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Research Article

A Comparison Between Methotrexate and Methotrexate with Biological Agents Treatment in Hand Deformities in Patients with Rheumatoid Arthritis

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Received: August 22, 2016; **Published:** October 14, 2016

Abstract

Objective: A comparison between the treatment used and hand deformities in patients with RA. The treatment includes conventional disease modifying drugs (DMARD) or DMARD and biological agents.

Methods: This study involved 70 female patients admitted between February 2016 and August 2016 to The Central Clinical Hospital in Warsaw to the Rheumatology Department. The group was divided as follows: 35 patients treated with methotrexate (MTX) alone and 35 patients treated with MTX and biological agents. 35 additional healthy volunteers were used as a control group.

Results: 35 hand deformities were noted in the group treated with MTX and biological agents and 42 hand deformities were noted in the group treated with MTX alone. The deformities and their frequencies were as follows: subluxation of the metacarpophalangeal joints (MCPJ) (20.0%) in both groups, ulnar deviation of the MCPJ (14.3 and 20.0%) respectively, radial deviation of the wrist (5.7 and 17.1%), boutonniere deformity of the fingers II - V (20% and 25.7%), swan neck deformity (8.6% and 14.3%), Z deformity of the thumb (11.4 and 2.9%).

According to the results, the average and maximum hand endurance, power grip strength, ability to rotate in the proximal and distal radio-ulnar joint were statistically significantly worse in both RA groups compared with the control group. Between both RA groups, the group treated with MTX and biological agents showed statistically significantly better results in number of rotations in radio-ulnar proximal and distal joints in the dominant hand. In the group treated with both MTX and biological agents, results showed a negative correlation in hand endurance, power grip strength and ability to rotate in the proximal and distal radio-ulnar joint, compared with DAS28 and HAQ. With disease progression, strength, ability and hand endurance decreases. It was observed that in the group treated with MTX alone, hand manipulation ability decreased over time with disease progression, but this correlation was not observed in the group treated with both MTX with biological agents. In the group treated with MTX alone, a negative correlation was noted in comparison to HAQ.

Conclusion: Effective management of RA includes slowing down the disease progression. The mode of treatment has an important role as wrist, hands and finger joints are most commonly affected.

Keywords: *Rheumatoid arthritis; Hand endurance; Handgrip strength; MTX; Biological agents*

Introduction

Rheumatoid arthritis (RA) is the most common inflammatory arthritis. It affects from 0.5 to 1% of the general population worldwide. The joints most commonly involved first in RA are the metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints, metarsophalangeal joints, wrist and knee. The disease affects symmetrically small and medium sized joints. The primary site of immune activation in RA is the synovium. Hallmark of the disease are infiltration of the synovium with mononuclear cells, especially T cells and macrophages, and synovial intimal lining hyperplasia. Immune cells invade the synovium, leading to the formation of inflammatory "pannus", which causes cartilage breakdown, bony erosion and loss of function of the affected joints. The patient has stiffness with movement and limited motion affected joints, which are swollen, painful and tender. Tendon and bursal involvement are frequent in early disease.

Hands deformities which are characteristic for RA cause distention of the joint capsules, muscle imbalances, ligament laxity, subluxations and decreased motion in the joints involved [1]. These deformities cause severe disabilities in patient and the inability to grip of hands provide to severe disability and the inability to grip.

Mechanical factors that damage rheumatoid joint are excessive movement and overloading the joints. Not only the joints but also the tendons are destroyed. The degenerative changes in tendons and joints can lead to spontaneous ruptures of tendons, which exacerbates dysfunctions of the hand.

The wrist

The wrist is the most common joint involved in RA. Typical deformities include scapho-lunate dislocation, translocation of the carpus in a lunar and volar direction, carpal supination, radial deviation of the carpus, dorsal subluxation of the ulnar and shortening of the wrists. The extensor carpi-ulnaris tendon often subluxes volarly. The characteristic changes include: radial deviation at the wrist with ulnar deviation of the digits often with palmar subluxation of the proximal phalanges (Z deformity) [2].

Wrist deformities include volar subluxation with a visible step opposite to the radiocarpal joint and radial deviation of the carpus from the axis of the wrist and hand.

The radial-wrist joint

The radial-wrist joint is one of the key elements determining the efficiency of the hand. Changes in the ligaments affects the anatomy of the metacarpals. This is due to the disorder in the arch cross-arm and hand in the development of deformation. Synovitis is observed especially around the distal ulnar, the area of the scaphoid and the temporal styloid process [2].

Radial deviation deformity consists of radial deviation in the radial-wrist joint and ulnar deviation of MCPJ in phalanges II-V. Destabilization of the joints plays an important role in this deformity.

MCP joints

Deformities of the MCP joints include flexion deformities, volar subluxation, which may be seen as a step, ulnar drift (often in combination with radial deviation of the wrist).

The MCPJ strengthen the longitudinal and transverse arch systems of the hand. Additionally, these joints guide active movements of the fingers in 2 degrees of freedom, while allowing sufficient laxity for passive accessory movements. In healthy hands, stability and mobility is maintained due to interactions between the joints, periarticular connective tissue and muscles. The two most common deformities in the MCPJ in patients with RA are ulnar "drift" and palmar subluxation [3].

The most frequent deformity of the hand affects the MCP joint and it is characterized by a volar subluxation of the proximal phalanges and ulnar drift of the finger [4]. This ulnar deviation of the MCP joint is usually caused by chronic synovitis, which disrupts the joints ligamentous support [3]. Ulnar deviation of the fingers is very characteristic for RA.

Frequently, the MCP ulnar deviation is accompanied by flexion and palmar subluxation in the proximal phalanges in the MCP joints. This is the result of contractures of the short muscles of the hand, with a tendency for ulnar deviation of finger and contractures of palmar ligaments [3].

The thumb

The thumb is frequently involved in RA patients. The deformities can be grouped according to the thumbs' posture. Deformity can be determined by a complex interaction between primary joints, tendon function and integrity. Joints adjacent to the primary affected joint are usually caused in the opposite direction. If they do not, we should suspect tendon ruptures [4].

Swan neck thumb deformity - CMC joint flexed, adducted, and subluxed, MP joint hyperextended, IP joint hyperextended. Disruption of the biomechanics in a normal thumb activity often leads to significant loss in the patient's ability to carry out daily activities. Activities such as buttoning clothing or manipulating small objects are difficult if the patient lacks either stability or control of the thumb joints.

Boutonniere thumb deformity - CMC joint is not involved, MP joint flexed, IP joint hyperextended. The boutonniere deformity is the most common rheumatoid thumb deformity. This consists of MP joint flexion and IP joint hyperextension.

Hyperextension of the IP joint is the result of the altered pull of both the intrinsic muscles and the extensor pollicis longus and it occurs secondarily. Each time the patient tries to pinch with the thumb, a cycle of MP joint flexion and IP joint hyperextension is initiated. With time, the IP joint deformity nears the MP joint deformity, and the result is often a $90^{o}/90^{o}$ deformity [4].

Swan neck deformity starts at the carpometacarpal (CMC) joint with subluxation of the first metacarpal, which then assumes an adducted and flexed position. After CMC joint subluxation and metacarpal flexion and adduction, the MP joint hyperextends and the distal joint flexes. This deformity is the opposite of the common boutonniere deformity.

The extensor pollicis longus is the most likely flexor tendon to rupture in rheumatoid patients. Rupture of the EPL occurs from infiltrative tenosynovitis. The functional loss varies and the tendon rupture may go undetected for some time.

Inflammatory changes in the thumb joint leads to loss of resistance, and consequently, the loss of function of the hand grip (monkey grip). Deformities of thumb play an important role, because the efficiency of the whole hand is dependent in 40-50% on the actions of the thumb [4].

PIP joints

Deformities of the PIP joints usually result from lack of ligament support.

The fingers

Besides the ulnar deviation of fingers, the Boutonniere (BN) finger and the swan neck finger (SN) and are the most common deformities detected in RA patients [5]

Flexion and extension contracture in the proximal and distal interphalangeal (IP) joint of the fingers lead to characteristic swan-neck deformity (flexion of the DIP and hyperextension of the PIP) or boutonniere deformity (flexion of the PIP and hyperextension of the DIP).

The SN deformity (SND) is characterized by a flexion of both MCP and DIP joints associated with the hyperextension of the PIP joint [6]. The SND represents the result of pathology involving PIP, DIP, MCP joints and the wrist [7].

The swan neck finger is the most severe deformity in RA. The patient loses fingertip grip and cannot close the hand. Only the ability to grip between the thumb and index finger on the radial side remains. Deformation of SND significantly limits the ability to grip. Hand movement ability is reduced by half. In this deformity the proximal and middle phalanx do not participate in the grip. This is often accompanied by ulnar deviation of the fingers. This results in fixed hyperextension of the PIP joints, which changes their anatomy and leads to a reduction in gripping force. Thus, both the quality of the grip and grip strength is limited.

Boutonniere deformity (BND) is characterized by extension of both MCP and DIP joints and a flexion of the PIP joint [8]. The BND is caused by intra-articular proliferation of the synovium of the PIP joint, which distends the capsuloligamentous apparatus, leading to extension of both MCP and DIP joints associated with a flexion deformity of the PIP joint [8].

A useful parameter to evaluate in RA patients is handgrip, since muscle weakness is a common symptom. One of the most important problems of rheumatoid hands is the reduced ability to grip. Impairment of grip is due to the limited mobility in PIP, DIP and MCP joints. Decreasing movement of the IP joint reduces the grip even less than in the changes in the MCP joint. There are three main reasons for the limitation of grip: muscles, ligaments and joints.

1. The joint mechanism depends on a joint capsule contracture or a joint surface deformation.
2. The ligament mechanism depends on contracture of collateral ligaments in the MCP joint.

Usually, ligaments are relaxed in extension, while contract as the proximal phalynx bends, increasing the pressure of the articular surface and thereby improving grip strength. During contractures, tension of ligaments rapidly increases during bend tests, so that the function of the hand grip is limited. Limitation of grip may be a result of contractures of two muscle groups, both internal and external.

Hand gripping plays an important role in performing everyday activities. The hand grip is a tool that enables objects to be grasped and manipulated. The proper functioning of the hand consists of 3 elements:

1. Grip quality
2. Grip value
3. Ability to handle the arm.

The aim of this study was to compare the treatment of RA patients, using MTX alone or in combination with biological agents, on the types at hand deformities at these patients.

Methods

Patients

Seventy female patients were enrolled in the study, 35 patients were treated with methotrexate alone and 35 with methotrexate and biological agents. The patients were admitted to the Central Clinical Hospital in Warsaw in the department of Rheumatology and Internal Diseases between February 2016 to August 2016. All patients fulfilled the 1987 ARA diagnostic criteria for RA [9].

A protocol was designed to record age, duration of the disease, rheumatoid factor, stage of RA according to Larsen and Dale [10], SNJ, PNJ, DAS28 [11], VAS (pain), VAS (disease activity), HAQ [12] and types of deformities.

A detailed history was taken and full clinical examination was done. The hands were examined to detect a dominant and non-dominant hand, the presence of subluxation of the wrist, radial deviation of the wrist joint, ulnar deviation of the MCPJ, subluxation of the MCPJ, boutonniere deformity of the fingers, swan-neck deformity of the fingers, Z deformity of the thumb, and handgrip strength.

The control group consisted of 35 female volunteers who work at the hospital.

The present study was approved by the local research ethics committee (protocol number 42/2015), and all the subjects signed a free informed consent before participating in the study.

Assessment

Radiographic damage was evaluated according to Larsen and Dale [10]. All of the women answered the Health Assessment Questionnaire (HAQ) [12] and were submitted to evaluate handgrip strengths.

To measure the handgrip strength, a standard adjustable-handle Jamar hydraulic dynamometer (model 18937009) was used on a (Kg) scale. For standardization, it was set at the second handle position for all subjects as suggested by the American Society of Hand Therapists [13]. The handgrip strengths of dominant and non-dominant hands were measured with the subjects seated on a chair, hips and knees flexed at 90°, feet kept on the floor, upper limbs in adduction position, elbow at 90° and wrists in neutral position. Each woman performed three sustained contractions for 6s, with a 30s rest interval between each contraction for both handgrips. A mean value was obtained from the three measurements. All evaluations were made by one examiner only.

The subjects sat with their shoulders adducted and neutrally rotated, elbows flexed at 90° and forearms and wrists in neutral position. They then had to grip with maximal efford for 3s. Verbal encouragement was given consistently throughout all measurements. Scores of three consecutive trials were recorded for each strength test for each hand. An average of these three trials and the highest grip strength for each hand was used for analysis. The trials for each measurement were separated by a rest of at least one minute to minimize fatigue.

Hand endurance was measured using a dynanometer. The examination depended on recording the amount of time (in seconds) the patient was able to grip the dynanometer using maximum effort. The normal standard was set as 60s before the examination. Next, the manipulation ability of the hands was assessed. This was done by recording the maximum number of rotations done by patients in the proximal and distal radioulnar joint, over a time span of 10s. This was done 3 times and the number of rotations was recorded.

Body weight and height were measured during the exam and values were expressed in kilograms and centimeters, respectively. To calculate BMI, height was converted into meters (BMI = weight/height^2).

Pharmacological treatment

In the first group, patients were treated with MTX as DMARD in doses of 25 mg per week, po (orally).

In the second group, besides MTX (as DMARD) patients were given the following biological agents:
TNF inhibitors 29 (Infliximab - 9, Adalimumab 10, Golimumab 6, Certolizumab 2, Etanercept 2), tocilizumab - 4, Rituximab 2.

Statistical analysis

In the first group, patients were treated with MTX as DMARD in doses of 25 mg per week, po (orally).

1. A value for an average quantitable variable was assessed on the basis of the ANOVA test. Post-hock analysis was performed with Tukey's test.

2. The Chi square test or the Fisher's exact test was used to check the discreet variables, presented in number and proportion. The threshold of significance used was 5%.

Results

Demographic and clinical characteristics of the groups are shown in Table 1.

Parameters	MTX+biological agent group N = 35	MTX group N = 35	Control group N = 35	p
Age	52.4 ± 12.4	56.4 ± 11.1	51.2 ± 10.6	0.2220
Female	35 (100%)	35 (100%)	35 (100%)	
BMI	26.2 ± 5.3	26.7 ± 6.6	26.7 ± 5.9	0.9442
Intellectual work	23 (65.7%)	22 (62.9%)	16 (45.7%)	0.1860
Right hand dominance	35 (100%)	35 (100%)	35 (100%)	1.000
RA duration	14.0 ± 7.6	12.5 ± 8.2	-	0.6251
Stage III	29 (82.9%)	32 (91.4%)	-	0.4773
Stage IV	6 (17.1%)	3 (8.6%)	-	
Tender joint	2.0 [0-6.0]	7.5 [2.0-10.0]	-	0.0074
Swollen joint	2.0 [0.0-3.0]	0.0 [0.0-6.0]	-	0.8300
VAS (pain)	23.7 ± 22.8	38.8 ± 21.3	-	0.0100
VAS (disease activity)	30.2 ± 22.7	42.8 ± 18.9	-	0.0222
VAS (morning stiffnes)	32.5 [0.0 – 50.0]	40 [20 – 60]	-	0.0307
DAS 28	3.53 ± 1.35	4.44 ± 1.21	-	0.0090
HAQ	0.65 ± 0.58	1.09 ± 0.61	-	0.0063

Table 1: *Baseline demographic and clinical characteristics of study population.*

No statistically significant differences were found between the examined RA groups apart from the DAS 28, HAQ, VAS (pain, disease activity, morning stiffness) values and the number of tender joints, which were statistically significantly lower in the "biological agent" group. All female patients had the right hand as dominant.

Values of laboratory data are shown in table 2. There was a statistically significant difference between the average values of erythrocytes and hemoglobin. In the "biological agent" group there were a statistically significant higher values of erythrocytes and hemoglobin.

Parameters	MTX+biological agent group N = 35	MTX group N = 35	P
RF	26.7 [13.3 – 168.5]	52.5 [11.4 - 212.0]	0.4471
ESR (mm/h)	24.4 ± 17.0	35.7 ± 28.2	0.0714
CRP (mg/l)	4.7 [3.6-13.4]	5.9 [4.3 -22.4]	0.2090
Leukocytem (G/l)	7.70 ± 2.34	7.56 ± 2.31	0.8228
Erythrocytes (T/l)	4.41 ± 0.29	4.15 ± 0.46	0.0128
Hemoglobin (g/l)	12.89 ± 0.73	12.0 ± 1.5	0.0053
Thrombocytes (G/l)	312.0 ± 73.4	294.8 ± 85.6	0.4149
AspAT (U/l)	20.5 ± 6.4	20.9 ± 12.0	0.9030

AlAT (U/l)	26.3 ± 16.5	19.2 ± 10.6	0.0570
Bilirubin (mg/dl)	0.38 ± 0.13	0.43 ± 0.17	0.2328
Creatinine (mg/dl)	0.66 ± 0.10	0.73 ± 0.14	0.0422
eGFR (ml/min)	88.1 ± 19.1	86.3 ± 18.7	0.7290

Table 2: *Values of laboratory data in RA patients.*

35 hand deformities were recorded in the group treated with MTX and biological agents and 42 treated with MTX only. The frequency of deformities was: swan neck deformity (8.6% and 14.3%), boutonniere deformity of the fingers II – V (20% and 25.7%), Z deformity of the thumb (11.4 and 2.9%), ulnar deviation of the MCPJ (14.3 and 20.0%), radial deviation of the wrist (5.7 and 17.1%), and subluxation of the MCPJ (20.0%) in both groups.

Distribution of different combinations of hand deformities are shown in Table 3 and 4. No statistically significant differences were found between examined RA groups and with the different combinations of hand deformities.

Hand deformity	MTX + biological agents group N = 35	MTX group N = 35	P
Swan neck fingers II – V	3 (8.6%)	5 (14.3%)	0.7096
Z deformity of thumb	4 (11.4%)	1 (2.9%)	0.3565
Buttonniere fingers II – V	7 (20.0%)	9 (25.7%)	0.5692
Buttonniere thumb	2 (5.7%)	4 (11.4%)	0.6737
Ulnar deviation of the wrist joint	3 (8.6%)	1 (2.9%)	0.6139
Radial deviation of the wrist joint	2 (5.7%)	6 (17.1%)	0.2595
Ulnar deviation of II-V MCP joints	5 (14.3%)	7 (20.0%)	0.5259
Subluxation of wrist joint	2 (5.7%)	2 (5.7%)	1.000
Subluxation of MCP joint of II-V fingers	7 (20.0%)	7 (20.0%)	1.000
All deformities	35	42	NS

Table 3: *Distribution of the different combinations of hand deformities.*

Swan neck: Hyperextension of the proximal interphalangeal joint with flexion of distal interphalangeal joint; Boutonniere finger: Flexion of the proximal interphalangeal joint with hyperextension of distal interphalangeal joint; Z-deformity of thumb: Flexion of the metacarpophalangeal joint and hyperextension of the interphalangeal joint; Ulnar deviation: Ulnar deviation of metacarpophalangeal joints

Parameters	MTX + biological agents group	MTX group	P
Without deformity	22 (62.9%)	21 (60.0%)	0.8245
Single deformity	6 (17.1%)	8 (22.9%)	
More than one deformity	7 (20.0%)	6 (17.1%)	

Table 4: *Number and % of patients without deformity, with a single deformity and with more than one deformity.*

The power grip strength, hand endurance and hand manipulation ability was compared between the RA groups and the control group and the results are show in table 5. It was observed that the average and maximum hand endurance, power grip strength, ability to rotate in the proximal and distal radio-ulnar joint were statistically significantly worse in both RA groups compared to the control group. Between both RA groups, the group treated with MTX and biological agents showed statistically significantly better results in the number of rotations in the proximal and distal radio-ulnar in the dominant hand. In the group treated with both MTX and biological agents, results showed a negative correlation in hand endurance, power grip strength and ability to rotate in the proximal and distal radio-ulnar joint, compared with DAS28 and HAQ. With disease progression, strength, ability and hand endurance decreases. It was observed that in the group treated with MTX alone, hand manipulation ability decreased over time with disease progression, but this correlation was not observed in the group treated with both MTX with biological agents. In the group treated with MTX alone, a negative correlation was noted in comparison to HAQ.

	MTXbiologic agent (1)	**MTX (2)**	**Control (3)**	**ANOVA 1 vs 2 vs 3**	**1 vs 2**	**1 vs 3**	**2 vs 3**
Power grip strength was measured with a dynamometer							
Right hand	kg	kg	Kg	P	P	p	P
Maximum	15.0 ± 7.2	13.4 ± 7.3	33.8 ± 6.8	< 0.0001	0.6638	< 0.0001	< 0.0001
Average	13.5 ± 7.0	11.7 ± 6.8	32.6 ± 6.5	< 0.0001	0.5818	< 0.0001	< 0.0001
Left hand							
Maximum	14.3 ± 6.3	13.7 ± 6.8	31.1 ± 6.7	< 0.0001	0.9341	< 0.0001	< 0.0001
Average	13.3 ± 6.3	11.9 ± 6.4	31.6 ± 6.5	< 0.0001	0.6724	< 0.0001	< 0.0001
Hand endurance measured with a dynamometer							
Right hand	S	s	S	p	P	p	p
Maximum	43.5 ± 22.0	35.9 ± 23.6	60.0 ± 0	0.0002	0.2926	0.0098	< 0.0001
Average	41.4 ± 22.5	31.5 ± 23.1	60.0 ± 0	< 0.0001	0.1258	0.0032	< 0.0001
Left hand							
Maximum	45.0 ± 20.6	34.2 ± 22.3	60.0 ± 0	< 0.0001	0.0640	0.0129	< 0.0001
Average	41.3 ± 21.3	30.7 ± 22.9	60.0 ± 0	< 0.0001	0.0832	0.0021	< 0.0001
Number of rotation in radio-ulnar proximal and distal joints (hand manipulation ability)							
Right hand	**Number of rotation in 10s**	**N of rotation in 10s**	**N of rotation In 10s**	**p**	**P**	**p**	**P**
Maximum	6.8 ± 2.8	5.1 ± 2.5	11.5 ± 2.6	< 0.0001	0.0305	< 0.0001	< 0.0001
Average	6.2 ± 2.6	4.7 ± 2.5	10.7 ± 2.4	< 0.0001	0.0465	< 0.0001	< 0.0001
Left hand							
Maximum	6.3 ± 2.6	5.1 ± 2.3	10.2 ± 2.5	< 0.0001	0.1271	< 0.0001	< 0.0001
Average	6.0 ± 2.4	4.7 ± 2.3	10.3 ± 2.3	< 0.0001	0.0665	< 0.0001	< 0.0001

Table 5: *The comparison of grip strength, hand endurance measurement in seconds, and manipulation ability of hands.*

Parameters	MTX + BIO group N = 35			MTX group N = 35		
	DAS28	HAQ	RA duration	DAS28	HAQ	RA duration
Grip strength max R hand	r = -0.61 p = 0.0004	r = -0.53 p = 0.0026	r = -0.32 p = 0.08	r = -0.39 p = 0.0419	r = -0.49 p = 0.0069	r = -0.30 p = 0.11
Grip strength mean R hand	r = -0.64 P = 0.0001	r = -0.54 p = 0.0018	r = -0.32 p = 0.052	r = -0.43 p = 0.02	r = -0.50 p = 0.0051	r = -0.23 p = 0.21
Grip strength max L hand	r = 0.53 0.0025	r = -0.50 p = 0.0051	r = -0.24 p = 0.19	r = -0.34 p = 0.07	r = -0.47 p = 0.0082	r = -0.10 p = 0.61
Grip strength mean L hand	r = -0.66 P < 0.0001	r = -0.55 p = 0.0015	r = -0.31 p = 0.058	r = -0.41 p = 0.0316	r = -0.49 p = 0.0058	r = -0.18 p = 0.33
Hand max endurance Right hand	r = -0.63 P = 0.0002	r = -0.58 p = 0.0007	r = -0.16 p = 0.39	r = -0.33 p = 0.08	r = -0.44 p = 0.0140	r = -0.31 p = 0.09
Hand mean endurance Right hand	r = -0.64 P = 0.0002	r = -0.56 p = 0.0012	r = -0.20 p = 0.30	r = -0.32 p = 0.09	r = -0.50 p = 0.0053	r = -0.33 p = 0.07
Hand max endurance Left hand	r = -0.64 P = 0.0001	r = -0.58 p = 0.0009	r = -0.01 p = 0.95	r = -0.34 p = 0.07	r = -0.54 p = 0.0021	r=-0.32 p=0.08
Hand mean endurance Left hand	r = -0.69 p= < 0.0001	r = -0.60 p = 0.0005	r = -0.17 p = 0.37	r = -0.33 p = 0.09	r = -0.51 p = 0.0037	r=-0.30 p = 0.11
N. of rotation max–R. hand	r = -0.61 p = 0.0004	r = -0.67 p < 0.0001	r = -0.25 p = 0.19	r = -0.21 p = 0.29	r = -0.48 p = 0.0067	r = -0.45 p = 0.0134
N. of rotation mean–R. hand	r = -0.63 p = 0.0002	r = -0.68 p < 0.0001	r = -0.29 p = 0.12	r = -0.20 p = 0.31	r = -0.49 p = 0.0061	r = -0.44 p = 0.0139
N. of rotation max–L. hand	r = -0.58 p=0.0009	r = -0.61 p = 0.0003	r = -0.08 p = 0.67	r = -0.16 p = 0.41	r = -0.42 p = 0.0198	r = -0.51 p = 0.0036
N. of rotation mean–L. hand	-0.64 P = 0.0001	r = -0.69 p < 0.0001	r = -0.26 p = 0.17	r = -0.18 p = 0.35	r = -0.48 p = 0.0077	r = -0.48 p = 0.0069

Table 6: *The correlation between grip strength, hand endurance measurement in seconds, and manipulation ability of hands and DAS28, HAQ and RA duration in both RA groups.*

Discussion

Rheumatoid arthritis (RA) is a chronic inflammatory disease and approximately 70% of RA patients develop pathologies of the hand [14]. Wrist involvement is seen in up to 50% of patients within 2 years of diagnosis and in up to 90% of patients following diagnosis [15]. A destructive overgrowth of the synovial tissue (pannus) is formed with prolonged synovitis. This can lead to mechanical injury due to the high pressure in the joint and the eroding effect of the pannus. RA causes pain, swelling, joint stiffness leading to impaired hand func-

tion and difficulty with work and daily activities. Hand deformities in rheumatoid arthritis have negative impact on the quality of life of RA patients [16]. RA is characterized by its lack of spontaneous remission; thus without medical management, the disease usually leads to progressive deterioration of hand function. Until recently, the rate of permanent work disability has been high despite development of anti-rheumatic therapy. Over the first 20 years at RA, joint damage progresses constantly It accounts for about 25% of disability in established RA [17].

In this study we examined RA patients, who were treated with biological DMARDs and compared them with patients who were treated with conventional DMARDS only (MTX). Hand deformities were assessed in both groups and it was observed that in the group treated additionally with biological agents, we obtained statistically significant lower values of DAS28, HAQ, VAS and a lower number of tender joints. This was assumed as we know biological agents have strong anti-inflammatory action. There was also a statistically significant difference between the average values of erythrocytes and hemoglobin.

Horsten., *et al*. [18] in their study determined the prevalence of hand and wrist symptoms and impairments, and the resulting limitations in activity in relation to disease duration in 200 RA patients in 4 categories of disease duration: 2-4, 4-6, 6-8 and ≥ 8 years. Of all patients, 94% suffered from at least one symptom, and 67% had at least one impairment, mostly from the earliest stages onwards. A high prevalence of hand and wrist symptoms and impairments is often already present after 2 years of disease duration.

The disease duration in this study was similar so the differences are the results of modes of treatment. In our study we compared the grip strength, hand endurance measured with a dynamometer and number of rotations in proximal and distal radio-ulnar joints in RA groups and in the control group. In this study we observed better results in patients treated more aggressively, with MTX as well as biological agents.

Bodur., *et al*. [19] in their study assessed grip strength, lateral, tip and three-fingered pinch in 105 RA patients. Disease duration, grip strength, pinch measurement, clinical and laboratory activity parameters were strongly correlated with hand disability. Grip strength and pinch measurements were the most comparable parameters in hand disability.

Papers regarding early RA and development of hand deformities are incredibly interesting [20-23]. Johnsson and Eberhards [20] stated that more than half of the patients in early RA had developed hand deformities after 10 years. The most prevalent deformities are ulnar deviation of the MCP joints, button hole deformity and swan neck deformity. The majority of deformities occurred during the first years of disease. Presence of hand deformities had an impact on daily life function and added useful prognostic information, being an early sign of a more severe disease.

Sheehy., *et al*. [21] concluded, that hand grip testing and subsequent conversion to z scores corrected for age and gender correlate with disease activity in early RA. They have shown that the grip strength z scores can discriminate between various disease states, and the strength seems to return to near normative data when the disease is in remission. Bjork., *et al*. [22] assessed hand function in women and men with early rheumatoid arthritis. In their prospective study over three years (the Swedish TIRA project) they stated that hand function was profoundly affected at diagnosis of RA, but improved significantly within 3 months and remained stable (but still affected) over 3 years. Women on average had significantly lower grip force than men.

Adams and Burridge [23] in their study concluded that in the early RA population handgrip strength as an accurate indicator of upper limb ability. Ulnar deviation at the MCP joints shows only a weak to moderate association with upper limb functional activity and ability. Although the Disability of the Arm, Shoulder and Hand (DASH) questionnaire and the Grip Ability Test (GAT) were strongly correlated, the DASH was a more discriminating measure than the GAT in assessing upper limb ability in this sample population.

Cima., *et al*. [24] cited that functional performance in RA hands is correlated with the grip strength. In their group of RA female patients, the mean age being 53, the mean handgrip strength of a dominant hand was 12 kg.

In our study the RA female patients treated with MTX and with biological agents the mean value of handgrip strength of a dominant hand was 13.5 kg, in the second group treated only with MTX the mean handgrip strength was 11.7 kg.

In the patients treated with MTX and with biological agents the maximum value of handgrip strength of a dominant hand was 15 kg, in the second group treated only with MTX it was 13.4 kg, but in the control group it was 33.8 kg.

Bergstra., *et al*. [25] cited that in literature the maximum strength for a healthy woman aged 50-54 years was reported to be 33.7kg for power grip. According to Gunther., *et al*. [26], which examined grip strength in healthy Caucasian adults, they stated that grip strength is significantly less in women than in men. Observed values in women ranged between 9 kg and 51 kg (right hand) and 7 kg and 45 kg (left hand). In both women and men, they observed an increase of grip strength until a maximum around the age of 35 years. Further on, increasing age was inversely related with grip strength. Grip strength is significantly higher in the right hand in both sexes. Mean values in women are 29 ± 7 kg for the right hand and 27 ± 7 kg for the left hand, thus strength of the left hand averages 95% of the right hand. Patients with RA are known to have lower grip strength compared to age and sex matched control [25].

Eberhardt., *et al*. [27] the goal of their work was to assess the usefulness of hand function measurements in a study of treatment effects of tumour necrosis factor (TNF) blockers and to define the relationship between different hand function tests and also relate hand function to general disability and disease activity. The study group consisted of 49 patients with established RA who were followed for 1 year while on TNF inhibitors. HAQ, DAS28, grip and pinch force, and GAT showed a highly significant improvement over time. The authors concluded that patients with advanced RA attained considerable improvement in hand function that was only partly reflected by measures of general disability and disease activity.

We conclude that rheumatoid arthritis is an important disease that affects the hand and causes deformities.

A key issue in this disease is to slow disease progression, mainly via the use of drug treatment, which could vastly improve the patients' quality of life, mainly by slowing down disease destruction of the wrist, hands and finger joints.

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