

# The Pharmacy of the Specialized Component of Pharmaceutical Policy of the 9<sup>th</sup> Regional Health Department of the State of Paraná and the Treatment of Ankylosing Spondylitis

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The objective of this study was to trace the profile of patients with Ankylosing Spondylitis treated at the Pharmacy of the 9<sup>th</sup> Regional Health Department of Paraná and evaluate the relationship between pharmacological treatment, quality of life and disease activity index of these patients. Data collection was performed through interviews, application of BASDAI index and the ASQoL questionnaire. Male patients presented better rates (ASQoL  $7.78 \pm 6.04$ , BASDAI  $4.26 \pm 2.40$ ) than female patients (ASQoL  $12.08 \pm 4.74$ , BASDAI  $6.25 \pm 2.43$ ;  $p < 0.05$ ). Retired patients had higher disease activity and lower quality of life (BASDAI  $6.59 \pm 1.53$ , ASQoL  $14 \pm 2.89$ ) than those who still worked (BASDAI  $4.59 \pm 2.87$ , ASQoL  $7.68 \pm 5.74$ );  $p < 0.05$ , and the quality of life of patients with comorbidity (ASQoL  $11.60 \pm 5.47$ ) was lower when compared to those without comorbidity (ASQoL  $6.83 \pm 4.90$ ,  $p < 0.05$ ). Patients who used immunobiological drugs had better results (ASQoL  $9.07 \pm 5.86$ , BASDAI  $4.73 \pm 2.55$ ) than those who used other drugs (ASQoL  $13.08 \pm 3.7$ , BASDAI  $6.88 \pm 2.15$ ,  $p < 0.05$ ), and patients who used adalimumab showed better rates (ASQoL  $7.42 \pm 4.81$ , BASDAI  $4.26 \pm 2.47$ ;  $p < 0.05$ ) when compared to other pharmacological treatments. Male patients showed a better response when compared to the female counterparts. Patients using adalimumab had a better quality of life and disease activity index than patients using other pharmacological treatments.

**Keywords:** Ankylosing Spondylitis. BASDAI. ASQoL. Public health.

## INTRODUCTION

Ankylosing Spondylitis (AS) is a chronic inflammatory disease, of autoimmune origin, which preferably affects the spine, causing lumbar pain and sacroiliitis, and may evolve into rigidity and progressive functional limitation of the axial skeleton. Over time, the quality of life of the patient deteriorates. It affects young adults, mainly caucasian male patients carrying the HLA-B27 antigen, with peak incidence in males aged 20 to 30 years. The HLA-B27 antigen is strongly correlated with

the onset of the disease. This marker was found in 80% to 98% of cases. In advanced stages, the disease can lead to complete ankylosis of the spine and extreme reduction in mobility (Ministério da Saúde, 2014a; Azevedo *et al.*, 2016).

The patient with AS initially presents an inflammatory low back pain, characterized by relief with movements and worsening with rest, with prolonged morning stiffness and predominance of axial symptoms during its evolution (Sampaio-Barros *et al.*, 2007). In addition to axial involvement, AS usually affects peripheral joints, but it may also cause enthesitis and affects other organs, leading to conditions such as uveitis and chronic intestinal inflammation (Braun, Sieper, 2007). Even in the early stage of the disease, inflammatory low back

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pain may cause significant morbidity in the patient and hinder daily activities and even require temporary leave from occupational functions. Many patients suffer from progressive loss of their work capacity, which can result in an early retirement and lead to additional costs to the public health system (Frauendorf, Pinheiro, Ciconelli, 2013).

The objectives of the AS treatment are to relieve pain, stiffness and fatigue, preserve proper posture, physical and psychosocial functions, in addition to obtaining control of the disease activity (Ministério da Saúde, 2014a).

The treatment of this pathology requires the association of non-drug therapies, such as psychological counseling and physiotherapeutic follow-up and pharmacotherapy. Drug treatments include Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), corticosteroids, Disease Modifying Antirheumatic Drugs (DMARDs) and Tumor Necrosis Factor (anti-TNF) alpha blocking agents. Anti-TNF agents are biological medicines indicated when the patient is still affected by the disease, for three months even after conventional treatment (Sampaio-Barros *et al.*, 2007; Ministério da Saúde, 2014a).

The disease activity assessment of a patient with AS can be performed by the Bath Ankylosing Spondylitis Activity Index (BASDAI), an instrument that has proven itself to be valid, reproducible and sensitive to health condition variations. The score is measured in Visual Analog Scale (VAS) from 0 to 10 (0 = good; 10 = bad), and it is considered one of the most important tools in clinical trials. A score equal or higher than 4 indicates active disease. In general, the response to treatments of axial AS occurs when there is a reduction of at least 50% or 2 absolute points in BASDAI, over a minimum period of 12 weeks (Garret *et al.*, 1994; Torres, Ferraz, Ciconelli, 2006; Ministério da Saúde, 2014<sup>a</sup>).

In 2003, Doward and colleagues proposed a specific tool to assess the quality of life in patients with AS, the Ankylosing Spondylitis Quality of Life (ASQoL), which is used and validated in many countries. The tool comprises 18 yes/no questions, resulting in a score from 0 to 18 and poor quality of life is associated with higher scores. ASQoL was developed in collaboration with patients with AS and is viable and sensitive to changes

over time (Doward *et al.*, 2003; Torres, Ferraz, Ciconelli, 2006; Davis *et al.*, 2007).

In the Unified Health System (SUS, from *Sistema Único de Saúde*), the pharmacological treatment of AS is included in the Basic Component and the Specialized Component of Pharmaceutical Policy (CEAF, from *Componente Especializado da Assistência Farmacêutica*), and treatment is available to patients with this disease free of charge by the public health system. The CEAF was regulated by Ordinance GM/MS n° 2,981, of November 26, 2009; on March 1, 2010. It replaced the former Exceptional Dispensing Drug Component, being one of its objectives to guarantee the completeness of drug treatment at the outpatient level, whose healthcare protocols are defined in Clinical Protocols and Therapeutic Guidelines (CPTGs) published by the Ministry of Health. AS was incorporated into the CEAF in March 2010. In the CPTG of AS, NSAID naproxen, MMCD sulfasalazine and methotrexate, and anti-TNF adalimumab, etanercept, infliximab and golimumab agents are standardized (Ministério da Saúde, 2017).

Therefore, this study aimed to understand the profile of patients with AS treated at the Pharmacy of the 9<sup>th</sup> Regional Health Department of Foz do Iguaçu, Paraná, as well as to characterize the relationship between the pharmacological treatment of AS with the quality of life and disease activity of patients treated at this pharmacy.

## METHODOLOGY

The study was conducted in the city of Foz do Iguaçu, near the pharmacy of CEAF of the 9<sup>th</sup> RHD of the State of Paraná after approval by the Ethics Committee of the *State University of Maringá* under the CAAE number: 79792817.2.0000.0104, with the population of interest being the population affected by AS.

The survey of the profiles and treatments was performed using a method developed by the researcher. On the other hand, data collection was performed through patient interview and the ASQoL questionnaire, answered physically by the patient without being biased by the researcher, as recommended by Doward *et al.* (2003). The BASDAI disease activity index was collected using

a validated form that, according to Garret *et al.* (1994), is widely used.

All patients with AS who were at the Pharmacy during the period of data collection (December 01, 2017 to February 28, 2018) were invited to participate in the study, and only those patients who agreed to participate and signed the Informed Consent Form were included in the study.

Data analysis was performed by applying the Variance Analysis (t test or ANOVA test) or Kruskal

Wallis and Nemenyi non-parametric tests, with a statistical significance level of 0.05.

## RESULTS AND DISCUSSION

A total of 104 patients with AS were registered to receive medication at the 9<sup>th</sup> RHD pharmacy in 2017, 59 (57%) female and 45 (43%) male. 42 patients participated in the study, representing 40% of the total population. Table I presents the profile of the participants.

**TABLE I – Profile of participants with AS treated at the Pharmacy of the 9<sup>th</sup> Regional Health of the State of Paraná**

Frequency			Frequency		
		%			%
<b>Gender</b>			<b>Marital status</b>		
Female	24	57%	Married	19	45%
Male	18	43%	Single	9	21%
			Divorced	9	21%
			Other	5	12%
<b>Age</b>			<b>Level of Education</b>		
Up to 30 years	2	5%	Primary Education	7	17%
31 to 40 years old	11	26%	Incomplete or complete		
41 to 50 years old	12	29%	Secondary Education	20	48%
51 to 60 years old	11	26%	Incomplete or complete		
Over 60 years old	6	15%	Higher Education	12	28%
			Incomplete or complete		
<b>Ethnicity</b>			<b>Family income</b>		
White	31	74%	Up to 1 minimum wage	8	19%
Pardo/ Mulatto	11	26%	1 to 5 minimum wages	25	60%
			Above 5 minimum wages	9	21%
<b>Physical Exercise</b>			<b>Diagnostic time</b>		
Yes	20	48%	<5 years	24	57%
No	22	52%	5 to 10 years	13	31%
			≥ 10 years	5	12%
<b>BMI</b>					
<18.5	1	2%			
18.5 to 24.9	13	31%			
25 to 29.9	15	36%			
≥ 30	13	31%			

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**TABLE I – Profile of participants with AS treated at the Pharmacy of the 9<sup>th</sup> Regional Health of the State of Paraná**

Frequency			Frequency		
		%			%
<b>Gender</b>			<b>Marital status</b>		
<b>HLAB-27</b>			<b>Age at diagnosis</b>		
Present	29	69%	Up to 30 years	8	19%
Absent	8	19%	31 to 40 years old	13	31%
Not performed	5	12%	41 to 50 years old	9	31%
			Over 50 years old	12	29%
<b>Work Activity</b>			<b>Diagnosis of another disease</b>		
Retired	17	40%	Yes	30	71%
In activity	25	60%	No	12	29%

Although AS is about six times more frequent in male people than in female people (Meirelles, Kitadai, 1999; Sampaio-Barros *et al.*, 2007), in Foz do Iguaçu, the majority of patients with an active process to receive medication at the CEAF pharmacy were female.

The youngest patient to receive the diagnosis of AS was 16 years old, and the oldest was 67 years old. Generally, AS involves young adults, usually starting between the second and fourth decade of life, especially those carrying the HLA-B27 that, in Brazil, represent about 60% of patients (Ministério da Saúde, 2014a). This study shows that 50% of patients participating in the study had been diagnosed with AS until their fourth decade of life.

Data on ethnicity and presence of HLA-B27 confirm that AS is predominant in caucasian people and HLA-B27 positive people (Meirelles, Kitadai, 1999; Sampaio-Barros *et al.*, 2007).

Hwang *et al.* (2017) in a study conducted in South Korea between 2012 and 2013 found normal body mass index (BMI) in 65%, overweight in 31% and obesity in 4% of AS patients. These data reflect the difference in weight control care between Brazilians living in Foz do Iguaçu and South Koreans. In the same study, the researchers found that a higher BMI and the presence of antidrug antibodies predict the interruption in the use

of anti-TNF agents due to failure of drug therapy. Thus, the higher the BMI, the greater the probability of failure with immunobiological drugs, and the findings in our study demonstrate that Brazilians from Foz do Iguaçu have a higher BMI than South Koreans, which may be a warning sign about the effectiveness of the treatment.

The prevalence of permanent disability at work varies from 10 to 40%, depending on the stage of the disease, the age of onset and the characteristics of each country, including access to the health system (Frauendorf, Pinheiro, Ciconelli, 2013). The work activity data in this study did not only refer to the permanent absence from work activities, but also to temporary absence.

Costa and Monteagudo (2008) found in a study carried out with patients enrolled in a National Association of AS Carriers that physical exercise promotes improvement in the quality of life of these patients, which was also evidenced in our study.

With respect to comorbidities, 71% of participants had, at least, one comorbidity. Among the comorbidities cited by the patients, fibromyalgia, hypertension, orthopedic diseases and depression were the most prevalent, with an incidence of 26%, 24%, 19%, and 14% respectively. According to the Ankylosing Spondylitis CPTG, 15% of patients with AS present fibromyalgia.

These patients are included in special cases because, according to CPTG, fibromyalgia may cause an increase in disease activity rates, reducing functionality and quality of life; therefore, fibromyalgia should be identified and treated for not to induce errors in the treatment (Ministério da Saúde, 2014a).

Concomitant diseases are more common in patients with chronic diseases. In patients with AS, the prevalence of comorbidities is twice as high as in healthy patients and are associated with worsening quality of life and retirement, especially psychopathological conditions such as anxiety and depression. The main extra-articular manifestations related to work incapacity are the presence of peripheral arthritis, inflammatory bowel disease, enthesitis, dactylitis and uveitis (Frauendorf, Pinheiro, Ciconelli, 2013; Januário *et al.* (2012). In our study, when asked about the manifestations of AS, 90% of patients reported having inflammatory low back pain at some point, 88% of participants reported having peripheral joint problems, 76% reported having morning stiffness, 36% reported having uveitis and 14% reported having chronic inflammatory bowel disease.

Nine patients (21%) reported performing some type of non-pharmacological treatment for AS, of which 8 (19%) reported attending physiotherapy sessions and 1 (2%) reported attending psychotherapy sessions, while 33 patients (79%) reported not performing any non-drug treatments.

Regarding the current drug treatment, 12 patients (29%) were using sulfasalazine (MMCD) associated with naproxen (NSAID), 1 patient (2%) was using only naproxen, 19 patients (45%) used adalimumab (12 in monotherapy, 4 associated naproxen with adalimumab,

1 associated sulfasalazine, 1 associated methotrexate and 1 associated methotrexate and sulfasalazine), 7 patients (17%) used monotherapy infliximab and 3 (7%) used etanercept (1 in monotherapy and 2 associated sulfasalazine with etanercept).

The drug golimumab was included in CPTG of AS in 2017 and started to be provided to patients at the end of the second semester of the same year. For this reason, we had no patients using this drug participating in the research.

The quality of life of the 42 patients who participated in the study was measured through the application of the ASQoL questionnaire, and the result was an average of  $10.24 \pm 5.70$ . The minimum value found for ASQoL was 0.00 and the maximum was 18.00. The disease activity index applied in the study was BASDAI, and the result found for the 42 participants showed an average of  $5.40 \pm 2.59$ . Twenty-nine patients (69%) had a BASDAI index greater than or equal to 4, that is, they had the disease in activity, while 13 patients (31%) had a BASDAI index lower than 4, which represents a disease with low or no activity. The minimum value found for BASDAI was 0.00 and the maximum was 9.5.

Male participants presented an average of the ASQoL and BASDAI indexes lower than the averages of female participants ( $p = 0.013$  and  $p = 0.0117$ , respectively) (Table II). The data obtained corroborated by the results published by Ribeiro *et al.* (2016), that may suggest that women with Ankylosing Spondylitis have worse quality of life indexes than men with the same pathology. According to this same author this may occur because women generally show greater dissatisfaction with the diseases than men.

**TABLE II** – Frequency distribution and analysis of variance for the ASQoL and BASDAI indexes, according to demographic variables

	Frequency	(%)	ASQoL			BASDAI		
			Average	SD	P	Average	SD	P
<b>Gender</b>								
Female	24	57%	12.08	4.74	0.0133 *	6.25	2.43	0.0117 *
Male	18	43%	7.78	6.04		4.26	2.40	
<b>Ethnicity</b>								

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**TABLE II** – Frequency distribution and analysis of variance for the ASQoL and BASDAI indexes, according to demographic variables

	Frequency	(%)	ASQoL			BASDAI		
			Average	SD	P	Average	SD	P
White	31	74%	10.23	5.26	0.9816	5.40	2.59	0.9292
Pardo/ Mulatto	11	26%	10.27	7.04		5.32	2.47	
<b>Physical Exercise</b>								
Yes	20	48%	8.90	6.19	0.1484	4.41	2.25	0.0162 *
No	22	52%	11.45	5.03		6.30	2.59	
<b>HLA-B27</b>								
Absent	8	22%	9.00	6.23	0.7859	5.27	2.39	0.3329
Present	29	78%	9.62	5.53		4.29	2.95	
<b>Non Pharmacological Therapy</b>								
Yes	9	21%	8.33	7.31	0.2623	5.17	3.06	0.7290
No	33	79%	10.76	5.18		5.53	2.51	
<b>Work Activity</b>								
Retired	17	40%	14.00	2.89	0.0000 *	6.59	1.53	0.0058*
In activity	25	60%	7.68	5.74		4.59	2.87	
<b>Diagnosis of another disease</b>								
Yes	30	71%	11.60	5.47	0.0123 *	5.78	2.62	0.1354
No	12	29%	6.83	4.90		4.45	2.35	
<b>BMI</b>								
Up to 24.9	14	33%	7.79	5.55	0.0518	4.67	2.74	0.2202
≥ 25	28	67%	11.46	5.45		5.76	2.48	
<b>Level of Education</b>								
PE	7	17%	11.86	6.31	0.6835	5.71	3.35	0.3164
SE	20	48%	10.30	5.42		5.45	2.35	
HE	12	28%	10.00	6.08		5.79	2.47	
PG	3	7%	7.00	6.08		2.72	2.45	
<b>Family income</b>								
Up to 1 MW	8	19%	14.25	4.20	0.0145 *	7.08	2.76	0.0801
> de 1 MW	34	81%	9.29	5.63		5.00	2.42	

Values of p refer to the test result for the difference between the averages. \*  $p < 0,05$ . SD: Standard Deviation; PE: Incomplete or complete primary education; SE: Incomplete or Complete Secondary Education; HE: Incomplete or complete higher education; PG: Postgraduate Education; MW: Minimum Wage.

In addition, AS have been strongly associated with the presence of fibromyalgia, which is more prevalent in females, a clinical situation that may influence

the results related to quality of life and the disease activity index (Mease, 2017). In this study, there were 11 participants (26%) with previous diagnosis of

fibromyalgia, all of them female. Thus, fibromyalgia may have an influence on the results of the averages of the ASQoL and BASDAI indexes.

Another factor related to quality of life is depression. Depressed patients tend to have worse quality of life indexes (Ribeiro *et al.*, 2016). In the present study, there were 6 patients (14%) with previous diagnosis of depression, 4 female and 2 male, and the study showed that patients with depression had a worse quality of life index (ASQoL  $12.17 \pm 5.49$ ) when compared to other patients (ASQoL  $9.91 \pm 5.73$ ;  $p > 0.05$ ).

The quality of life of patients who practiced physical activity was not statistically different from the quality of life of patients who did not practice any physical activity, despite presenting a difference of 2.7 points on average ( $p = 0.1484$ ). However, the Disease Activity Index of patients who practiced physical exercise was statistically lower ( $p = 0.0162$ ) than the index of patients who did not practice any physical exercise, showing that patients who exercise have a less active disease compared to patients who are not exercising (Table II).

This data is confirmed by the results obtained by Costa *et al.* (2015), who tested the performance of BASDAI in a Brazilian cohort of 1492 patients and revealed that the patients who practiced physical exercises had a lower index when compared to the patients who did not. It has been demonstrated that physical activity seems to have an additional or synergistic effect to biological therapy (Ministério da Saúde, 2017). Physical activity is usually recommended for patients with AEs. Exercises reduce the symptoms, contribute to a more appropriate posture, improve mobility, help to preserve function and reduce the use of NSAIDs (Frauendorf, Pinheiro, Ciconelli, 2013).

Patients who were retired from their activities had higher disease activity index and worse quality of life when compared to patients who were still in work activities. These differences were statistically significant at a level of 0.05 (ASQoL  $p = 0.000$  and BASDAI  $p = 0.0058$ ) (Table II). High rate of disease activity is a risk factor for loss of productivity and withdrawal from work activities (Frauendorf, Pinheiro, Ciconelli, 2013). Consequently, high disease activity is related to deterioration of quality of life. Frauendorf, Pinheiro,

Ciconelli, 2013 demonstrated that some factors such as female sex, low educational level, housing in rural areas, manual work, exposure to cold environments in the workplace, high workload and lack of collaboration of colleagues, are associated with the high risk of absence from retirement, in people affected by AS.

Patients with comorbidities had worse quality of life rates when compared to patients without them ( $p = 0.0123$ ). There was no statistically significant difference between the averages of the BASDAI index for patients with and without comorbidities ( $p = 0.1354$ ) (Table II).

Patients with BMI up to 24.9 presented better quality of life ( $p = 0.0518$ ) and lower rates of disease activity ( $p = 0.2202$ ) than patients with a BMI greater than or equal to 25, but only the average values of quality of life presented statistical differences.

The averages of ASQoL and BASDAI among the different ethnic groups did not differ significantly, as well as the presence or absence of HLA-B27 and the use of non-pharmacological therapies (Table II). The performance of BASDAI in a Brazilian cohort of 1492 patients tested by Costa *et al.* (2015) revealed that ethnicity and presence or absence of HLAB-27 did not affect the result of BASDAI. The use of non-pharmacological therapy was not tested. On the other hand, the quality of life, tested by Ribeiro *et al.* (2016) in a Brazilian cohort of 1,465 patients, showed better quality of life in caucasian patients when compared to patients of other ethnic groups. The presence or absence of HLAB-27 did not affect the result of ASQoL, and the use of non-pharmacological therapy was not tested.

The average of ASQoL was higher in patients with lower educational levels and, although the p-value for the average comparison test was  $> 0.05$  (Table II), Davis *et al.* (2007) indicated through their research that a difference of 1 to 2 points in the ASQoL score is clinically significant. The comparison between the averages of the BASDAI index in the different levels of education did not present a value of  $p < 0.05$  (Table II) either. However, patients with a post-graduation title obtained an average of the BASDAI index with three points of difference compared to the other patients, which suggests that the disease activity of patients with higher educational levels was lower than patients with lower educational levels. In

addition, the average value of BASDAI for postgraduates was  $2.72 \pm 2.45$ , which indicates disease with no activity or low activity. This data is corroborated by the studies of Frauendorf, Pinheiro and Ciconelli (2013), who stated that education is a protective factor against the retirement of patients with AS from their work activities, which usually occurs when the disease is highly active in the patient and, consequently, worsens their quality of life. This connection between education, quality of life and disease activity, according to the researchers, may be explained by a better socioeconomic level of these patients, a better ability to adaptation and an adherence to ergonomic behaviors.

The quality of life of patients with family income of up to 1 minimum wage was lower than the quality of life of patients with higher family income ( $p = 0.0145$ ). Patients with a family income of up to 1 minimum wage had a higher BASDAI index than patients with family income above 1 minimum wage. However, if a level of significance of 0.05 is established, family income had no influence on the average of BASDAI ( $p = 0.0801$ ) (Table II). The higher the socioeconomic level, the better the quality of life and the lower the disease activity of these patients. Several criteria may

justify these results, including those already mentioned for level of education and easier access to specialized rheumatology services.

In this study, we found the quality of life index of 2 patients (5%) with a postgraduate degree, good family income, practicing physical activity and BMI  $<25$  was better (ASQoL  $5.5 \pm 7.78$ ) than the other patients (ASQoL  $10.48 \pm 5.59$ ;  $p > 0.05$ ), confirming that all these factors together provide an improvement in quality of life.

Regarding pharmacological treatments, it was observed that patients who used adalimumab presented better quality of life and a lower rate of disease activity when compared to patients who were using other pharmacological treatments. However, only the comparison between the averages for ASQoL showed statistical significance (ASQoL  $p = 0.0250$  and BASDAI  $p = 0.0655$ ) (Table III). After applying the average difference test, the Kruskal Wallis and Nemenyi tests were applied to compare the averages of ASQoL between each pair of medication (Table IV) and, if a significance level of 0.05 was established, it was observed that the statistical difference for the averages of ASQoL occurs only for comparisons between Adalimumab and Naproxen + Sulfasalazine ( $p = 0.032$ ).

**TABLE III** – Frequency distribution and analysis of variance for the ASQoL and BASDAI indexes, according to pharmacological treatment

Medications	Frequency	(%)	ASQoL			BASDAI		
			Average	Standard Deviation	p	Average	Standard Deviation	p
Adalimumab	19	46%	7.42	4.81	0.0250 *	4.26	2.47	0.0655
Etanercept	3	7%	11.67	8.50		5.33	3.79	
Infliximab	7	17%	11.43	7.14		5.75	2.29	
Naproxen + Sulfasalazine	12	29%	13.08	3.70		6.88	2.15	

Values of p refer to the test result of the difference between the averages (Kruskal Wallis). The Kruskal Wallis tests were applied and after the Nemenyi test, a non-parametric test to compare three or more populations, used to test the null hypothesis that all populations have equal distribution functions against the alternative hypothesis that, at least, two of the populations have different distribution functions.\*  $p < 0.05$ .

**TABLE IV** – Results of the Nemenyi's test (p-values) after comparison between the averages of ASQoL between each pair of drugs

	Adalimumab	Etanercept	Infliximab
Etanercept	0.456	-	-
Infliximab	0.203	1.000	-
Naproxen + Sulfasalazine	0.032 *	0.999	0.991

\*Only the comparison between the averages of ASQoL between adalimumab and naproxen + sulfasalazine showed  $p < 0.05$ .

The results for quality of life are confirmed by the study of Ribeiro *et al.* (2016), who evaluated the quality of life in spondyloarthritis of a large Brazilian cohort and showed better quality of life in patients who used adalimumab when compared to other pharmacological treatments.

When evaluating the quality of life and disease activity index data by dividing patients by pharmacological

treatment with immunobiological medication or MDM + NSAIDs, it was observed that patients who used immunobiological medication presented better quality of life ( $p = 0.0265$ ) and less disease activity ( $p = 0.0145$ ) than patients who did not use immunobiological medications (Table V). The results of disease activity are compatible with the results observed by Costa *et al.* (2015), which demonstrate that patients using immunobiological drugs have less disease activity than patients who do not use immunobiological drugs.

About 33.5% of patients with rheumatic diseases do not adhere to treatment due to several factors, including low income, making CEAF a very important strategy in the public system of the country because for most of the population is the only way to access some medicines, especially those with higher prices. Free access to high-cost medicines is an important legacy of SUS in pharmaceutical policy. (Ministério da Saúde, 2014b; Dabés, Almeida, Acurcio, 2015; Vieira, 2010).

**TABLE V** – Frequency distribution and analysis of variance for the ASQoL and BASDAI indexes, according to the use or non-use of immunobiological drugs

Medications	Frequency	(%)	ASQoL			BASDAI		
			Average	Standard Deviation	P	Average	Standard Deviation	P
Imunobiological (Adalimumabe, Etanercepte or Infliximabe)	29	71%	9.07	5.86	0.0265 *	4.73	2.55	0.0145 *
MMCD + AINES (Naproxen + Sulfasalazine)	12	29%	13.08	3.70		6.88	2.15	

Values of p refer to the test result for the difference between the averages. \* $p < 0.05$ .

## CONCLUSION

Most of the patients involved in the study are female, caucasian, positive for HLAB-27, BMI higher than 25, with diagnosis of another concomitant disease, especially fibromyalgia, in work activity and has a family income between 1 and 5 minimum wages.

Male patients had a better response to treatment than female patients, and patients using adalimumab had a lower rate of disease activity and better quality of life than patients using other medications.

Patients using anti-TNF therapy had better quality of life and disease activity rates than patients using other drugs.

Patients with comorbidities presented worse quality of life indexes. Family income proportionally affected the quality of life of individuals. The performance of any physical activity, lower body mass indexes and higher level of education seem to improve the quality of life of patients with AS. Although there is no statistical evidence on the data, patients who fit the three variables have a better quality of life index than the others.

Only 31% of the patients examined suffered from the disease without performing physical activity. Based on the results obtained, it is possible to infer that despite the fact that the treatment of AS is well described in the CPTG prepared by the Ministry of Health and that a complete and sufficient therapeutic arsenal for the treatment of this pathology is available at SUS, several factors may negatively influence the outcome of the treatment of these patients.

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## REFERENCES

- Azevedo VF, Rossetto CN, Lorenzeti PG, Tramontin MY, Fornazari B, Araújo DV. Indirect and direct costs of treating patients with ankylosing spondylitis in the Brazilian public health system. *Rev Bras Reumatol.* 2016;56(2):131-137.
- Braun J, Sieper J. Ankylosing spondylitis. *Lancet.* 2007;369(9570):1379-1390.
- Costa IP, Bortoluzzo AB, Gonçalves CR, Silva JAB, Ximenes AC, Bértolo MB et al. Avaliação do desempenho do BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) numa coorte brasileira de 1.492 pacientes com espondiloartrites: dados do Registro Brasileiro de Espondiloartrites (RBE). *Rev Bras Reumatol.* 2015;55(1):48-54.
- Costa RMD, Monteagudo MDG. Espondilite Anquilosante: o exercício físico como reabilitação e promotor da qualidade de vida. *Motri.* 2008;4(2):11-20.
- Dabés CG, Almeida AM, Acúrcio FA. Não adesão à terapia biológica em pacientes com doenças reumáticas no Sistema Único de Saúde em Minas Gerais, Brasil. (Non-adherence to biological therapy in patients with rheumatic diseases in the Brazilian Unified National Health System in Minas Gerais State, Brazil). *Cad Saúde Pública.* 2015;31:2599-2609.
- Davis-Jr JC, Revicki D, van der Heijde DM, Rentz AM, Wong RL, Kupper H et al. Health-Related Quality of Life Outcomes in Patients With Active Ankylosing Spondylitis Treated With Adalimumab: Results From a Randomized Controlled Study. *Arthritis Rheum.* 2007;57(6):1050-1057.
- Doward LC, Spoorenberg A, Cook SA, Whalley D, Helliwell PS, Kay LJ et al. Development of the ASQoL: a quality of life instrument specific to ankylosing spondylitis. *Ann Rheum Dis.* 2003;62(1):20-26.
- Frauendorf R, Pinheiro MM, Ciconelli RM. Variables related to work productivity loss in patients with ankylosing spondylitis. *Rev Bras Reumatol.* 2013;53(3):303-309.
- Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. *J Rheumatol.* 1994;21(12):2286-2291.
- Hwang J, Kim HM, Jeong H, Lee J, Ahn JK, Koh EM et al. Higher body mass index and anti-drug antibodies predict the discontinuation of anti-TNF agents in Korean patients with axial spondyloarthritis. *Rev Bras Reumatol.* 2017;57(4):311-319.
- Januário F, Almeida J, Serra S, Amaral C, Machado P, Rodrigues LA. Caracterização de doentes com espondilite anquilosante em hidrocinestoterapia – uma avaliação multidimensional. *Acta Med Por.* 2012;25(5):301-307.
- Mease PJ. Fibromyalgia, a Missed Comorbidity in Spondyloarthritis: Prevalence and Impact on Assessment and Treatment. *Curr Opin Rheumatol.* 2017;29(4):304-310.
- Meirelles ES, Kitadai F. Aspectos clínicos e epidemiológicos da espondilite anquilosante. *Rev Bras Reumatol.* 1999;39(1):30-34.
- Ministério da Saúde (Brasil). Componente Especializado da Assistência Farmacêutica: inovação para a garantia do acesso a medicamentos no SUS. 2014b.
- Ministério da Saúde (Brasil). Portaria Conjunta SAS – SCTIE/MS nº 7, de 17 de julho de 2017. Aprova o Protocolo Clínico e Diretrizes Terapêuticas da Espondilite Anquilosante. *Diário Oficial da União* 19 jul 2017; Seção 1.
- Ministério da Saúde (Brasil). Portaria Conjunta SAS/MS nº 640, de 24 de julho de 2014a. Aprova o Protocolo Clínico e Diretrizes Terapêuticas da Espondilite Anquilosante. *Diário Oficial da União* 24 de jul 2014; Seção 1.
- Ribeiro SLE, Albuquerque EN, Bortoluzzo AB, Gonçalves CR, Braga da Silva JA, Ximenes AC, et al. Quality of life in spondyloarthritis: analysis of a large Brazilian cohort. *Rev Bras Reumatol.* 2016;56(1):22-27.



Sampaio-Barros PD, Azevedo VF, Bonfiglioli R, Campos WR, Carneiro SCS, Carvalho MAP, et al. Consenso Brasileiro de Espondiloartropatias: Espondilite Anquilosante e Artrite Psoriásica Diagnóstico e Tratamento – Primeira Revisão. *Rev Bras Reumatol.* 2007;47(4):233-242.

Torres TM, Ferraz MB, Ciconelli RM. Instrumentos de Avaliação em Espondilite Anquilosante. *Rev Bras Reumatol.* 2006;46:52-59.

Vieira FS. Assistência farmacêutica no sistema público de saúde no Brasil. *Rev Panam Salud Publica.* 2010;27(2):149-56.

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