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## 6 **Abstract**

7 Anal fissure is a linear or oval shaped tear in the anal canal starting just below the dentate  
8 line extending to the anal verge. Topical glyceryl trinitrate cream a nitric oxide donor  
9 compound has been shown to cause relaxation of anal sphincter and thus effective in the  
10 treatment of anal fissure. Objective: The main goal is to evaluate the efficacy and  
11 complication of GTN with Vaseline base in period between January 2014 to June 2018 in  
12 Almak Nimir university hospital Shendi university (Sudan). Methodology: This study was a  
13 prospective, hospital based, small scale study conducted in the period between January 2014  
14 to June 2018 in Almak Nimir university hospital Shendi university (Sudan). 155 patients with  
15 acute chronic anal fissure treated with GTN with Vaseline base (22 patients were excluded  
16 due to incomplete follow up). Result: One hundred and fifty-five patients were enrolled;  
17 twenty-two patients were excluded due incomplete follow up. Maximum number of cases of  
18 anal fissure in ano belonged to 21 to 30 age group. Success rate up to 94

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20 **Index terms**— glyceryl trinitrate (GTN), chronic anal fissure (CAF), internal anal sphincter (IAS), resting  
21 anal pressure (RAP).

## 22 **1 I. Introduction**

23 Anal fissure is a linear or oval-shaped tear in the anal canal starting just below the dentate line extending to  
24 the anal verge. It was first described in 1934 by Lockhart-Mummery. [1,2] Chronic fissures may associate with  
25 a sentinel pile or anal papilla. The majority of occur in the posterior midline (90%), although anterior midline  
26 fissures seen in 10-20% of affected women and 1-10% of affected men (3).

## 27 **2 II. Etiology**

28 The pathogenesis of chronic anal fissure remains poorly understood. The sphincter spasm seems to cause relative  
29 local ischemia that precludes the healing (4) (5).

30 Many reports have documented that anal hypertonia means elevated maximal resting anal pressures (RAP)  
31 higher than 90 mm Hg ??6 -9] and is related to the internal anal sphincter because resting pressures returned to  
32 normal values after internal sphincterotomy [10,11]. Anal hypertonia of IAS produces ischemia of the posterior  
33 commissure of the anus [9,12,13]. It was postulated that increased anal pressure precedes the development of  
34 anal fissure, and there is evidence that psychological stress produces a sustained tonic rise in anal canal pressure,  
35 translating into an increased tone in the IAS ??12 -15].

36 A morphological description offers a more precise definition. The CAF presents thickened edges with usually  
37 visible, internal anal sphincter fibers at the fissure base. It may also be associated with skin tag (the sentinel  
38 pile) at the lower end of the fissure and/or a papilla at the upper end of a fissure (hypertrophied anal papilla)  
39 [16,17,18].

40 The presenting complaints documented in the study by Khubchandani and Reed were the pain (23.5%),  
41 bleeding (76.2%), itching (34.9%) and an anal lump (24.3%) and burning sensation in the anal region (33%) (19).

## 7 V. RESULTS

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### 42 3 a) Medical Therapy

43 Initial therapy for an anal fissure is medical, and more than 80% of acute anal fissures resolve without further.  
44 The goals of treatment are to relieve constipation and to break the cycle of hard bowel movement and associated  
45 pain. Softer bowel movements are less painful for the patient to pass.

46 First-line medical therapy consists of therapy with stool-bulking agents, such as fiber supplementation and  
47 stool softeners. Laxatives used as needed to maintain regular bowel movements. Mineral oil may be added to  
48 facilitate passage of stool without as much stretching or abrasion of the anal mucosa, but it was not recommended  
49 for indefinite use. Sitz baths after bowel movements and as needed provide significant symptomatic relief because  
50 they relieve some of the painful internal sphincter muscle spasms.

51 Recurrence rates are in the range of 30-70% if the high-fiber diet abandoned after the fissure healed. This  
52 range can be reduced to 15-20% if patients remain on a high-fiber diet.

53 Second-line medical therapy consists of an intra-anal application of 0.4% nitroglycerin (NTG: also called  
54 glycerol tri-nitrate) ointment directly to the internal sphincter. [20].

### 55 4 b) Pharmacological Sphincter Relaxants

56 Interest in the pharmacologic manipulation of the IAS was spurred by the recognition that sphincter hypertonia  
57 associated with fissure persistence, and that surgical approaches to decreased tone may lead to permanent  
58 dysfunction. The IAS consists of smooth muscle whose tone is caused partially by intrinsic myogenic properties  
59 and partly to extrinsic neural influences [21,22,23] Nitric oxide is the principal noradrenergic, noncholinergic  
60 neurotransmitter in the IAS [24,25] and its release results in IAS relaxation. IAS contraction is mediated by  
61 increased cytosolic levels [21,26] Calcium-channel blockers conversely reduce IAS tone. ?1-Adrenergic stimulation  
62 leads to IAS contraction, whereas ?-adrenergic and muscarinic cholinergic agonists lead to IAS relaxation (21).

63 Topical Glyceryl trinitrate cream a nitric oxide donor compound has been shown to cause relaxation of anal  
64 sphincter (27).

65 Conventional myorelaxant creams such as topical nitroglycerin, nifedipine, and calcium channel blockers have  
66 all proven to be efficacious in treating anal fissures, albeit less so than lateral internal sphincterotomy [28,29].  
67 Unfortunately, different studies have reported associated moderate to severe side effects, ultimately resulting in  
68 non compliance and treatment failure [30,31]. Nitroglycerin causes headaches and hypotension in over 70% of  
69 patients [32,33], and diltiazem causes perianal itching [34].

70 The drawbacks to topical GTN are intolerance due to side effects and overall poor patient compliance. Systemic  
71 absorption of the compound can result in vasodilation and severe headaches. Headaches are a problematic side  
72 effect of topical GTN, and up to 20% of patients had to discontinue therapy. (35).

## 73 5 III. Patients and Methods

74 This study was a prospective, hospital-based, small-scale study conducted in the period between January 2014  
75 to June 2018 in Almak Nimir University Hospital Shendi University (Sudan). 155 patients with acute & chronic  
76 anal fissure treated with GTN with Vaseline base (22 patients excluded due to incomplete follow up), the anal  
77 fissure was defined as ulceration in the posterior or anterior anoderm or post de factory pain. Patients with  
78 other conditions (perianal fistulas or abscesses) excluded.

## 79 6 IV. Methods

80 A total of 133 patients, 43 patients (32.3%) with chronic anal fissure and 90 patients (67.7) with acute anal fissure  
81 aged between 15 and 70 years were included in this study / and were subjected to nonoperative management  
82 with 2% GTN in Vaseline base twice daily for six weeks.

83 Patients re-evaluated at 2 and, six weeks, during follow-up, history and perianal examination were performed,  
84 and patients' records reviewed, parameters, relief of symptoms, pain relief, bleeding per rectum and healing of  
85 fissure were evaluated. Complications of treatment, headache, dizziness and significant drop in blood pressure  
86 recorded.

87 The response to treatment registered as complete (symptomatic remission and complete fissure cicatrization),  
88 partial (symptomatic improvement but the persistence of the fissure), refractory (without symptomatic improve-  
89 ment or fissure cicatrization) and relapse (recurrence of symptoms and appearance after complete response).

90 The primary endpoint of the study was complete healing and symptomatic improvement after GTN treatment.  
91 Statistical analysis was performed using SPSS.

## 92 7 V. Results

93 Most of the patients belonged to the age group 21-30 (39.1%), and the age of 71-80 is less affected, with a  
94 slight male preponderance (51.1% 49.9%). 100 patients (75.2%) had pain during defecation as their presenting  
95 symptom, bleeding per rectum in 8 patients (6 %), while both pain and bleeding in 25 patients (18.8%) and of  
96 whom 72.2% of patients had a history of constipation The clinical signs in the study were a posterior anal fissure  
97 in 112 patients (84.2%), an anterior anal fissure in 9 patients (6.8%), while six patients (4.5%) in both and 12  
98 patients (9%) had a tender digital rectal examination. 131 patients (98.5%) not express a headache or symptom  
99 of hypotension after treatment with GTN.

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## 100 8 VI. Discussion

101 An anal Fissure is a disease of young adults as most of the published studies agreed on, Hananel and Gordon, they  
102 state that Fissure most commonly seen in middle-aged and younger patients (1) Jensen SL studied 90 patients  
103 with acute anal fissure, and reported a mean age of 46(36) Raj V. K. and Kadam M. M. has observed that 36.67%  
104 of acute fissure and 43.33% of chronic fissure cases occurs in the age group between 21-30 years old (39). We had  
105 similar results in the present study, with the maximum number of cases of anal fissure belonged to 21 to 30 age  
106 group. There were six cases of an acute anal fissure in less than 10-year age group. The lax anal sphincter is the  
107 reason for the rarity of the disease among the patients above the age of 60 years (figure 1).

108 Concerning gender there was no variation in distribution, Jensen SL reported an equal incidence of male and  
109 female patients (36) Giridhar C. M. et al. have observed that 56.6% male patients and 43.3% female patients  
110 had an anal fissure (37). According to Kari S. S. et al, while studying 100 patients with an anal fissure, 56 % of  
111 patients were males (38) In the present study there is a slight male predominance with 51.1% of patients being  
112 males. (table 1). Raj V. K. and Kadam M., found that Intense pain during and after defecation with or without  
113 bleeding per rectum are the symptoms with which a patient of an acute anal fissure usually presents to (93.33%)  
114 (39). Hananel N. and Gordon in a review of 876 patients, pain and bleeding were the main complain (90.8% &  
115 71.4%) respectively (1).

116 In the present study, the most common presentation of an anal fissure was pain during defecation 100 patients  
117 (75.2%), followed by both pain & bleeding per rectum 25 (18.8%) cases. Constipation was present in 96(72.2%)  
118 cases (Table 2).

119 Hananel N. and Gordon in their study found, 75 % of the anal fissure was anterior, while posterior anal fissure  
120 in 25% (1). In our study posterior location, the figure was higher 107 (80.5%) cases, while anteriorly was found  
121 in 8 (6%) cases, both posterior and anterior was in 6 patients (4.5%).Painful on examination without fissure in  
122 12 (9%) cases (Table

123 The majority of acute anal fissures managed medically. In fact, almost half will heal with conservative therapy  
124 alone using warm baths and increased fiber intake. (5,40) [20]. In his study, Shubetal, found that 44% of fissure  
125 healed conservatively within four weeks. (41).

126 All the patients enrolled in the present study 133 patients,128 patients (96.2%) achieved symptom relief  
127 within two weeks by using GTN (in Vaseline base) stool softeners, sitz bath, and lignocaine ointment, while five  
128 patients (3.8%)not responded. Patients in whom there was no relief of symptoms after two weeks of conservative  
129 management, were subjected to surgical management. By the six weeks the number decrease to 125 patients who  
130 respond to the treatment (94%) achieved symptom relief (no pain or bleeding, ulcer healing) (table 4).

131 Chemical sphincterotomy with nitrates may generate headache in 20%-30% (35)(42) of cases or even a higher  
132 rate (43).Other study, nitroglycerin causes both headache and hypotension in over 70% of patients [32,33].  
133 Systemic absorption of the compound was the cause of the problem due to vasodilation and up to 20% of patients  
134 had to discontinue therapy (35), which was absent in this study no patient stops the treatment due to side effect,  
135 either a headache or symptoms of hypotension and increase the success rate up to 94 % (table ??).

136 Nelson R & Perry WB and his group in two different studies they conclude that the dose of GTN (0.2%  
137 or 0.4%) was not found to influence the efficacy but did increase the incidence of side effects, headache, which  
138 occurred in about a quarter of patients [42,44]. In our study a headache is not significant, was only noticed in  
139 two patients (1.5%).

140 A systematic review of the literature was undertaken two databases (Pub Med, MEDLINE) were searched,  
141 this is the first study in the literature used GTN 2 % in Vaseline base, they use GTN ointment with different  
142 concentration (0.2% & 0.4%) [42,44] in spite of that we have two patients (1.5%) who experience headache,  
143 Vaseline base was found to be the major contributing factor in preventing absorption of GTN systemically.<sup>1</sup>

## 144 9 VII. Conclusion

145 GTN 2% in Vaseline base was very good in the treatment of anal fissure with an efficacy up to 94% and negligible  
146 site effect (1.5%). So we can conclude that a headache is not a headache in patients using GTN.

## 147 10 Global

148 1

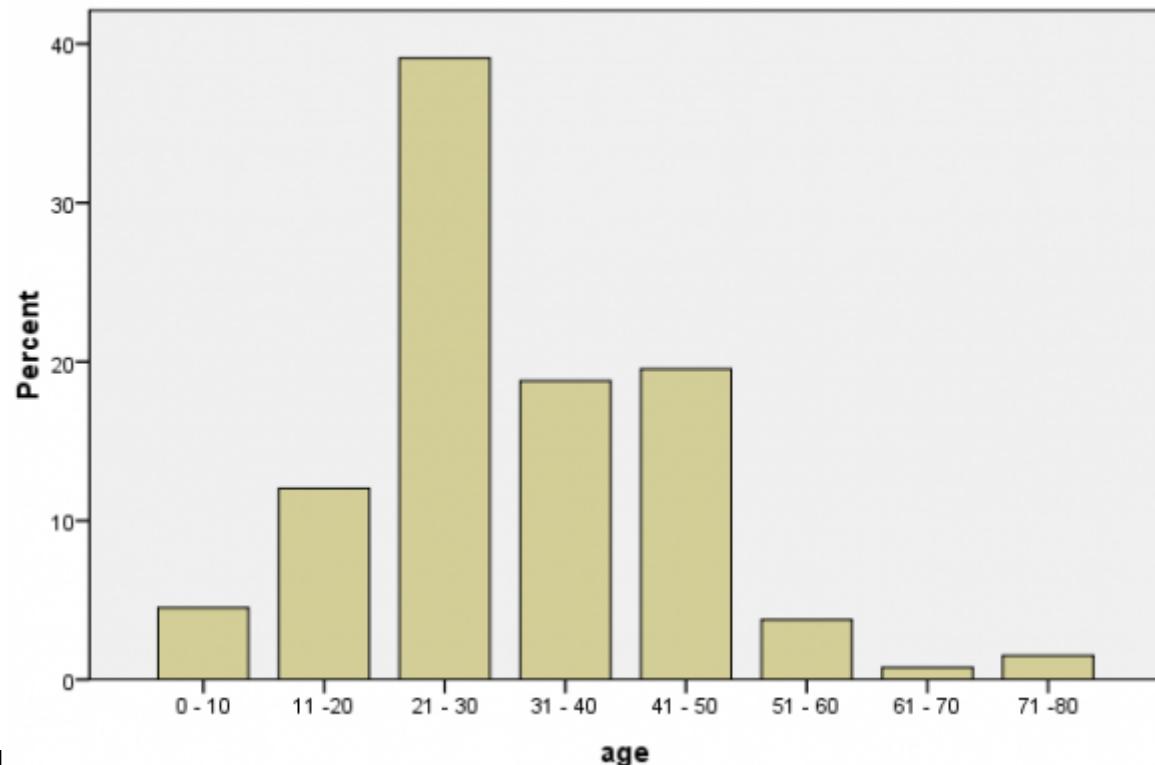


Figure 1: Fig. 1 :

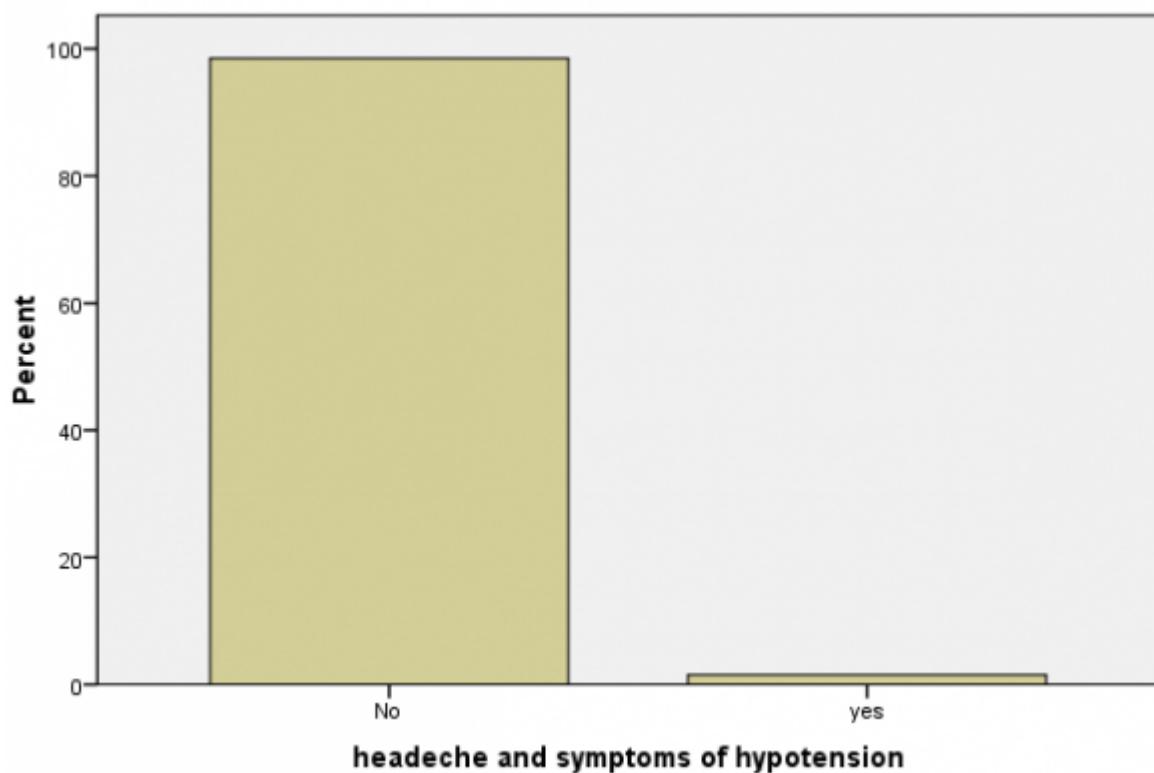


Figure 2:

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**1**

Gender	No. of Patients %
Male	68 (51.1%)
Female	65 (48.9%)

Figure 3: Table 1 :

**2**

Symptoms	No of Patients N=134	Percentage (%)
Pain During Defecation	100	75.2 %
Pain & Bleeding	25	18.8 %
Bleeding	6	8 %
Constipation	72	54.5 %

Figure 4: Table 2 :

**3**

Clinical Signs	No. of Patients
Posterior Anal Fissure	107 Patients (80.5%)
Anterior Anal Fissure	8 Patients (6%)
Both	6 Patients (4.5%)
Tender Digital Rectal Examination	12 Patients (9%)

By two weeks 128 patients (96.2%) achieved symptom relief, by the six week the number decrease to 125 patients who respond to the management (94%)

Figure 5: Table 3 :

**4**

	Relief of Symptoms
2 Weeks	6 Weeks
Respond	128 (96.2%)
Not Respond	5 (3.8%)

125 (94%)  
8 (6%)

Figure 6: Table 4 :



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