

Sustainability of Lower Disease Activity Levels in a Rheumatoid Arthritis Patient's Cohort Maintaining High Adherence to Appointments and Treatment

Pedro Santos-Moreno (✉ pedrosantosmoreno@hotmail.com)

Biomab IPS

Juan Alvis-Estrada

ALZAK Foundation

Laura Villarreal

Biomab IPS

Maria Carrasquilla-Sotomayor

ALZAK Foundation

Omaira Valencia

Universidad de Los Andes

Fernando Rodriguez-Florido

Biomab IPS

Nelson Alviz-Zakzuk

ALZAK Foundation

Research Article

Keywords: rheumatoid arthritis, treatment, comprehensive healthcare, adherence

DOI: <https://doi.org/10.21203/rs.3.rs-150979/v1>

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Abstract

Objective: To describe sustainability of low disease activity levels in patients with rheumatoid arthritis (RA) who were followed-up in a specialized center based on a healthcare model maintaining adherence to appointments and treatment.

Material and methods: As part of a comprehensive RA healthcare model, services related to care like rheumatology, physiatry, physiotherapy, occupational therapy, nutrition, and psychology can be found in the specialized center. Patients with RA are followed-up at least six times a year to ensure retention in care model and adherence to the treatment. Using this approach, a cohort of RA patients were followed-up during 2018. Demographical and clinical data were extracted retrospectively from the electronic health records. The association between clinical and demographic variables was studied by means of the Chi-square test and analyzed using the McNemar test for changes in disease activity levels.

Results: 2,239 RA patients were followed-up, 82.76% were women. The average disease duration was eight years (IQR: 3-18 years). During the follow-up year, 91.62% of patients with conventional therapy had at least six rheumatology appointments, while for those who received biological therapy 81.51%. For the ones treated with biological therapy, there were no significant changes for each level of disease activity during study period; nevertheless, in patients who received conventional therapy there was a significant increase of patients in remission (p -value = 0.004).

Conclusions: The results evidence that the model used guarantees high levels of adherence for medical appointments and keeps remission levels for RA under control.

Key Points

1. A multidisciplinary care model in RA improves adherence to medical appointments and treatment.
2. The improvement in adherence rates improves the sustainability to maintain low levels of disease activity by RA patients.

Introduction

Rheumatoid arthritis (RA) is an autoimmune and chronic disease characterized by being multisystemic and inflammatory, and by having multifactorial etiology, along with causing pain, rigidity, and swelling of the joints (1, 2). Studies about RA establish that early diagnosis and treatment prevent joint damage and improves people's long-term situations, allowing them to engage in routine activities normally. Additionally, low impact exercises, such as walking, strengthen the muscles, and relieve the pressure in the joints improve the general health condition (3–6). Nowadays, two types of treatment are administered for RA: first, conventional disease-modifying antirheumatic drugs (DMARDs), and second, biologic DMARDs. The former are usually used in previous or early disease stages, while the latter are used in stages where the severity of the disease is higher, but they are high cost medications (3).

The prevalence of RA varies depending on the population, but in general it is between 0.2-5% around the world (7). In developed countries, the prevalence varies between 0.3-1% (8); in the United States only, by 2013–2015, it was estimated that per year, approximately 22% of the adult population had some variety of arthritis (9). In Latin America, studies have reported prevalence values in the general population of 0.9% and 0.45%, in countries like Argentina and Brazil, respectively (10, 11); for Colombia, in 2005 a prevalence of 0.9% in the general population was estimated (12).

On the other hand, as one of the implications of living with RA, there is a progressive loss of joint functionality; suffering this disease causes disability and impairs the quality of life, which leads to an important economic burden for the health system, the patients, their families, and society in general, mainly for using biologic treatment (13, 14).

To evaluate RA activity, clinical and laboratory parameters and the indicators of the activity of the disease have been used, for instance the American College of Rheumatology (ACR) criteria, the Simplified Disease Activity Index (SDAI), and the Disease Activity Score (DAS) (15). The latter has a modified version known as DAS28 (16), which classifies patients with RA into four activity levels, namely: remission (REM), low activity (LDA), moderate activity (MDA) and severe disease activity (SDA). This index has become one of the main indicators for therapeutic decision-making, including starting and changing biological treatments (17).

Thus, it is important to study how DAS28 scores vary over time in patients treated with conventional DMARDs and biologic DMARDs, depending of adherence to appointments and treatment. This study describes disease activity levels (DAS28) in a cohort of patients with RA who received conventional and biological therapy in a SCRA in Colombia, in which the care model is focused on the patient adherence to appointments and treatment.

Material And Methods

Study design, population, and context

We described a retrospective RA patient's cohort who went during a year to the SCRA in Bogota, Colombia. This center follows a patient centered care model based on a treat to target strategy, in which different services related to patient care like rheumatology, physiatry, physiotherapy, occupational therapy, nutrition, and psychology, are easily accessible (18). Patients have access to rheumatology consultation at least three times per year in order to ensure retention in care and adherence to treatment; but in general, the idea is to assure 6–9 consultations per year. On the other hand, the health care model used in the SCRA classify by the DAS28 score, the needs of frequency of appointments, LDA every 9–10 weeks; remission every 11–12 weeks; while MDA every 5–6 weeks and HDA every 3–5 weeks (Fig. 1).

The study population was composed of RA patients who were 18 years-old or older who attended the center and had at least six appointments per year in all specialties.

The information used for this study came from patient's electronic health records including data about comorbidities, RA disease duration, sociodemographic data, DAS28 measurements for each appointment, and the type of treatment.

Statistical analysis

Descriptive relative and absolute frequency statistics were used to evaluate demographic variables, clinical and treatment backgrounds. Means, medians, interquartile ranges, and standard deviations were also used to analyze diagnosis time and patients ages. The relations among categorical variables were studied by using the chi-square test. Also, the McNemar test was used to analyze whether disease activity levels DAS28 (remission, LDA, MDA, and SDA) changed between the first and sixth appointment during the follow-up year. Lastly, the score tendency of DAS28 during the study year was established by controlling the invariable factors like gender and the presence or absence of comorbidities. The statistical analysis of the data was conducted in R version 3.5.2.

Ethical considerations

The BIOMAB institutional research board (IRB) in ordinary session on April 4, 2019, registered in folder 25, evaluated and approved the research, which was reviewed in the medical, methodological, and bioethical aspects; the IRB also approved the collection and analysis of information from medical records. This study was classified as research with no risk for the patients, according to resolution Number 8430 of 1993 of the Colombian Ministry of Health (19); no data that can identify the patients were published or disclosed, but an informed consent form was obtained from patients.

Results

Demographic characteristics and background

In total, 2,239 RA patients were followed-up between January and December 2018 at SCRA; patients had a disease diagnosis time mean of eight years (IQR: 3–18 years) and a treatment median time of two years at the SCRA (SD: \pm 2 years). The population consisted mainly of women (82.76%, n = 1,853). Additionally, 95.27% of the patients had, at the start of the cohort, an age range of over 40 years of age and a mean of 62 years (IQR: 54–69 years) (Table 1).

Table 1
Demographic and clinical characteristics of the patients

Characteristic	Conventional therapy (N = 1265)	Biological therapy (N = 974)	Total (N = 2239)
Time with RA (years)			
Mean (SD)	12 (11)*	13 (11)**	12 (11)***
Median (IQR)	7 (3–17)*	9 (2–20)**	8 (3–18)***
Time in care at SCRA (years)			
Mean (SD)	4 (2)	4 (2)¥	4 (2)¥¥
Median (IQR)	4 (2–6)	4 (2–7)¥	4 (2–6)¥¥
Age (years), median (IQR)			
Mean (SD)	63 (11)	59 (12)	61 (12)
Median (IQR)	64 (56–71)	59 (52–66)	62 (54–69)
Age group (years) [% (n/N)]			
18–30	0.79 (10/1265)	2.36 (23/974)	1.47 (33/2239)
31–40	2.06 (26/1265)	4.83 (47/974)	3.26 (73/2239)
41–50	9.72 (123/1265)	12.63 (123/974)	10.99 (246/2239)
50–60	24.43 (309/1265)	35.22 (343/974)	29.12 (652/2239)
61–70	35.65 (451/1265)	29.98 (292/974)	33.18 (743/2239)
> 70	27.35 (346/1265)	14.99 (146/974)	21.97 (492/2239)
Gender: female [% (n/N)]	82.13 (1039/1265)	83.57 (814/974)	82.76 (1853/2239)
Comorbidities [% (n/N)]			
High blood pressure	24.94 (303/1215)	21.14 (182/861)	23.36 (485/2076)

* missing = 209, ** missing = 68, *** missing = 277

¥ missing = 1, ¥¥ missing = 1

Characteristic	Conventional therapy (N = 1265)	Biological therapy (N = 974)	Total (N = 2239)
Diabetes mellitus	4.66 (56/1203)	4.9 (42/857)	4.76 (98/2060)
Heart disease	0.5 (6/1203)	0.47 (4/850)	0.49 (10/2053)
Chronic kidney disease	0.58 (7/1201)	1.42 (12/847)	0.93 (19/2048)
Osteoporosis	13.71 (167/1218)	13.48 (126/935)	13.61 (293/2153)
Sjogren síndrome	3.86 (47/1218)	4.18 (39/932)	4 (86/2150)
At least a comorbidity	37.19 (456/1226)	32.81 (311/948)	35.28 (767/2174)
* missing = 209, ** missing = 68, *** missing = 277			
¥ missing = 1, ¥¥ missing = 1			

From the medical background described in the clinical records, we found that 35.28% (767/2174) showed a comorbidity, with high blood pressure being 23.36% (485/2076), and osteoporosis 13.61% (293/2153) as the most frequent ones (Table 1). There were no significant differences between females (35.65%) and males (33.51%) who had a comorbidity. However, the prevalence of having a comorbidity varied between the groups of 41–50, 51–60, 61–70, and >70 years old, with 14.29%, 21.84%, 37.73%, and 58.24%, respectively, which ended up being statistically different (p-value = 0.000).

Of the 2,239 patients who were followed-up during the study period, 93.39% went to between four and seven rheumatologic appointments. The mean number of appointments was six (min:1, max:12). Those who received conventional therapy attended at least six rheumatologic appointments during follow-up, as opposed to the group that received biological therapy, for which the attendance rate to six or more appointments was 57.49% (Table 2).

Table 2
Appointment attendance during the follow-up year

	Conventional therapy		Biologics		Total	
	n	%	n	%	n	%
Fulfilled appointments						
1	0	0.00	21	2.16	21	0.94
2	0	0.00	20	2.05	20	0.89
3	0	0.00	29	2.98	29	1.30
4	0	0.00	127	13.04	127	5.67
5	0	0.00	217	22.28	217	9.69
6	1159	91.62	370	37.99	1529	68.29
7	86	6.80	132	13.55	218	9.74
8	14	1.11	43	4.41	57	2.55
9	5	0.40	11	1.13	16	0.71
10	1	0.08	3	0.31	4	0.18
12	0	0.00	1	0.10	1	0.04

Treatment

From all analyzed patients, 56.5% were treated with conventional DMARDs. In similar proportions, biological treatment was applied by gender, 43.93% for females and 41.45% for males. Both conventional and biological therapies were administered in different proportions to the age groups 41–50, 51–60, 61–70, and >70 years (p-value = 0.000). There was also a statistically significant difference between patients with some degree of comorbidity who received conventional treatment (37.19%) and the ones that received biological treatment (32.80%) (p-value = 0.0377).

Disease activity

DAS28 measurement had a mean value of 2.52 (SD: ± 1) from the first to the sixth appointment for conventional therapy, while for the biological one it was of 2.85 (SD: ± 1.2). These value distributions were similar according to the type of therapy administered during the first six medical appointments. Regarding the variation of the RA activity levels, those who received biological therapy and attended at least six medical appointments, did not experience significant changes in the state of their disease. This means that they kept the activity level reported at the beginning of the follow-up. Nonetheless, for the subgroup of patients who had been receiving treatment at the SCRA (n = 20) for less than a year, there was an increase in the number of patients obtaining remission, going from 4/20 in the first appointment to 10/20 in the sixth appointment [p-value: 0.0771 (McNemar test)]. In the group who received

conventional therapy, there was an increase of approximately 5% of the remission level from the first to the sixth appointment.

On the other hand, the score tendencies of DAS28 associated with the patients throughout the different appointments were similar, regardless of the prescribed therapy type, gender, and whether they showed comorbidities or not (Table 3).

Table 3
Activity level of rheumatoid arthritis in the first and sixth appointments

DAS28	Conventional therapy (N = 1242) †			Biologics (N = 554) †		
	Appointment 1	Appointment 6	p-value†	Appointment 1	Appointment 6	p-value†
REM	61.92%	66.83%	0.004	55.05%	56.14%	0.725
LDA	18.20%	13.77%	0.002	15.88%	13.54%	0.309
MDA	19.00%	17.07%	0.201	24.01%	25.63%	0.550
SDA	0.89%	2.33%	0.006	5.05%	4.69%	0.890
† McNemar test						
‡ Patients who attended at least six appointments						

Discussion

In this research, patient's profiles were described in terms of gender, age, time with the disease, comorbidities, attendance to appointments, and the prescribed treatment. According to this, the results showed that RA affects more women (82.76%) than men (17.24%), which is like other studies results (20–22). Additionally, people 40 years-old or older are treated with approximately eight years living with RA. It was also found that the most common comorbidities were high blood pressure and osteoporosis, which is comparable to previous studies conducted in Saudi Arabia and Cuba, where they were found among the main three main comorbidities in the studied subjects (5, 20). In addition, it was observed that the patients with conventional therapy attended medical appointments more often.

Alternatively, DAS28 results showed that there was an improvement among the patients that received conventional therapy, as the number of patients in remission increased. Although for most the patients that received biological therapy no statistically significant changes in disease activity were observed, the population did not get worse during the duration of the study. Nevertheless, when only considering the subpopulation that was just recently included in the SCRA care program, i.e. those with less than a year of RA specialized care program, we found evidence that prescribing biological therapy was useful for

reducing RA's severity levels with a level of remission that matches with the fact that this treatment is recommended for better control of the disease (23).

In Colombia, according to the register of RA patients led by the *Cuenta de Alto Costo* (High cost diseases account of Ministry of Health), in average an RA patient received three rheumatology consults during 2017 (24). In contrast, our results showed that approximately 70% of RA patients treated in the SCRA had appointments to the rheumatologist at least six times showing that comprehensive care programs guarantee better access to healthcare for these patients.

This study has some limitations that should be considered when generalizing its results. When comparing the SDA change in levels of RA, there were only a few cases with stated level against many others that were not in that disease severity level; this happened mainly with the ones treated with conventional therapy. Additionally, in this study it was not possible to evaluate the reason for the fluctuation of the DAS28 score among patients; maybe external factors to the SCRA program that cannot be controlled, such as people's day to day activities, could play a big role to explain this situation.

Patient adherence to long-term therapies is alarmingly low in both low-and middle and high-income countries (25). Our results evidenced how retention in care and improved adherence to appointments and treatment allow controlling the disease activity levels.

Conclusions

DAS28 disease activity levels were controlled by means of periodical follow-up and integral comprehensive care. The results of this study help characterize a population seen at the specialized in RA center and serve to focalize the efforts on operative aspects to improve retention in care. Future research focused on patients who were recently linked to a program like the one offered by the SCRA will be important to determine key factors that affect the changes in the state of DAS28 disease activity levels.

Declarations

Ethical considerations

The BIOMAB institutional research board (IRB) in ordinary session on April 4, 2019, registered in folder 25, evaluated and approved the research, which was reviewed in the medical, methodological, and bioethical aspects; the IRB also approved the collection and analysis of information from medical records. This study was classified as research with no risk for the patients, according to resolution Number 8430 of 1993 of the Colombian Ministry of Health (19); no data that can identify the patients were published or disclosed, but an informed consent form was obtained from patients.

All methods were carried out in accordance with the institutional ethic guidelines and regulations.

All methods were conducted in accordance with the ethical standards of the Declaration of Helsinki. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication

Consent was obtained from the participants for the publication of the data and results of the study.

Availability of data and materials

The authors declare that the database and other study materials are available for review at any time. All files, databases and other documents related to the study are available on a computer in our research office and with access only to the team of researchers. In any case, please contact PSM.

Disclosure / Conflicts of interest

PSM has received fees for conferences, counseling, advisory boards; also travel to academic meetings expenses and research grants from: Abbvie, Abbott, Biopas-UCB, Bristol, Janssen, Pfizer, Roche, Sanofi.

The other authors declare that they have no conflicts of interest regarding this article

Funding

Not apply

Authors' contributions

PSM and NAZ conceived the research idea and study design, the acquisition of data, gathered the initial database for analysis, drafted the initial version of the manuscript, provided a critical review of study results, worked together on manuscript preparation and approved the final version for submission. JPAE, LV, MCS, OV, FRF gathered the initial database for analysis, drafted the initial version of the manuscript and worked together on manuscript preparation and approved the final version for submission.

Acknowledgements

We thank Biomab IPS – Center of Rheumatoid Arthritis for the administrative data provided for this study

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