)	107.9 ± 7.8	136.2 ± 169.0	NS	NS

NS: not significant.

4. Discussion

Recently, it has become possible to control RA by administering biologics. However, we experience many patients in which joint swelling and pain are complained despite the administration of biologics, but surgery is not desired. In these patients, triamcinolone acetonide 20 mg and 1% lidocaine hydrochloride 5 ml were injected into the wrist joint for the purpose of reducing joint swelling and pain, and their usefulness and safety were reported [1]. Recently Yoshii et al. [5] reported intra-articular injection is useful for disease activity and pain control, and improvement of activity in daily living. There remains some debate about effect determined by frequency of injection.

"Steroid arthropathy" is caused by steroid injection, and

frequent intra-articular injection of steroid have been reported and cautioned [6]. However, although there have been many reports of intra-articular steroid injections. Chandler et al. [7] and clinical studies have reported that the number of intra-knee steroid injections is not directly related to joint destruction [8, 9]. Koski et al. [10] showed that 68% of patients could maintain clinically normal condition 3 months after intra-articular injection of steroids, and 20% of cases had normal synovial condition and intra-articular condition by ultrasonography. Early 2000s, steroids have been reported to be useful by intra-articular injection of steroids as a treatment for RA patients in Europe and the United States [11-13].

However, there are no reports of long-term intra-articular steroid injection for wrist joint pain in Japan. Nagano et al. [14] conducted a follow-up after wrist arthroplasty prior to the

launch of biologics, with 18 of 45 patients who underwent only synovectomy relapsed. 90 patients with Sauvé-Kapandji method were reported that mild wrist pain occurred in 2 patients. After that, we used a modified Sauvé-Kapandji method with an improved surgical method was performed in 40 patients, and no changes were observed in CHR, RCDR and RRA 33 months after surgery [15].

In simple X-ray images before/after injection, wrist bone destruction showed a significant difference in RRA only triamcinolone acetonide injection group by one-side test ($p < 0.05$), but no significant differences were observed a two-sided test.

However, no significant difference was observed between the only triamcinolone acetonide injection and triamcinolone acetonide injection & the biologics group, so it is considered that the change in RRA due to the triamcinolone acetonide injection is minimum.

On the other hand, in light of the fact that no changed in CHR, RCDR, or RRA were observed even in the group receiving the only anti-rheumatic drug or biologics.

The duration of the illness ranged from 2 to 20 years (average 8.9 years). In other words, it seems that it will take a long time for the wrist joint destruction to progress. As this reason the wrist joint is a non-loaded joint, so the burden on the wrist joint is small.

With the above results and 5 injections / year, wrist joint destruction did not progress, so there was an opportunity to increase the number of injections, which reduced the degree of swelling and pain.

In grade III and IV, the growth of synovium is suppressed in the biologic-administered cases, but the pain due to joint destruction remains. Therefore, we understand that joint injection of triamcinolone acetonide is effective in suppressing the pain. It is thought that the administration of the anti-rheumatic drug alone causes joint destruction, but the joint pain is tolerable and the injection is not desired. In our case, the disease duration was 8.9 years on average, and the age at the time of injection was 64 years on average. It is considered that there are many patients that could not be treated with highly effective rheumatoid drugs or biologics. Injecting triamcinolone acetonide into the wrist joint is an effective method for suppressing joint swelling and pain in patients with advanced OA. It can be handled by injection without any surgery. Nowadays, the progress of OA can be suppressed by using biologics from the onset of RA.

EULAR [16] in 2020 recommends careful injection of steroids into the joints to prevent infection. The author only disinfects the injection site with Povidone iodine, but has not experienced infection.

In recent years, differences between doctors and patients have been reported in RA evaluation methods. That is, doctors regard joint swelling as the main symptom, and patients complain of joint pain. Paul Studenic et al. [17] reports that shared decision making is important to eliminate this discrepancy in evaluation methods. In the future, it will be most important for patients to reduce synovial swelling and pain under basic treatment.

5. Conclusion

1. At an average follow-up period of 5.9 years, no significant changes in the wrist joint were observed on X-ray images regardless of the presence or absence of the administered drug.
2. It was speculated that the unloaded joint was the reason why the progress of wrist joint destruction was not observed in the follow-up test for an average of 5.9 years regardless of the presence or absence of drug use.

Acknowledgements

We would like to express our deep gratitude to Mrs. Mori, a nurse who cooperated in the preparation of this paper.

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