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Original Article

Assessment of nutritional and biochemical status in patients with rheumatoid arthritis undergoing pharmacological treatment. A pilot study

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Abstract: Objective: To assess the nutritional status of patients with rheumatoid arthritis (RA), correlating it with the laboratory tests and pharmacological treatment used in cases of this pathology. Method: Seventy-two women diagnosed with RA were included. Assessment of their nutritional status was classified by anthropometric assessment, and food consumption was assessed by the Semi-quantitative Food Frequency Questionnaire (SFFQ). The results of the patients' biochemical tests were obtained from their medical records. Results: 45.8% of the sample studies were diagnosed to be overweight, followed by obesity, eutrophy and malnutrition. The biochemical tests showed alterations in C-reactive protein parameters, blood sedimentation rate and rheumatoid factor. The SFFQ results showed low intake of calories, calcium, vitamins D and E, zinc, copper and magnesium. Low calorie intake was found statistically among patients undergoing combined treatment with leflunomide+methotrexate, and leflunomide+prednisone. Conclusion: Patients with RA under treatment present high incidence of overweight or obesity and deficient intake of trace elements which protect against the development of RA. The use of combined pharmacological treatment determines the high incidence of reduced calorie intake in patients with RA.

Keywords: Nutritional assessment, rheumatoid arthritis, inflammation, pharmacological treatment

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease with progressive, systemic, idiopathic aetiology. It affects all ethnic groups and both sexes, being more frequent in women [1, 2]. RA is manifested in chronic inflammatory disturbances which may affect organs and tissues, primarily the joints where it produces non-suppurative proliferative synovitis, which in most cases evolves to the destruction of articular cartilage and anquilosis of the joints [3].

The object of pharmacological treatment of RA is to maintain articular function and to reduce pain, inflammation and structural damage [4]. Nevertheless, these medicaments affect the synthesis of prostaglandins and reduce production. Treatment with glucocorticoids for example inhibits inflammation through mechanisms which are independent of transcription effects, controlling the activity of the disease and helping to relieve pain. However prolonged use of these products may cause intestinal problems such as irritation, ulcers, acid reflux and even kidney failure [5]. Disease-modifying anti-rheumatic drugs (DMARDS) have the potential to diminish the effects of the disease when used in the initial phase [6].

Studies show that with the evolution of the disease the nutritional profile of patients carrying rheumatoid arthritis is affected. This occurs because the medicaments used to control the activity of the disease causes gastrointestinal changes which affect the ingestion, digestion and absorption of food [7]. The inflammatory nature of the disease provokes alterations to the metabolism; one of the main causes of

these is activation of nuclear factor kappa-B (NF-κβ) which generates metabolic changes, leading to depletion of lean tissue [8, 9]. Carriers suffer considerable loss of lean mass, known as rheumatoid cachexia, which affects the immunological system, the skeletal muscles and the viscera [10].

As a consequence of the inflammation, joint stiffness and structural damage caused by the disease, the physical activity of RA patients is reduced. Physical exercise has been identified as an important part of rehabilitation in this group [11, 12].

The object of this work is to assess the nutritional status of patients with rheumatoid arthritis, correlating it with laboratory tests and the pharmacological treatment used in cases of this pathology.

Materials and methods

This investigation was approved by the Research Ethics Committee of Centro Universitário Estácio FIC in decision no. 863,488. All the participants agreed to take part in the research and signed a free informed consent form.

The research used standardised questionnaires with information on the patients' age, sex, height, weight, practice of physical activity, time since diagnosis of the disease and use of vitamin supplements. The questionnaire also included the pharmacological treatment used by the patient. Inclusion criteria: adult women, aged between 18 and 60 years, diagnosed with rheumatoid arthritis meeting the RA diagnosis criteria drawn up by the American College of Rheumatology in 1987 [13]. The study was carried out between January and May 2015 in the rheumatology out-patients department of a public hospital in Fortaleza-CE, Brazil. Pregnant women and patients in wheelchairs were excluded.

The nutritional status of the patients was classified by anthropometric assessment: bodyweight, height, arm circumference (AC), triceps skinfold thickness (TST) and biceps skinfold thickness (BST). The patients were weighed using a Toledo® (2098PP) digital scales, accurate to 50 g and with capacity of 200 kg, and their height was measured with a Toledo® stadiometer, with maximum 2.07 m. The arm circumference was measured with a Vonder® inelastic tape measure, length 2 m, interval 0.1 cm. All the skinfolds were measured with a Sanny® clinical adipometer (AD1009) following the protocol described by Pollock and Wilmore [14].

Food consumption assessed by the Semi-quantitative Food Frequency Questionnaire (SFFQ), applied after medical consultations. The SFFQ was validated by Pereira et al. [15] and contains 60 foods divided into 10 groups and 7 food frequencies: never, less than once per month, 1-3 times per month, once per week, 2-4 times per week, once per day and twice or more per day.

A household measurement table was used to convert the foods in the SFFQ to grams [16]. Food consumption frequency was multiplied for each food unit and the result was divided by seven to obtain the mean daily intake. The food composition table was used to find the values of macronutrients and micronutrients [17]. Classification to fit food consumption followed the references for sex and age of *Dietary References Intakes* (DRIs) [18], since there is no reference for patients with rheumatoid arthritis. Energy needs were characterised using the Harris and Benedict form, supported by Avanutri software.

The body mass index (BMI) [19] was obtained by dividing the bodyweight (Kg) by height in meters squared. The arm muscle circumference (AMC) was calculated using the formula AMC = AC (cm)-3.14 × [TST (mm) ÷ 10] [20]. The reference value table adapted by Blackburn and Thorton [21] was used to fit the skinfolds, arm muscle area (AMA) and arm fat area (AFA).

The patients' medical records were reviewed to obtain information on their biochemical tests from 2012 to 2015. The data collected were calcium (Ca), 25-hydroxy vitamin D, C-reactive protein (CRP), rheumatoid factor (RF), blood sedimentation rate (BSR), HDL cholesterol, LDL cholesterol, total cholesterol (TC), triglycerides (TG), creatinine (Cr), urea (Ur), glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT).

Descriptive statistical analysis was applied in the first place to the values obtained from data

Table 1. Fitting and classification of anthropometric measurements; mean values and interval

	Malnourished	Eutrophic	Overweight	Obese	Mean	Interval
BMI	4.2%	23.6%	45.8%	26.4%	27.25 ± 0.57	15.79-38.83
AC	26.4%	33.3%	34.7%	5.6%	96.39 ± 1.76*	59.87-129.25*
AMC*	33.8%	53.5%	9.9%	2.8%	92.57 ± 1.64*	58.5-122.77*
TST*	21.1%	28.2%	15.5%	35.2%	110.83 ± 3.49*	39.22-170*
AFA*	33.7%	25.4%	11.3%	29.6%	108 ± 4.69*	33.98-200.52*
AMA*	31%	33.8%	15.5%	19.7%	102.56 ± 3.51*	39.75-174.26*

*Values obtained by percentage fit, BMI-Body Mass Index, AMC-arm muscle circumference, TST-triceps skinfold thickness, AFA-arm fat area, AMA-arm muscle area, ± standard error.

Table 2. Mean values of results of laboratory tests for years 2012 to 2015

Tests	2012 Mean	2013 Mean	2014 Mean	2015 Mean
Calcium (mg/dL)	9.54 ± 0.18	9.45 ± 0.11	9.59 ± 0.14	10.28 ± 0.36
HDL (mg/dL)	53.38 ± 2.65	49.45 ± 2.62	48.8 ± 2.07	52.21 ± 2.04
LDL (mg/dL)	137.45 ± 8.52	124.88 ± 6.05	120.4 ± 5.15	130.99 ± 4.54
CRP (mg/dL)	14.26 ±4.05	14.91 ± 4.16	13.19 ± 0.3	9.01 ± 1.47
HB (mg/dL)	12.77 ± 0.23	12.83 ± 0.27	9.55 ± 1.96	12.64 ± 0.24
GOT (mg/dL)	24.52 ± 2.38	25.52 ± 2.14	23.84 ± 2.77	25.72 ± 2.42
GPT (mg/dL)	30.86 ± 4.79	30.62 ± 3.95	26.65 ± 3.13	31.12 ± 4.71
25-hydroxy D (mg/dL)	25.68 ± 1.26	27.08 ± 1.89	25.65 ± 2.34	26.6 ± 2.42
BSR (mg/dL)	41.95 ± 4.92	39.82 ± 4.44	128.17 ± 8.41	43.28 ± 13.6
TG (mg/dL)	152.25 ± 19.3	140.24 ± 25.67	32.9 ± 3.28	124.84 ± 10.6
RF (mg/dL)	129.08 ± 63.48	86.62 ± 33.49	66.4 ± 45.42	83.13 ± 25.95
TC (mg/dL)	213.03 ± 9.21	195.06 ± 6.05	193.35 ± 6.39	202.10 ± 7.06

± standard error, HDL-high density lipoprotein, LDL-low density lipoprotein, CRP-C-reactive protein, HB-haemoglobin, GOT-glutamic oxaloacetic transaminase, GPT-glutamic pyruvic transaminase, BSR-blood sedimentation rate, TG-triglycerides, RF-rheumatoid factor, TC-total cholesterol.

collection. The mean and the interval were described with the sample stratified into classes by BMI, medicaments and laboratory tests. Subsequently Shapiro-Wilk normality tests ($P< 0.05$) were applied with sample-size up to $n = 50$, or Kolmogorov-Smirnov ($P\leq0.05$) for samples larger than 50. To analyse the influence of the classes on the mean values of the variables assessed, Student's t-test was used for samples with parametric distribution or the Mann-Whitney test for non-parametric variables. Pearson's and Spearman's correlations were used as necessary to verify ratios between quantitative variables. The chi-square test was used to verify the influence of the pharmacological treatment used by patients and the calorie intake in the SFFQ. Statistical analysis used the Software Statistical Package for the Social Science (SPSS, version 22.0) with significance value $P<0.05$.

Results

Descriptive analysis of anthropometric assessment

The sample consisted of 72 women patients, in the age band 29 to 59 years, average time since diagnosis 13.26 years (± 1.18). 89% of the patients said that they do not practice physical activity. Descriptive analysis of the anthropometric data, such as BMI, AC, AMC, TST, AFA and AMA, is presented in **Table 1**. The subdivision by classes shows a concentration of BMI and AC in the Overweight class, AMC and AMA in the Eutrophy class, TST in the Obese class, and AFA in the Malnutrition class.

Clinical and laboratory data

Biochemical data for the years 2012-2015 were extracted from medical records. The short

Table 3. SFFQ stratified by BMI classification

	Eutrophic Mean	Overweight Mean	Obesity Mean
Kcal	1330.31 ± 93.61	1348.79 ± 77.02	1247.76 ± 67.89
Fibre (g)	15.1 ± 1.35	15.49 ± 1.18	13.97 ± 0.96
Vit. B1 (mg)	1.07 ± 0.11	1.03 ± 0.85	1.04 ± 0.87
Vit. B2 (mg)	1.29 ± 0.14	1.14 ± 0.11	1.17 ± 0.99
Vit. B6 (mg)	1.36 ± 0.96	1.44 ± 0.12	1.31 ± 0.72
Vit. B12 (mg)	4.37 ± 0.91	3.72 ± 0.61	6.75 ± 1.97
Fe (mg)	9.37 ± 0.95	8.28 ± 0.55	9.57 ± 0.93
Ca (mg)	595.43 ± 63.78	563.29 ± 42.19	492.51 ± 51.15
Vit. A (mcg)	910.48 ± 124.57	741.83 ± 71.10	1192.94 ± 192.92
Vit. D (mg)	3.56 ± 0.47	2.7 ± 0.35	9.41 ± 5.85
Vit. E (mg)	11.22 ± 1.79	10.65 ± 0.55	11.2 ± 1.12
Vit. C (mg)	1015 ± 390.26	699.83 ± 252.13	312.82 ± 93.22
Mg (mg)	185.53 ± 19.99	163.69 ± 9.11	185.11 ± 23.56
Zn (mg)	5.7 ± 0.57	4.83 ± 0.26	5.57 ± 0.37
Se (mg)	74 ± 6.92	70.66 ± 5.36	74.23 ± 5.76
Cu (mg)	0.83 ± 0.73	0.8 ± 0.5	1247.76 ± 67.89

± standard error, Kcal-kilocalory, Vit-Vitamin, Fe-iron, Ca-calcium, Mg-magnesium, Zn-zinc, Se-selenium, Cu-copper.

time-frame was selected in order to minimise variation in the number of test samples between years.

It may be inferred from **Table 2** that only CRP, BSR and RF present higher than acceptable mean levels each year. Conflicting behaviour was found for Ca, HDL cholesterol, GOT, GPT, 25-hydroxy vitamin D (25-hydroxy D) and HB, which maintained acceptable mean levels each year. High mean levels were observed for TG in 2012, LDL in 2015 and TC in 2012 and 2015.

In terms of pharmacological data, 34 (47.2%) of the women interviewed said that they make concomitant use of methotrexate and prednisone, 25 (34.7%) of methotrexate and leflunomide, 28 (38.9%) of prednisone and leflunomide and 28 (38.9%) of prednisone, methotrexate and leflunomide. The food supplements used were: folic acid, 63% of the sample; calcium and vitamin D, 40.3%; folic acid and calcium, 36.1%; vitamin D and folic acid, 27.8%; and calcium, vitamin D and folic acid, 23.6%.

Descriptive analysis of the SFFQ

A Semi-quantitative Food Frequency Questionnaire (SFFQ) was applied to assess and quantify food intake based on DRI. Of the minerals analysed, 91.7% of the sample presented a deficiency of calcium, 94.4% magnesium, 75% zinc and 100% copper. The other minerals presented a reasonable match in the 72 SFFQs analysed, e.g. phosphorus (100%), iron (83.3%) and selenium (84.7%). According to DRI, considering sex and age, 61.1% of the sample presented deficiency of vitamin D and 79.2% of vitamin E. However adequate levels were found of vitamins A (76.4%), B1 (55.6%), B2 (65.3%), B3 (93.1%), B6 (81.9%), B12 (87.5%) and C (93.1%).

The sample was also examined on the basis of BMI class (eutrophy, overweight, obese) in order to establish a connection between these groups and the patients' sufficiency in micronutrients. The malnutrition class was excluded from the analysis as it represented only 4.2% of the sample. Descriptive analysis found that all the groups present sufficient intake of iron, selenium and vitamins A, B1, B2, B3, B6, B12 and C, while the intakes of calcium, magnesium, zinc, copper and vitamin E were insufficient.

Vitamin D intake was found to be sufficient only in the obese group. The whole sample presented low intake of fibre, while intake of polyunsaturated fats was sufficient in the eutrophy group, deficient in the overweight group and very low among the obese. In terms of calorie requirement, 52% of the eutrophy class present a correct energy intake, while 66% of the overweight and 55.5% of the obese presented an insufficient energy intake.

Analysis of correlations between nutritional and clinical states

A correlative analysis between anthropometric and biochemical variables, between biochemical variables and micronutrients, and between anthropometric variables, was applied in the BMI classes eutrophy, overweight and obese.

It may be inferred from **Table 4** that there was a moderate negative association between AFA and TST, and the time since diagnosis, and between AC and AFA, and the CRP for the overweight class only. The same class presents a

Table 4. Correlation between time since diagnosis and anthropometric measurements and between time since diagnosis and CRP in eutrophic, overweight and obese patients

	Eutrophic		Overweight		Obese	
	Time since diagnosis	CRP (2015)	Time since diagnosis	CRP (2015)	Time since diagnosis	CRP (2015)
TST	P = 0.21	P = 0.40	P = -0.36*	P = -0.38	P = -0.02	P = -0.25
BST	P = 0.10	P = 0.12	P = -0.24	P = -0.44*	P = -0.17	P = 0.28
AMC	P = 0.08	P = -0.08	P = -0.03	P = -0.24	P = -0.17	P = 0.44
AFA	P = 0.18	P = 0.27	P = -0.37*	P = -0.42*	P = -0.10	P = 0.09
AMA	P = -0.04	P = 0.02	P = -0.04	P = -0.26	P = -0.15	P = 0.44
Age	P = 0.41	P = 0.15	P = 0.51*	P = 0.12	P = -0.16	P = 0.06

*Statistically significant, CRP-C-reactive protein, TST-triceps skinfold thickness, BST-biceps skinfold thickness, AMC-arm muscle circumference, AFA-arm fat area, AMA-arm muscle area.

moderate positive association between age and the time since diagnosis. No statistical significance was found for the other ratios.

Pearson's test showed a strong positive correlation between serum calcium and food calcium in the eutrophy (r = 0.71, P<0.05) and overweight classes (r = 0.80, P<0.01), and likewise between serum cholesterol and food cholesterol for the obese group (r = 0.78, P<0.05). In the overweight group a moderate directly proportional association was also found between CRP and polyunsaturated fat (P = 0.42, P<-0.05), and between CRP and food selenium (P = 0.43, P<0.05). Magnesium presented a moderate negative association with CRP (P = -0.56, P<0.05) in the obese group only. Vitamins A and C presented no statistical significance for the correlation with CRP in any of the BMI classes.

A comparative study between the means of the SFFQ variables (polyunsaturated fat, calcium, selenium, potassium, magnesium, zinc, calorie intake, vitamins A, E and C) was carried out using the Mann-Whitney test for non-parametric independent samples, between the BMI classes grouped in pairs. Of the above-mentioned variables, only Vitamin A in the overweight and obese groups presented significant differences between the mean values (P<0.05), with values of 23.03 for overweight and 32.53 for obese; and Vitamin C between the eutrophy and obese groups (P<0.05), with mean values of 22.41 for eutrophy and 15 for obese. For the sufficiency of anti-oxidant micronutrients (selenium, zinc, magnesium and vitamins A, E and C), the Mann-Whitney test showed statistical significance only for CRP among the selenium classes (*P*<0.05), with a mean value of 19.50 for individuals with insufficiency and 31.34 for those with sufficient levels. The *p* values for BSR and RF were not significant. BMI as a quantitative parametric variable was assessed by Student's t-test in independent samples, for the use of methotrexate, leflunomide and prednisone separately. The analysis showed, with significance P<0.05, that the participants who took prednisone had a lower mean BMI (26.70) than those who did not take the drug (29.62), while the mean of those who took leflunomide (29.01) was higher than the mean of those who did not (26.01). Mean BMI presented no significant differences among methotrexate users (**Table 3**).

Analysis was done using the χ^2 test in order to investigate the influence of the combined use of methotrexate, leflunomide and prednisone on the correct calorie intake of patients. For associations of methotrexate and leflunomide, and for prednisone and leflunomide, values of $\chi^2 = 6.49$ and $\chi^2 = 7.63$ were obtained respectively for a significance of P<0.05, confirming the existence of an influential association between these groups. Of the individuals who used methotrexate and leflunomide, 76% had insufficient calorie intake, 29.2% normal and 15.3% higher than the recommended level. Of those using prednisone and leflunomide concomitantly, 71.4% had a low calorie intake, 10.7% sufficient and 17.9% high. No significant values for the test were found among users of methotrexate and prednisone. The influence of the use of methotrexate and leflunomide on the observed values of GOT and GPT was assessed, but statistically no significant probability of an association between these variables was identified.

Discussion

During its evolution RA causes great nutritional changes, which directly influence the patient's nutritional status. High body composition is a predictor for complications in treatment of the disease. Excess weight in RA is directly related with a reduced quality of life and physical condition, as well as an increase in pain and comorbidity [22].

The required energy intake varies with the clinical condition of each patient and consequently the metabolic rate changes according to the degree of inflammatory response [23]. People with RA suffer a greater depletion of proteins in the whole body, which is related with the production of the growth hormone, glucagon and of TNF-α. Patients with low fat reserves generally have low levels of vitamins A and E; this stimulates the peroxidation of lipids and worsens the RA condition [5].

Joint pain, stiffness, loss of bone density and muscular weakness are caused by the worsening of the disease [24]. Consequently the patients present reduced amplitude of movement in the affected joints and functional limitation in carrying out everyday physical tasks [25], as well as difficulty in doing regular physical exercise. This may lead to increased weight and greater risk of cardiovascular disease, raising morbidity and mortality among RA patients [8, 26]. In our study 45.8% of the participants presented overweight and 26.4% were obese. These data agree with the results of a multicentre study [27] in which 18% of patients with RA were obese. A longitudinal study by Wolfe and Michaud [28] included participation of 24,535 patients, of whom 63-68% presented BMI≥30 kg/m^2. Ajeganova et al. [22] carried out nutritional assessment on completion of a study involving 2,608 people, finding that 33% of the study patients were overweight and 12.9% were obese; both groups had initial RA. High weight in these patients was associated with worsening of the disease, increased risk of co-morbidity, total joint replacement, increased pain and a lower quality of life [22, 26].

As the disease evolves over time, patients tend to present a BMI above the eutrophy band [23, 29]. In our study the AFA and TST presented a correlation with the time since diagnosis only in overweight individuals. These results are similar to those reported by Zarpelon et al. [29], who found an association between the TST and the duration of the disease in an anthropometric assessment of 102 patients.

In terms of sufficiency levels in the biochemical tests, the sample presented inappropriate values in TC, CRP, BSR and RF, while the means of the other lipid factors (HDL-cholesterol, LDL-cholesterol and TG) and the HB were normal. Some authors suggest that the inflammation caused by RA is associated with changes in the lipids profile, which is a risk factor for cardiac disease [30]. Avelar et al. [31] also found changes in TC tests, observing a significant increase in TC and LDL-cholesterol with the activity of the disease; our study did not corroborate these findings as there was no worsening of the lipid profile during the course of the disease.

Due to the chronic nature of RA, as the disease progresses the carriers suffer various functional changes which prevent proper calorie intake, finally leading to changes in their nutritional status [32]. In our study the patients presented a deficit in their intake of vitamins D and E, zinc, magnesium and calcium. Morgan et al. [33] analysed food intakes in RA patients over a 6-month period: the mean consumption of zinc, magnesium, folic acid, vitamin B6 and vitamin E was only 67%. Vitamin D deficiency was also noted by Rossini et al. [34] in a study of 1,191 patients, 85% of whom were women. Of the patients who did not receive Vitamin D food supplements, 52% presented reduced serum levels of 25-hydroxy vitamin D. It was observed that calorie intake and zinc consumption were below the minimum needed in 55.6% and 75% of the sample respectively. Sarkis et al. [35] assessed food intake of serum calcium in 83 women and observed that despite the low food intake level, the serum calcium levels of these patients were not compromised, which agreed with the findings in our study.

Despite the strong positive correlation between food cholesterol and serum cholesterol in the obese sub-group, the other groups presented no statistically significant correlations. This may be explained by the large number of patients (53.8%) with altered serum cholesterol indices. High cholesterol in patients with rheumatoid arthritis has been associated with increased cardiovascular risk. The traditional risk factor for cardiovascular risk and inflammation would probably be one of the predictors for cholesterol alteration. Inflammation provokes oxidative changes which lead to an alteration in HDL structure, reducing its cardio-protective effect [36].

The role of the poly-unsaturated fatty acids Ʊ3, Ʊ6 and Ʊ9 has been reported as an important regulator of inflammation, as well as having a protective effect and reducing pain [37]. Salvador et al. [38] reported measurements of poly-unsaturated fat intake by RA patients, find-

ing that patients with slight, moderate and high disease activity presented a reduced intake of fatty acids, like the patients in this study.

Kremer and Bigaouette [39] assessed nutrient consumption in RA patients, and observed low intake of pyridoxine, zinc and magnesium. In our study patients with active RA presented deficiencies in calcium, zinc, magnesium and copper; a correlation was also found between selenium levels and CRP. Products of oxidation by free radicals can be found in the synovial fluid of RA patients [40]. Antioxidant micronutrients play an important role in the protective mechanism against tissue damage caused by reactive oxygen species [41]. Some of these micronutrients, namely β-cryptoxanthin and supplementary zinc, and possibly diets rich in fruits and crucifer vegetables, may offer protection against the development of RA [42]. Some authors suggest that routine diet supplementation with multi-vitamins and trace elements are important for patients with RA [39].

Because it is a systemic disease, RA affects other organs as well as the joints, such as bone marrow, eyes and lungs. The presence of the antibody known as rheumatoid factor (RF) is one of the indicators for prognosis of the disease. This antibody attracts leukocytes into the joint space, causing an inflammatory response through the release of chemical mediators, such as thromboxanes, prostaglandins and leukotrienes [43]. In our work the rheumatoid factor proved quite high, however correlative studies or studies of the influence of this variable found no significance.

Drugs to modify the course of the disease act by preventing and minimising damage to joints and tissue. Methotrexate and leflunomide are among this class of medicaments and are noted as powerful treatments, however it has been reported that the combination of these two drugs has a hepatotoxic effect. Curtis et al. [44] found no statistical correlation between people using these medicaments and a change in GOT and GPT. The nutritional status of carriers of rheumatoid arthritis is weakened as the disease evolves. They become unable to carry out everyday activities, and experience difficulties in mastication which may lead to alterations in their food consistency. The high intake of medicaments causes gastrointestinal changes, which in turn affect the ingestion, digestion and absorption of the medicaments [43]. In our study we observed that the concomitant use of drugs affected the patients' calorie intake: 76% of the patients who took methotrexate and leflunomide presented low calorie intake, 29.2% sufficient intake and 15.3% a higher than recommended intake. Of the patients who took prednisone and leflunomide concomitantly, 71.4% presented reduced calorie intake, 10.7% normal intake and 17.9% a high intake.

Maintaining a good nutritional status, including weight control and healthy food intake, is essential for RA carriers. In our study more than half the sample analysed presented excess weight, which helped to increase pain and hindered remission of the disease. Patients being treated for RA presented insufficient calorie intake as well as deficiencies in vitamins D and E, calcium, zinc, magnesium and copper. We found significant muscular depletion and the patients did not present weight gain or alteration of the lipid profile in the course of the disease.

The results found in our study enable us to conclude that combined treatment with certain drugs (methotrexate with leflunomide and prednisone with leflunomide) results in a high incidence of reduced calorie intake in RA patients. Furthermore, our study reveals the importance of a balanced diet, emphasising specific nutrients, for RA patients under treatment, since they present a high incidence of overweight or obesity and deficient intake of trace elements which offer protection against the development of the disease.

Disclosure of conflict of interest

None.

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