Abstract. – Background: The medical treatment for hemorrhoids has undergone significant changes on introduction of new pharmaceutical agents in the last decade. Euphorbia Prostrata is a new molecule used for grade I and II hemorrhoids. Beneficial effects of the Euphorbia prostrata in hemorrhoids have multiple mechanisms that are due to its active constituents flavonoids, tannins and phenolic acid. This pilot study was performed to assess the effectiveness of this molecule in early grades of symptomatic hemorrhoids.

Materials and Methods: In the present retrospective study, the effect of Euphorbia prostrata on patients with hemorrhoids was observed over a follow up period of 12 weeks. In all, 120 patients were studied. This included 63 males and 57 females. Patients with grade 1 and 2 were prescribed with one tablet of Euphorbia prostrata (Tab Sitcom, Panacea Biotec, India) to be consumed on empty stomach every morning for two weeks. Follow-up was carried out at 2, 4 and 12 weeks after commencement of treatment. The primary end point of the study was control of bleeding and secondary end points were regression of hemorrhoid mass, pruritus and discomfort in the anus.

Results: Ninety-nine patients (82%) had complete cessation of bleeding at the end of two weeks. Six patients needed another 2 week’s treatment to achieve complete relief, amounting to a success rate of 87%. Anal itch was relieved in 73% of patients, while anal discomfort subsided in 90% of patients. None of the patient had reported any adversity with consumption of the drug.

At the follow-up after 3 months of treatment, no patient reported with symptomatic recurrence. However, 37 of the 79 patients (46%) still had residual hemorrhoids on anoscopic examination.

Conclusions: This pilot study shows that Euphorbia prostrata can be used as an effective and well-tolerated pharmaceutical agent in the treatment of early grades of hemorrhoids. Long-term follow-up and randomized control trials by comparing with other established formulations is necessary to justify reliance on this medication.

Key Words: Hemorrhoids, Euphorbia prostrata, Flavonoids, Bleeding.

Introduction

Hemorrhoids are one of the most frequent anorectal disorders encountered in the primary care setting. They are the most common cause of bleeding per rectum and are responsible for considerable patient suffering and disability1.

Drug treatment for various anorectal conditions has been known since ancient times. Today, modern as well as traditional drugs are being increasingly used in all grades of symptomatic hemorrhoids. These drugs (oral and local) are used as a part of conservative management or as an adjuvant to invasive outpatient procedures. While drug treatment is aimed at curing early grade of hemorrhoids which does not need any intervention, the role of drug therapy in advanced grades of hemorrhoids is to control the acute phase so that definitive office procedures or surgery can be scheduled at a convenient time2.

Bioflavonoids, particularly diosmin, oligomeric proanthocyanidin complexes (OPCs), and hesperidins, have demonstrated efficacy in the treatment of hemorrhoids3. These bioflavonoids exhibit phlebotonic activity, vasculoprotective effects, and antagonism of the biochemical mediators of inflammation. OPCs, diosmin, and hesperidin have been the subject of numerous clinical trials on efficacy and safety in the treatment of varicose veins and hemorrhoids4.
*Euphorbia prostrata* is an annual herb, which belongs to family Euphobeaceae and is abundantly found in India and Africa. It is been traditionally used in several digestive system disorders⁵.

The active principles in *Euphorbia prostrata* are chiefly flavonoids, phenolic acid and tannins. Flavonoids and phenolic acid have been reported to have anti-inflammatory, analgesic, antioxidant, haemostatic, antithrombotic and vasoprotective actions⁶.

The chemical analysis of *Euphorbia prostrata* revealed that it contains phenolic compounds like Gallic acid which activates Hageman factor which causes hypercoagulability and ellagic acid which suppress histamine release.

It also contains flavonoids like apigenin, which inhibits I kappa B and suppresses inflammatory mediators and luteolin, which inhibits protein tyrosin phosphorylation and IkB mediated inflammation. Tannins are known to possess astringent and haemostatic properties. Preclinical studies carried out on the extract have confirmed its wound healing and anti-haemorrhoidal activity⁷.

With these properties of *Euphorbia prostrata*, we tried to evaluate its usefulness in controlling symptoms of grade 1 and 2 symptomatic hemorrhoids.

**Materials and Methods**

In the present retrospective study, the effect of *Euphorbia prostrata* on patients with hemorrhoids was observed over a follow up period ranging from 6 to 12 weeks. In all, 168 patients were included in this study. This included 94 males and 74 females. The study was conducted at Fine Morning Hospital and Research Center, Nagpur, India, between January 2009 and December 2009.

The diagnosis of hemorrhoids was made on a detailed history of symptoms and was confirmed on per rectal and anoscope examination. Patients having first and second degree symptomatic hemorrhoids were included. While 71 of the patients were having Grade I hemorrhoids, remaining 97 patients had Grade II hemorrhoids, which used to prolapse during defecation and to get reduced by their own.

**Exclusion Criteria**

Patients having associated anal fissure or infective anal pathologies, like cryptitis or proctitis, and patients who had been treated with some office procedure in the past were excluded from the study.

All the patients received written explanation about this medicinal prescription including potential drawbacks such as relapses and a possible need for a repeat medication or a resort to other mode of treatment. The study was approved by the local Ethical Committee and was performed according to the Declaration of Helsinki.

The molecule is available in the market as a tablet of 100 mg with the brand name Sitcom (Pannecia Biotec Ltd., New Delhi, India).

The patients were provided with a pack of 14 tablets of Sitcom which was to be consumed once daily before breakfast for two weeks. They were asked not to use any other oral or local medication during this therapy. They were encouraged to consume high fiber diet along with plenty of oral fluids. They were cautioned not to strain at stool and that they should expect some bleeding in the first week after commencement of the treatment.

The understudied were called after 2 weeks for first follow up. They were also warned to report early if the symptoms aggravated or in case of any adversity noted with use of the medication.

A worksheet was prepared for each patient which included four points for assessment for this trial. This included 1. Bleeding; 2. Prolapse; 3. Pruritus; and 4. Heaviness or discomfort in the anal canal. Each of the above points was noted before commencement of the treatment and at each follow-up.

A treatment protocol was also framed where those patients who got complete relief from the symptoms were asked to discontinue medication after 2 weeks but to report at 4 and 12 weeks.

Patients showing partial relief of symptoms after 2 weeks were prescribed a further course of 14 tablets of *Euphorbia prostrata*.

Patients having no relief at the end of 2 weeks of treatment were asked to discontinue and were suggested other treatment options.

Anoscopic examination was performed at 4 and 12 weeks. Any adversity with consumption of Sitcom was noted. Patients having symptomatic relief but with persistence of hemorrhoids were kept on regular follow up along with instructions on dietary measures and lifestyle modification.

**Results**

Of the 168 patients, one hundred and twenty completed the study protocol. There were 63
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males and 57 females. The mean age of patient was 33 years (range 21-67 years). 79 patients had grade 2 hemorrhoids while 41 had grade 1 hemorrhoids. Out of the remaining 48 patients, thirty-six patients did not complete the study for various reasons, like violation of treatment protocol by irregular consumption of Sictom tablet, use of other medication, irregular follow up and the remaining 12 patients were lost to follow-up.

None of the patient withdrew from the study due to adversity of the study medication.

As regard bleeding per rectum, ninety-nine patients (82%) had complete cessation of bleeding at the end of two weeks. Eight patients (7%) had some amount of bleeding, so they were asked to continue consuming Sitcom for 2 more weeks. The remaining 13 patients had no relief at all, and the treatment was discontinued in these patients. At the end of 4 weeks, five of the eight patients with partial relief responded with complete stoppage of bleeding while the remaining three patients continue to have bleeding and thus they were considered treatment failures amounting to a total of 13% treatment failure.

At the first follow-up, 73% patients complaining of anal pruritus were relieved of this symptom, while the remaining continued to have anal itch even at the subsequent follow up.

88% patients complaining of discomfort or heaviness in the anal canal reported complete relief at the first follow up. Another 2% got relieved at the last follow up while the remaining continued to complain the discomfort.

Of the 79 patients having prolapse or protrusion, 58 patients (73%) did not notice this symptom at 12 week follow up. However, anoscopic examination performed during this follow-up revealed that 37 patients (46%) still had residual hemorrhoids.

**Discussion**

Symptomatic hemorrhoid is not only a subject of interest for coloproctologists, but is also encountered in the practice of gynecology, gastroenterology, urology and family medicine.

Numerous medications in the form of oral preparation or as local application have been proposed, used and studied since the time of Hippocrates. There are many oral antihemorrhoidal preparations widely prescribed by physicians in the treatment of acute symptoms of hemorrhoids. These preparations contain semi synthetic agents or plant extracts such as escin, diosmin, and rutin related compounds that have been shown to have regulatory effects on veins, venules, and capillaries.

Bioflavonoids, particularly diosmin, oligomeric proanthocyanidin complexes (OPCs), and hesperidin, have demonstrated efficacy in the treatment of hemorrhoids. These bioflavonoids exhibit phlebotonic activity, vasculoprotective effects, and antagonism of the biochemical mediators of inflammation. Animal studies have shown that flavonoids reduce neutrophil activation, mediate inflammation, and decrease soluble endothelial adhesion molecules. Human trials have shown the ability of flavonoids to improve venous tone and vein elasticity assessed by plethysmography and to decrease plasma markers of endothelial activation.

*Euphorbia prostrata* is an annual herb, which has traditionally been used to treat several ailments like asthma, diabetes mellitus, bloody dysentery and sores since time immemorial. Tannins are known to possess astringent and haemostatic properties. Preclinical studies carried out on the extract have confirmed its wound healing and anti-hemorrhoidal activity.

Beneficial effects of *Euphorbia prostrata* in hemorrhoids have multiple mechanisms, which include improvement of venous tone, increased lymphatic drainage, protection of capillary bed microcirculation, inhibition of inflammatory reactions, and reduced capillary permeability. Flavonoids in Euphorbia are potent inhibitors of prostaglandin E2 (PGE2) and thromboxane A2 (TXA2) as well as being inhibitors of leukocyte activation, migration, and adhesion. Five new compounds were discovered and identified by the inventors in *Euphorbia prostrata* namely luteolin, 6-methoxyquercetin-glycoside, quercetin, and glycosides of luteolin and apigenin. The extract of *Euphorbia prostrata* is water soluble.

The pharmaceutical composition containing the standardized extract of *Euphorbia prostrata* as the active ingredient contains 35-62% flavonoids. Of this, apigenin glycoside amounts to 30-45%, luteolin glycoside to 3-9%, 6-methoxyquercetin glycoside is 1-6% while quercetin and luteolin is 1-2%. Studies with the standardized extract of *Euphorbia prostrata*, when administered orally showed an inhibition of both carrageenan-induced edema and histamine-induced edema.
Ellagic acid is one of the major constituents of *Euphorbia prostrata* extract and is reported to suppress histamine release mediated by histamine liberators. This property of Sitcom has been seen to control anal pruritus in majority of patients in this study.

It is speculated that analgesic, anti-inflammatory and antioxidant activity of various flavonoids components of *Euphorbia prostrata* extract may contribute in healing of inflammatory tissue damage in hemorrhoidal conditions. Phenolic acids are reported to activate intrinsic blood coagulation by activation of Hageman factor and cause a state of hypercoagulability. It is well reported that tannic acid has antimicrobial properties, which is associated with the ester linkage between gallic acid and other sugar or alcohol groups.

This investigation has confirmed that *Euphorbia prostrata* is quite effective in controlling hemorrhoidal bleeding and alleviating symptoms of the disease because of the various contents it has. It is non-toxic and may be given orally without loss of efficiency. This reinforces data found in previous clinical trials using varying dosages and of different study lengths, in which flavonoids was more effective than placebo in reducing the duration and intensity of symptoms (e.g., bleeding, pain, and anal discharge) of acute hemorrhoid attacks. Bleeding from non prolapsed internal hemorrhoids resolved more quickly with flavonoids.

Studies have shown that flavonoid is an “edema-protective” drug in treatment of acute hemorrhoids. It has been hypothesized that the positive effect of flavonoids on anal mucosa is through decreasing the edema. This may be the reason that patients in this study who felt that the hemorrhoids have been regressed after treatment with Sitcom actually had experienced reduced hemorrhoidal edema, as anoscopic examination did showed presence of residual hemorrhoids in most of the patients with grade 2 hemorrhoids.

As with all diseases, the primary treatment for hemorrhoids is the prevention. Patients with risk factors for developing these conditions should be identified through history and physical exam and helped out with conservative treatment lest an aggressive intervention is called for.

Conclusions

The study indicates that two weeks of treatment with 100 mg of *Euphorbia prostrata* could be adopted as one of the drug of choice for the treatment of early grades of symptomatic hemorrhoids. While the findings are promising, further long-term follow-up and randomized controlled trials with other established formulations are required to confirm long term efficacy and sustainability of this medication.

References

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