Eight weeks of *Curcuma longa* L. supplementation improves disease activity and quality of life in Ulcerative Colitis patients: a pilot study

Suplementação de *Curcuma longa* L. por oito semanas melhora a atividade da doença e a qualidade de vida de pacientes com Colite Ulcerativa: um estudo piloto

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ABSTRACT
This study evaluated the effects of *Curcuma longa* L, combined with Mesalamine on inflammation and quality of life in patients with Ulcerative Colitis (UC). A randomized, double-blind, pilot study was undertaken with nine patients, age ≥18 years, who were exclusively using Mesalamine (3g/day). These patients were kept under observation in a university hospital for eight weeks. An experimental group (EG) (n=5) received three capsules daily, containing 500mg of dry extract of *Curcuma longa* L and a control group (CG) (n=4), 500mg of microcrystalline cellulose. The groups were evaluated for the following, before and after the intervention: rectosigmoidoscopy, fecal calprotectin, body mass index (BMI), interleukin 10 (IL10), C-reactive protein (CRP), haemoglobin and haematocrit. A Short Form Health Survey (SF36) questionnaire was used to assess quality of life. When individually evaluated, EG patients showed histological improvement (Effect size: 0.706) in the rectosigmoidoscopy examination. 80% of them presented calprotectin values within the normal range. BMI analysis showed that 78% of the patients were overweight, but without difference between groups (p=0.456). The inflammation markers (IL10, CRP and calprotectin) as well as haemoglobin and haematocrit were not different in any of the groups. There was no difference in the SF-36 quality of life domains between groups, but the effect size was medium to large for the domains physical functioning, bodily pain, general health, social functioning, role-emotional and mental health. As conclusion the turmeric supplementation for eight weeks was able to reduce the Mayo score and improve the quality of life in patients with UC.

Keywords: Ulcerative Colitis; Turmeric; Inflammation; Nutritional assessment; Quality of life.
suplementação com cúrcuma por oito semanas reduziu o score de Mayo e melhorou a qualidade de vida de pacientes com colite ulcerativa.

**Palavras-chave:** Colite ulcerativa; Cúrcuma; Inflamação; Avaliação nutricional; Qualidade de vida.

**1 INTRODUCTION**

Ulcerative Colitis (UC) is a common inflammatory bowel disease\(^{(1)}\) characterized by recurrent episodes of inflammation in the mucosa of the rectum and colon. Symptoms include diarrhea, bleeding, rectal tenesmus and joint pain, which generate negative repercussions on quality of life due to changes in physical, psychological and socio-professional domains.\(^{(2)}\) The commonly used drug to treat UC is Mesalamine, which has an anti-inflammatory action.\(^{(3)}\) Treatment combining Mesalamine with a herbal medicine, through the use of *Curcuma longa* L., aims to reduce inflammation and prolong the period without disease activity.\(^{(4)}\)

*Curcuma longa* L. is considered a functional food belonging to the Zingiberaceae family.\(^{(5)}\) It has antioxidant, gastrointestinal healing, antimicrobial and anti-inflammatory properties, which act by suppressing the nuclear factor kappa B and proinflammatory cytokines of the colon mucosa, collaborating in the treatment of inflammatory bowel diseases.\(^{(6)}\)

Studies have shown that oral administration of curcumin reduces intestinal inflammation in active UC patients.\(^{(7,8)}\) Mesalamine plus 3 g/d of *Curcuma longa* L. for one month improved clinical remission compared with Mesalazine alone.\(^{(4)}\) Thus, our hypothesis is that Mesalamine associated with Curcuma supplementation decreases inflammation and improves the quality of life in patients with active UC.

**2 METHODS**

2.1 PATIENTS AND DESIGN OF STUDY

A double-blind, randomized, pilot and clinical trial design was performed with active UC patients, using Mesalamine 3 g/day exclusively under observation at a University Hospital were enrolled for eight weeks. The protocol was approved by the Ethics Committee of the hospital, under registration number 1.745.720 / 2016 and CAAE: 56646216.0.0000.5078.

The selected patients for the study were clinically stable outpatients, male and female, aged ≥ 18 years, all of them diagnosed with UC by Truelove or de Mayo’s score\(^{(9,10)}\) and presenting abnormal fecal calprotectin levels (> 150.1 mg/g). The rectosigmoidoscopy examination showed endoscopic alterations from Mayo’s standards. Patients who reported dysphagia, allergy to turmeric and who had heart disease, liver disease, leukopenia,
thrombocytopenia, pancreatitis, gallstone, kidney disease, decompensated diabetes, pneumonia, sepsis or infection, pregnant women and nursing mothers were excluded from the study group. Fifty patients were selected for the study but only 12 of them had active symptoms of the disease. They were included in the research after signing the Informed Consent Form. Then, they were randomly divided in two groups: an Experimental Group (EG) (n = 6) and a Control Group (CG) (n = 6) (Figura 1).

2.2 SUPPLEMENTATION

EG received three capsules/d, each containing 500 mg of dry extract of *Curcuma longa* L. (> 96% of curcuminoids) one hour before each meal: breakfast, lunch and dinner, reaching a final therapeutic dose of 90g turmeric for the diet treatment of patients with UC. (4) CG
received three capsules/d containing 500 mg of microcrystalline cellulose each, of similar size, colour and arrangement to the capsules with turmeric. Patients were instructed to maintain Mesalamine treatment 3 g/day and not to consume turmeric during the study.

2.3 CLINICAL ASSESSMENTS

Each participant was evaluated for intestinal disease activity by rectosigmoidoscopy using the Pentax EC-390i1 video endoscope. Healing was interpreted by endoscopic healing values (0-3) associated with Mayo's histological classification (≤2-12).(10) The quantification of fecal calprotectin was performed by the Elisa method. In addition, anthropometric evaluation was performed by calculating BMI(11,12), quantification of interleukin 10 (IL-10) by the Elisa method and C-reactive protein (CRP) by the automated immunoturbidimetry method. Hemoglobin concentrations were analysed using spectrophotometer and hematocrit by indirect measurement. Socioeconomic and quality of life questionnaire (SF-36) variables were also applied.(13) All examinations were performed at the beginning and end of the study by trained nutritionists and physicians.

2.4 STATISTICAL ANALYSES

For the socioeconomic, anthropometric, body composition, biochemical and calprotectin variables, estimates were obtained for the mean and standard error of the mean. The means between groups in the raw data were performed using Student's t-test, paired or unpaired for the variables with normal distribution or by the Mann-Whitney or Wilcoxon test for non-normal distributions. For categorical variables, the Fisher's exact chi-square test was used. The impact was calculated by Cohen and the values were identified as: Small Effect: 0.20-0.50, Medium Effect: 0.50-0.80, Large Effect: ≥0.80. (14) The analyses were performed using STATA 14.0 software and a significance level of 5% (p <0.05) was adopted.

3 RESULTS

Of the 12 participants who started the study, three of them discontinued the study due to disease remission or clinical complication, with nine patients remaining, being five of them from the EG and four from the CG. In the sample there was a predominance of males (55.6%), with an average age of 49.89 ± 13.34 years.

When evaluated individually, EG patients showed histological improvement (Effect Size: 0.706) on rectosigmoidoscopy examination (Figure 2). Although 80% of EG patients had calprotectin values within the normal range, these did not differ between groups (Table1).
For BMI, 78% of patients were overweight, with no difference between groups (p = 0.456). The inflammation markers (CRP, IL10), as well as haemoglobin and haematocrit, showed no significant differences between groups (Table 1).

In addition, quality of life evaluated by SF-36 domains showed no difference between groups (p > 0.05). But, the intervention effect (EF) revealed a medium to large effect size for the physical functioning, bodily pain, general health, social functioning, role-emotional and mental health domains (Table 2).
Table 1. Influence of turmeric intervention on evaluation of body mass index and biochemical analysis of UC patients.

| Variables                  | Experimental group | Control group | Effect Size |
|----------------------------|--------------------|---------------|-------------|
|                            | Pre    | Post | ∆      | p†       | Pre  | Post | ∆      | p†       | p‡       | d Cohen | Effect |
| Body mass index (kg/m²)    | 28.43±1.16  | 28.43±1.16 | 0.00 | 0.99 | 27.11±1.20  | 27.03±1.35 | -0.08 | 0.965 | 0.456 | 0.28 | Small  |
| Interleukin-10 (mg/dL)     | 0.12±0.02 | 0.11±0.00 | -0.01 | 0.80 | 0.23±0.10  | 0.11±0.01 | -0.13 | 0.289 | 0.65 | 0.66 | Medium |
| C-reactive protein (mg/dL) | 0.77±0.34 | 0.40±0.09 | -0.49 | 0.46 | 0.37±0.11  | 0.42±0.33 | 0.05 | 0.564 | 0.31 | 0.69 | Medium |
| Haemoglobin (mg/dL)        | 13.80±0.55 | 14.76±0.53 | 0.96 | 0.24 | 13.67±0.74  | 13.77±0.47 | 0.10 | 0.913 | 0.21 | 1.14 | Large  |
| Haematocrit (mg/dL)        | 41.32±1.45 | 42.28±1.46 | 0.96 | 0.65 | 41.62±2.56  | 39.22±0.98 | -2.40 | 0.415 | 0.14 | 1.65 | Large  |
| Calprotectin (mg/dL)       | 494.14±202.81 | 200.04±115.71 | -294.10 | 0.24 | 688.67±401.16  | 345.17±216.5 | -8 | 343.50 | 0.480 | 0.55 | 0.18 | Small  |

Values are presented as means ± standard error of the mean.

Δ: delta
†: Difference between the pre- and post-moments (p-value obtained by paired Student’s t-test).
‡: Difference between groups (p-value obtained by unpaired Student’s t-test of delta values).
Fonte: Elaborado pelos autores (2020)
Table 2. Quality of life domain of UC patients.

| Variables          | Experimental group | Control group | Effect Size |
|--------------------|--------------------|---------------|-------------|
|                    | Pre                | Post          | Δ            | p†         | Pre          | Post          | Δ            | p‡         | d Cohen |
| Physical functioning| 90.00±3.16         | 87.00±4.64    | -3.00        | 0.595      | 37.50±11.27 | 67.50±11.81  | 30.00        | 0.146      | 0.081    | 1.71    | Large  |
| Role physical      | 75.00±11.18        | 65.00±21.79   | -10.00       | 0.910      | 50.00±20.41 | 50.00±28.87  | 0            | 1.000      | 1.000    | 0.17    | Small  |
| Bodily pain        | 67.00±18.99        | 55.60±12.78   | -11.40       | 0.399      | 20.50±14.61 | 49.25±10.08  | 28.75        | 0.189      | 0.085    | 1.38    | Large  |
| General health     | 79.60±8.53         | 84.40±8.30    | 4.80         | 0.697      | 49.00±13.36 | 84.50±16.97  | 35.50        | 0.083      | 0.086    | 1.02    | Large  |
| Vitality           | 55.00±6.52         | 57.00±7.52    | 2.00         | 0.916      | 43.75±8.26  | 43.75±2.39   | 0            | 0.882      | 0.607    | 0.14    | Small  |
| Social functioning | 82.50±11.59        | 95.00±5.00    | 12.50        | 0.288      | 37.50±11.41 | 31.25±15.73  | -6.25        | 0.767      | 0.302    | 1.00    | Large  |
| Role emotional     | 86.67±13.33        | 73.33±19.44   | -13.33       | 0.520      | 50.00±21.52 | 66.66±19.24  | 16.66        | 0.544      | 0.590    | 0.70    | Medium |
| Mental health      | 61.60±10.55        | 68.80±13.29   | 7.20         | 0.673      | 48.00±13.56 | 46.00±13.22  | -2.00        | 0.884      | 0.537    | 0.57    | Medium |

Values are presented as mean ± standard error of the mean.

Δ: delta

†: Difference between the pre- and post-moments (p-value obtained by paired Student’s t-test).
‡: Difference between groups (p-value obtained by unpaired Student’s t-test of delta values).

Fonte: Elaborado pelos autores (2020)
4 DISCUSSION

It was observed that turmeric supplementation was able to reduce the Mayo’s Ulcerative Colitis activity score and the quality of life domains. Previous studies had observed endoscopic remission in 36% of UC patients after a 3 g/d dose of Curcuma longa L. associated with 4 g/d Mesalamine for one month\(^4\), and significant improvement in endoscopic scores with lower turmeric dosage (2 g/d) for six months, combined with Sulfalazine or Mesalamine at a maximum dose of 3 g/d.\(^7\)

Despite the behavioural changes to which the patients are susceptible during disease activity, such as altered dietary intake and nutritional absorption, the patients in our study were overweight at baseline and maintained this nutritional status during the eight weeks of intervention. This finding corroborates with other studies that also found a higher prevalence of overweight among patients\(^{15,16}\), thus suggesting that the symptoms of these patients have no influence on weight loss.

In vitro evidence indicates that turmeric, due to its curcumin content, is capable of increasing IL-10 promoter activity, with consequent increase in IL10 production and secretion.\(^{17}\) Thus, this increase may positively contribute to anti-inflammatory activity, causing the reduction of pro-inflammatory markers such as CRP. In our study, we observed a significant increase of IL10 in the GE group, which may be a result of turmeric action, and be associated with the improvement found in these patients’ quality of life domains.

The SF-36 questionnaire has been used in patients with active UC to assess energy levels, vitality and health perception in general, being able to indicate changes in behaviour, which affect social relationships. In the present study, we verified this profile in CG patients, who maintained the disease symptoms during the intervention and reported avoiding socialization.\(^{18}\) Thus, the large effect size for the domains of physical capacity, pain, general health and social aspects of SF-36 allows us to say that the consumption of Curcuma longa L. had a positive impact on quality of life.

5 CONCLUSION

Turmeric supplementation for eight weeks was able to reduce the Mayo’s score and improve the quality of life of patients with UC. Although this study has a small sample size, the results were promising and justify further long-term, randomized, double-blind studies in order to verify the influence of turmeric supplementation on remission time, biochemical inflammatory markers and quality of life.
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