

Clinical Study of the Ginko biloba - Troxerutin-Heptaminol Hce† in the Treatment of Acute Hemorrhoidal Attacks

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Abstract

Objective : The aim of this study was to assess the clinical efficacy, compliance and safety of Ginko biloba - Troxerutin-Heptaminol Hce in the treatment of patients with acute hemorrhoidal attacks in Thailand.

Material and Method : In a prospective clinical study on hospital outpatients, the authors studied the effect of Ginko biloba - Troxerutin-Heptaminol Hce for a week in adults (18-70 years old) with acute hemorrhoidal attacks.

Result : Twenty-two patients, with a mean age of 41.7 years were included in the study. The male to female ratio was 1 : 1.2. Most patients (77%) had grade 1 and 2 hemorrhoids with an average duration of attacks of 3 days. On intention to treat analysis, bleeding, pain, tenesmus and discharge were significantly improved. Treatment was well accepted and safe.

Conclusion : In the short-term, Ginko biloba - Troxerutin-Heptaminol Hce is effective, acceptable and safe in the treatment of patients with acute hemorrhoidal attacks.

Key word : Acute Hemorrhoidal Attacks, Ginko Biloba - Troxerutin-Heptaminol Hce

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Having a hemorrhoids is a common clinical condition with a prevalence of 24.8 per cent⁽¹⁾. Most of the symptoms can be treated with outpatient

measures such as drugs, sclerotherapy, infrared photo-coagulation and rubber band ligation, etc⁽²⁻⁷⁾. The goal of treatment for acute hemorrhoidal attack is

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† Ginko biloba - Troxerutin-Heptaminol Hce = Ginkor Fort® (Beaufour Ipsen International, Thailand).

to achieve rapid resolution of symptoms with minimal risk of complications. Though fiber supplements alone are safe and effective for such purposes, a period of up to six weeks may be required for resolution of symptoms(8). Techniques such as rubber band ligation, sclerotherapy and infrared photocoagulation may give more rapid control of bleeding but are not appropriate for the general practitioner who may not be adequately trained or does not have the equipment required to perform the mentioned techniques safely.

Ginkgo biloba - Troxerutin-Heptaminol Hce (Beaufour Ipsen International, Thailand) which consists of Ginkgo biloba extract (EGb 761 : 14 mg), Heptaminol hydrochloride (300 mg) and Troxerutin (300 mg) is one of the phlebotonic agents recommended for the treatment of hemorrhoids. Effects of EGb 761 and Troxerutin on the improvement of hemorrhoid symptoms are caused by improving venous flow rate, decreasing capillary hyperpermeability and decreasing inflammation, while Heptaminol hydrochloride increases venous tone and reduces capillary hyperpermeability(9,10). These drugs have their own as well as synergistic favorable effects which are in accordance with the most recent etiopathogenetic concept of hemorrhoidal disease(11-14). Ginkgo biloba - Troxerutin-Heptaminol Hce has an action on the hemorrhoidal vascular system at the tissue level, acting against congestion, edema and the inflammatory process (resulting from a hemorrhoidal attack). It has been used to treat patients with acute hemorrhoidal attacks effectively(15-18).

However, there are no data regarding the efficacy, compliance and safety of Ginkgo biloba - Troxerutin-Heptaminol Hce in Thai patients who present with acute hemorrhoidal attacks. This prospective clinical study was performed to evaluate the result of such treatment.

MATERIAL AND METHOD

Patients with acute hemorrhoidal attacks attending the ano-rectal clinic of the Department of Surgery, Ramathibodi Hospital Medical School during September 2000 and November 2001 were enrolled into this prospective clinical study. Informed consent was obtained from all patients in the study. The study was approved by the Ramathibodi Hospital Ethics Committee.

All patients included in the study presented with recently untreated acute hemorrhoidal attacks as defined by Prof. Jean-Clauded SARLES(15), by the presence of at least two of the following:

- Ano-rectal bleeding.
- Burning or throbbing pain.
- Discharge.
- Pruritus ani.
- Tenesmus.

Ano-rectal bleeding was classified according to intensity as follows :

- 4 : presence of fresh blood in the toilet bowl.
- 2 : presence of fresh blood on the toilet paper.
- 0 : absence.

Pain was measured by using visual analog score on the scale of 0 to 10.

Presence of discharge, pruritus ani and tenesmus were recorded.

Physical signs

Through a complete ano-rectal examination with proctoscopy, the severity of the hemorrhoids were classified into 4 grades as follows:

- Grade 1 : bleeding only with no prolapse.
- Grade 2 : prolapse with spontaneous reduction.
- Grade 3 : prolapse with manual reduction.
- Grade 4 : permanent prolapse.

Overall assessment was characterized as:

Good	: Symptoms has disappeared at the end of the treatment.
Average	: Obvious improvement of symptoms.
Poor	: Minimal or no improvement.

Compliance with treatment was rated as good (all medications were taken and the patient available for all appointments), fair (the patient was available for follow-up but medication was not completely taken) and poor (the patient was lost to follow-up).

Adverse drug effects were recorded during and at the end of the treatment.

Inclusion criteria

1. Patients aged between 18 and 70 years old.
2. Patients with acute hemorrhoidal attacks who had not taken any treatment in the same therapeutic class as Ginkgo biloba - Troxerutin-Heptaminol Hce since the beginning of the attacks.
3. Absence of other anorectal lesions with symptoms defined as acute hemorrhoidal attacks.

Exclusion criteria

1. Pregnant or nursing women.
2. Patients with contraindication to heptaminol.
3. Patients with anal fissure, anorectal abscess, fistula-in-ano, inflammatory bowel disease and anal cancer.
4. Patients who required NSAIDs and/or vasoactive agents which may affect the course of acute hemorrhoidal attacks.
5. Patients with anti HIV positive result.

Treatment and evaluation protocol

Patients with acute hemorrhoidal attacks enrolled into the study were assessed for symptoms and physical signs before treatment (D0) then received 4 capsules of Ginko biloba - Troxerutin-Heptaminol Hce each day for 7 days and assessed again at the end of the treatment period (D7).

The study outcome consists of clinical efficacy, compliance and drug adverse effect.

Clinical efficacy was estimated by:

- Comparison between clinical parameters before treatment (D0) and at the end of the treatment (D7).

- Whether there was agreement of an overall assessment of treatment by patient and the physician.

Response of acute hemorrhoidal attacks to treatment was analyzed on an intention to treat basis. Changes in categorical response variables were compared using McNemar's chi-square test and asymptotic marginal homogeneity test, and continuous response variables using the Wilcoxon signed rank test. A p-value of less than 0.05 was considered significant.

RESULTS

Twenty-two consecutive patients were included in the study. The baseline characteristics of the patients are shown in Table 1.

The mean age of the patients was 41.67 years. Male to female ratio was 1 : 1.2. The majority of patients (77.26%) had grade 1-2 internal hemorrhoids with a median acute symptom duration of 3 days. After treatment, rectal bleeding, pain, tenesmus and discharge were significantly improved (p < 0.05). Pruritus ani was not significantly changed (Table 2).

Overall assessment by doctor and patients were significantly in agreement (Table 3).

Table 1. Baseline characteristics (n = 22).

	%	
Age (years): mean (sd)	41.67 (11.65)	
Male : female	1 : 1.2	
Grade of hemorrhoids		
Grade 1 : number	5	22.72
Grade 2 : number	12	54.54
Grade 3 : number	5	22.72
Duration of acute attack (days) : median (range)	3 (1-10)	

Table 2. Response of acute hemorrhoidal attacks to treatment (n = 22).

Outcome	Day 0	%	Day 7	%	P-values
Bleeding					
Score 0 : patients	0	0	15	68.2	
Score 2 : patients	3	13.6	2	9.1	
Score 4 : patients	19	86.4	5	22.7	0.001 ^a
Pain (score) : median (range)	3 (0-10)		1 (0-7)		0.034 ^b
Tenesmus : patients	11	50.0	5	22.7	0.014 ^c
Pruritus ani : patients	8	36.4	4	18.2	0.103 ^c
Discharge : patients	6	27.3	2	9.1	0.045 ^c

^a p-value by asymptotic marginal homogeneity test,

^b p-value by Wilcoxon signed-rank test,

^c p-value by McNemar's chi-squared test.

Table 3. Overall assessment of treatment^a.

Patient assessment	Doctor assessment			Total
	Good	Moderate	Poor	
Good	11	2	0	13
Moderate	0	4	2	6
Poor	0	1	2	3
Total	11	7	4	22

^a Crude agreement : 88.64%, expected agreement : 61.57%,
weighted kappa statistic (se) : 0.704 (0.169), p-value < 0.001

Compliance was rated as good in twenty patients and fair in two patients. Adverse effects were found in two patients: headache in one patient and dizziness in another. Both patients were able to continue taking the medication.

DISCUSSION

Acute hemorrhoidal attacks are one of the major reasons for patients with hemorrhoids to consult a doctor. The goal of treatment for acute hemorrhoidal attacks involves rapid resolution of symptoms with minimal complications. For outpatient treatment of the condition, techniques such as rubber band ligation, sclerotherapy and infrared photocoagulation may result in rapid control of rectal bleeding but may not be applicable for general practitioners. Among the phlebotonic agents recommended for treatment of hemorrhoids, Ginko biloba - Troxerutin-Heptaminol Hce has been used to treat patients with acute hemorrhoidal attacks effectively(15-18).

This prospective study showed that patients with acute hemorrhoidal attacks had clinically important benefits when treated with Ginko biloba - Troxerutin-Heptaminol Hce. As shown in Table 2, bleeding, pain, tenesmus and discharge were significantly reduced by the 7th day. Pruritus ani was not significantly changed after treatment but this may be due to small sample size of the patients presenting with this symptom. Overall assessment by doctor and patients were significantly in agreement, compliance was satisfactory and the side effect minimal. The beneficial effects of Ginko biloba - Troxerutin-Heptaminol Hce in the present study is in agreement with other placebo-controlled and comparative studies reported previously(15-18).

The authors concluded that Ginko biloba - Troxerutin-Heptaminol Hce can be used as an alternative treatment for patients with acute hemorrhoidal attacks safely and effectively particularly in patients who present with rectal bleeding, pain, tenesmus and discharge.

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การรักษาภาวะริดสีดวงทวารหนักกำเริบเฉียบพลันด้วยยา Ginko biloba–Troxerutin–Heptaminol Hce

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จุดมุ่งหมาย : ศึกษาประโภชาน ผลแทรกซ้อน และการยอมรับยา

วิธีการ : เป็นการศึกษาในปัจจุบันในผู้ป่วยผู้ใหญ่ที่เป็นริดสีดวงทวารหนัก (อายุ 18–77 ปี) ที่มารับการรักษาภาวะริดสีดวงทวารหนักกำเริบเฉียบพลันที่คลินิกศัลยกรรมผู้ป่วยลำไส้ใหญ่และทวารหนัก โรงพยาบาลรามาธิบดี โดยให้ยา Ginko biloba – Troxerutin–Heptaminol Hce เป็นเวลา 7 วัน และบันทึกประโภชาน ผลแทรกซ้อน และการยอมรับยาของผู้ป่วยมาวิเคราะห์ทางสถิติ

ผล : ผู้ป่วยร่วมในการวิจัยทั้งหมด 22 ราย อายุเฉลี่ย 41.7 ปี ชาย : หญิง เท่ากัน 1 : 1.2 ผู้ป่วยส่วนใหญ่ (ร้อยละ 77) เป็นริดสีดวงทวารหนักชนิดรุนแรงน้อยถึงปานกลาง (ระยะที่ 1 และ 2) หลังรักษาพบว่า ภาวะเลือดออก ปวดปอดบ่ง และมีสารคัดหลั่งให้หลอกจากทวารหนักลดลงอย่างมีนัยสำคัญ ผู้ป่วยสามารถรับยาได้อย่างต่อเนื่องและมีผลแทรกซ้อนไม่รุนแรงและน้อย

สรุป : ในระยะลั้น Ginko biloba – Troxerutin–Heptaminol Hce เป็นยาที่ใช้ได้ผลดีในผู้ป่วยผู้ใหญ่ที่เป็นริดสีดวงทวารหนักที่มีภาวะริดสีดวงทวารหนักกำเริบเฉียบพลัน ผู้ป่วยสามารถรับยาได้อย่างต่อเนื่องและปลอดภัย

คำสำคัญ : ริดสีดวงทวารหนักกำเริบเฉียบพลัน, Ginko biloba – Troxerutin–Heptaminol Hce

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