

Beneficial effects of Flavonoids after ambulatory therapy with Combined Hemorrhoidal Radiocoagulation (CHR)

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Abstract. – OBJECTIVE: Phlebotropic activity, protective effect on the capillaries and anti-inflammatory properties of the Flavonoids have been reported in literature. Recently, we evaluated the effect of these drugs in controlling post-operative symptoms of proctologic surgery. In this randomized study we compared the results obtained in two groups of patients, with grade II haemorrhoids, submitted to radiofrequency coagulation of the hemorrhoidal nodule with radiofrequency scalpel (CHR), to verify the effects of Flavonoids to reduce further symptoms after treatment.

PATIENTS AND METHODS: Out of 70 patients initially randomized, a total of 59 patients regularly returned to outpatient visit at least for 1 month of follow-up. Consequently, two groups of patients were considered: Group A, represented by 28 individuals treated with Flavonoids, and Group B, consisting of 31 patients as a control group. Our purpose was to determine: grade of pain after procedure and at first evacuation (score from 1 to 10), bleeding, incidence of failures and complications, patient's satisfaction after 30 days from the treatment (score from 1 to 10).

RESULTS: We observed that the results obtained regarding the pain reported at the end of procedures (2.51 ± 1.4 for group A and 2.54 ± 1.15 for group B) and at the first evacuation (2.6 ± 1.52 for group A and 2.7 ± 1.18 for group B) are similar in both study groups. Instead, the mean score on overall satisfaction at 30 days from the treatment showed a statistical significance (8.32 ± 1.72 for group A and 6.64 ± 1.78 for group B; $p < 0.05$). There were no reported other important issues.

CONCLUSIONS: Our findings confirm the usefulness of Flavonoids to make more comfortable the post-treatment period.

Key Words:

Flavonoids, Hemorrhoids, Radiofrequency scalpel, Proctology.

Introduction

All methods for the ambulatory therapy of hemorrhoids have advantages and disadvantages

and, often, the results reported in the literature are controversial. A very important aspect for the patient is represented by post-treatment symptoms. We, recently, published some analysis in which we compared different methods with the rubber band ligation combined with radiofrequency coagulation of the hemorrhoidal nodule (CHR)^{1,2}. We observed that patients treated with CHR reported an average score about pain and satisfaction more favorable.

In this prospective randomized study we compared the results obtained in two groups of patients with grade II hemorrhoids submitted to CHR. Group A was treated with Flavonoids while the Group B did not receive any medical treatment.

The purpose of our analysis was to verify the beneficial effects of Flavonoids to reduce further symptoms after ambulatory therapy with CHR.

Patients and Methods

For the development and description of this randomized clinical trial, we followed CONSORT criteria³. The trial was undertaken in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice⁴ and with the ethical principles laid down in the Declaration of Helsinki⁵. The randomized trial was performed by the sealed envelopes method, after careful explanation of the advantages and risks of the study.

Seventy patients with grade II hemorrhoids were selected and studied in the Department of Experimental Medicine and Surgery, University of Rome, Tor Vergata.

Before being admitted to the study, all patients underwent a proctology visit and a sigmoidoscopy to exclude other proctological diseases associated. They were also excluded from the study: pregnant women and the patients with oth-

er diseases that require the use of medications (anticoagulants, painkillers, etc.) that could change final results. In the days before the treatment was not prescribed any specific preparation or a special diet.

All patients were placed in left lateral position sec. Sims and, using a disposable proctoscopy, treated in ambulatory with CHR^{1,2}. A 4MHz Radiofrequency generator was used; it was equipped with an handle which can be mounted on various types of electrodes. In those procedures we indifferently used ball electrodes or large tip electrodes for the coagulation. The intensity of the output power of radiofrequency generator was adjusted as required to obtain coagulation, without causing charring. The gradual variation of the nodules aspect to a grayish white color indicated a sufficient state of coagulation.

All selected patients had three internal hemorrhoidal nodules located in the usual positions. We proceeded to ligation of a single hemorrhoidal node every 15 days, so each patient underwent a total of 3 procedures.

The ligation was performed just above the dentate line, sufficiently distant from the skin edge to avoid the involvement of neural structures. Any kind of anesthetic was used. The method resulted painless: patients reported only minor discomfort, however, tolerable. All patients were immediately discharged after the procedure. A high-fiber diet and administration of paraffin oil (3 spoons/day) were prescribed during following weeks in order to make softer stool and reduce traumatism in the anal canal. A careful hygiene and use of local emollient and disinfectant soap were recommended. At discharge, the patients were randomized in two groups. Group A: we prescribed Flavonoids (tablets containing Quercetin 200 mg and Hesperidin 50 mg in combination with Resveratrol, Bromelain, Folic Acid, vitamins C and E) (Deflanil Plus®) at a dose of two times a day for a week and then at a dose of once a day for the next week. We preferred this product because is formulated for once daily dosing, compared to others. Group B represented the control group, without Flavonoids therapy.

All patients were clinically visited and underwent to anoscopy after 3, 15 and 30 days from the procedure.

In this study primary endpoint was to evaluate the beneficial effects of Flavonoids to reduce further symptoms after ambulatory therapy with CHR.

We considered the grade of pain immediately after the procedure and at the first evacuation, bleedings, appearance of failures and complications and patient's satisfaction after 30 days from the treatment.

For pain evaluation we used a score based on overall impressions reported by patients at the end of treatment: 1 was the minimum value (no pain) and 10 the maximum value (maximum pain reported). We also assessed the degree of patients satisfaction at 30 days from the last procedure using a score that goes from 1 (minimum) to 10 (maximum), that indicated the highest satisfaction in relation to expectations.

Descriptive statistics for qualitative variables were performed with occurrences and described with relative frequencies. Comparison was performed with the Student's *t* test for parametric continuous variables, the Mann-Whitney test for non-parametric variables and the Fisher's exact test for categorical variables in which the occurrence of observations within cells was inferior to 5. All *p* values were considered significant if less than 0.05.

Results

Between January 2013 and December 2013 we conducted a randomized study on 70 patients in two equal groups. Seven patients in group A (Flavonoids) and 4 patients in group B (Control) were lost during the follow-up, and therefore they were excluded from the final evaluation of results. Altogether, we enrolled 59 patients with a total of 177 procedures. The study was completed in January 2014 with the last visit. Group A consisted of 11 male and 17 females with mean age of 31 years (range 19-43), group B included 12 males and 19 females with mean age of 36 years (range 23-51). Preoperative symptoms reported by 70 patients and appeared at least 6 months are showed in Table I.

Table I.

| Preoperative symptoms | N. | % |
|-----------------------|----|------|
| Pain | 52 | 74.3 |
| Bleeding | 31 | 44.2 |
| Anal Itching | 22 | 31.4 |
| Perianal Irritation | 20 | 28.6 |
| Secretions | 11 | 15.7 |

The mean pain score reported at the end of procedures was 2.51 ± 1.4 (range 1-6) for group A and 2.54 ± 1.15 (range 1-7) for group B (Figure 1). In both groups, the first evacuation generally occurred after 24-36 hours from the ligation. The mean pain score at the first evacuation was 2.6 ± 1.52 (range 1-6) for group A and 2.7 ± 1.18 (range 1-6) for group B (Figure 2). Therefore there were no statistically significant differences between the two groups about pain at the end of the procedures and after the first evacuation, as well as after the successive evacuations.

In both groups bleedings, occurred at the end of the procedures, after the first evacuation and in following days, were irrelevant and didn't require any particular interventions and/or coagulants. We observed no other issues of great importance.

At first visit after 3 days, an early lost of elastic ligatures were observed in 10 cases of 84 procedures in group A (11.9%) and in 18 cases of 93 ligatures in group B (19.3%). However, in all these patients after 15 days we observed eschars as results of CHR. During all the study no complications were observed.

The mean score on overall satisfaction at 30 days from the treatment was 8.32 ± 1.72 (range 3-10) and 6.64 ± 1.78 (range 4-10) for group A and group B, respectively (Figure 3). The mean score on overall satisfaction showed, therefore, a statistical significance between the two groups ($p < 0.05$).

Two patient in group A and 5 patients in group B required analgesics (Ketorolac 20-25 drops, sporadically). No patient assumed benzodi-

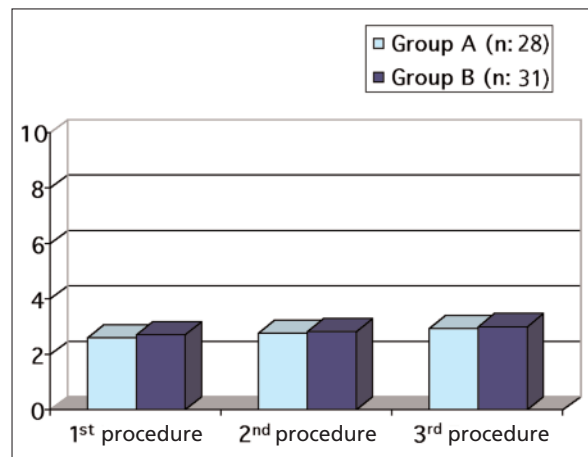


Figure 2. Comparison of pain scores (1-10) between group a (*Flavonoids*) and group B (*Control*) after 1st, 2nd and 3rd procedure.

azepines. Readmission to work was straightforward in all cases, without correlation with the type of work.

Discussion

In this study, we evaluated the beneficial effects of Flavonoids to reduce further symptoms after ambulatory therapy with CHR.

We used a new instrument, "HF Radioscalpel", able to cut and coagulate tissues using heat generation from high frequency radio waves passage^{6,7}. The main difference with traditional electric

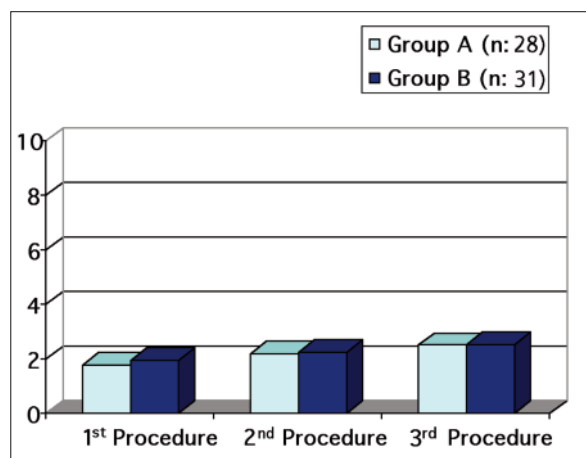


Figure 1. Comparison of pain scores (1-10) between group A (*Flavonoids*) and group B (*Control*) after 1st, 2nd and 3rd procedure.

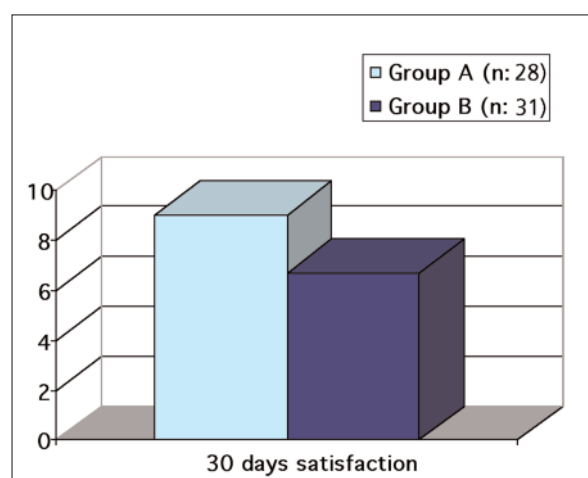


Figure 3. Comparison of satisfaction scores at 30 days (1-10) between group A (*Flavonoids*) and group B (*Control*).

scalpel is in increased frequency (4 MHz compared to 500 KHz traditional electrical scalpel) that results in using less power (60 W versus more than 300 W) and developing lower temperatures (45-70°C vs. 300-600°C). Final result is minimization of traumatic effect related to heat damage^{8,9}. Currently HF radioscalpel is applied in General Surgery, Plastic Surgery, Vascular Surgery, Dermatology, Orthopedics, Neurosurgery and Ophthalmology. More recently, radiosurgery founded application in Proctology. The finding that the HF radioscalpel can further improve immediate and remote results of all proctologic interventions encouraged massive spreading of this instrument. In our previous experiences we already used HF radioscalpel in proctology and our personal conviction was that it led to better final results^{10,11}, in comparison to traditional techniques. In literature reports, numerous Authors described their experience about radio frequency in proctology. In particular Gupta describes a radiocoagulation technique for ambulatory treatment of grade I or II hemorrhoids and affirms his personal failure rate of 13%¹². The same Author previously conducted a randomized trial to compare results obtained with radiocoagulation and band ligation¹³, noting that this latter method, despite being effective in the same way, had a higher pain incidence. In a precedent article, we compared in the ambulatory treatment the traditional Rubber Band Ligation (RBL) vs CHR, to evaluate immediate efficacy and optimize long-term result¹.

The analysis results are excellent in both groups and there is no statistical significance regarding the pain after the CHR and after the first evacuation. We did not consider other symptoms, such as bleeding, because their incidence is irrelevant. Regarding instead the satisfaction expressed after 30 days, we observed better results in the group of patients treated with Flavonoids. Probably this result is in relation with the characteristics of the drug. The Flavonoids therefore seem to have a beneficial effects on all the other hassles that arise after the CHR (pruritus, tenesmus, perianal weight, etc).

The Flavonoids are polyphenolic compounds, secondary metabolites of higher plants, water-soluble and usually present as glycosides. Flavonoids are ubiquitous in nature and currently we know of more than 4.000 flavonoid glycosides. These compounds reduce the inflammation by inhibiting prostaglandin PGE₂ e PGE₂ α and thromboxane B₂ release from macrofages and increasing endothelial nitric oxide synthase activity. Levels of

oxygen-derived free radicals, generated during the inflammatory response, are also reduced. These proinflammatory mediators would otherwise excessively weaken the collagen in the vessels basement membrane and in the tunica media of venules. As a result, the inflammatory process is inhibited and edema subsequently reduced.

Flavonoids improve venous tone and reinforces capillary resistance. This protective effect on capillary fragility may prevent postoperative bleeding. In addition, they increase lymphatic drainage and protect the microcirculation from inflammatory mediators, resulting in reduced edema and pain^{14,21}.

Many authors have studied the effects of Flavonoids in the treatment of medical proctologic disorders and after outpatient and surgical treatments^{18,19}. La Torre et al¹⁵ conducted a randomized trial of patients undergoing Milligan-Morgan hemorrhoidectomy. They observed an improvement in the postoperative comfort and a reduction of pain and bleeding.

We had already experienced these drugs in the postoperative treatment after hemorrhoidectomy²² and we noticed a significant decrease in symptoms. We did not have significant results regarding bleeding and pain, but we observed a significant difference about the tenesmus, perianal itching and weight compared to the control group.

The results obtained in this study confirm the usefulness of Flavonoids in patients undergoing to ambulatory therapy of hemorrhoidal disease for their contribution in a more comfortable post-treatment period.

Conclusions

In this study Flavonoids (tablets containing Quercetin 200 mg and Hesperidin 50 mg in combination with Resveratrol, Bromelain, Folic Acid, vitamins C and E), at a dose of two times a day for a week in single dose and then at a dose of once a day for the next week, were administrated in patients with grade II hemorrhoids after ambulatory therapy with CHR, in order to evaluate the their effectiveness.

Our results confirm the usefulness of this drugs to make more comfortable the post-treatment period.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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