Intractable Headache as a Side Effect of Topical Nitroglycerin Ointment

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ABSTRACT

Objective: To determine the pattern of severe intractable headache with the use of topical Glyceryl Trinitrate (GTN) cream for treatment of fissure in ano, necessitating stoppage of treatment.

Methods: The Cross sectional, descriptive, quasi-experimental study was conducted on fifty patients with acute fissure in ano, presenting in surgical OPD of Islamic International Medical College (IIMC) Trust Railway General Hospital, Maryam
Memorial Hospital, and Burhani Medical Center, Rawalpindi.
The diagnosis was based on clinical history and examination findings. GTN 0.2% ointment was used topically, in a quantity of 1-2 ml 8 hourly for initial ten days. No concomitant analgesic therapy was advised. Ispagula husk 2 tablespoonfuls at bedtime was prescribed to all patients. Incidence of headache and its severity was assessed using verbal descriptor pain scale, rating the severity of pain from 0-10. A score of 0-3 was interpreted as mild, 4-7 as moderate and 8-10 as severe pain.

Results: Out of 50 patients, four (8%) complained of severe headache. In three (6%) patients the treatment had to be abandoned. Thirteen (26%) patients had a disturbance of daily routines due to headache; however, therapy could still be continued.

Conclusions: Headache is common, and only occasionally is severe enough to compel the patient to discontinue treatment. The treatment has the advantages of ease, recurrent use and cost-effectiveness. (Rawal Med J 2008;33:15-17).
Key Words: Anal fissure, topical nitroglycerin, intractable headache.

INTRODUCTION

Fissure in ano is a very common condition affecting mainly young people. It is an extremely painful condition causing significant morbidity.\(^1\) For a long time it has only been amenable to anal dilatation or lateral sphincterotomy under general anesthesia.\(^2\) Surgical treatment has been associated with some derangement of sphincter mechanism in addition to the morbidity associated with general anesthesia. This led to an ongoing quest for medical therapies for treatment of this condition. Newer therapies include topical applications of GTN, diltiazem, and clove oil. GTN Ointment 0.2-0.5% applied topically thrice daily for up to six weeks has showed satisfactory results in several clinical trials.\(^3\)\(^-\)\(^4\) When used as a gel for fissure in ano, it still carries a side effect of headache. Sometimes it is so severe and intractable that the treatment has to be abandoned and some other method has to be resorted to for the treatment.
This study was focused on the frequency with which the treatment has to be abandoned due to severe headache.

**PATIENTS AND METHODS**

The study was performed on 50 consecutive patients with acute fissure in ano, seen at the surgical OPD of IIMC Railway Hospital, Maryam Memorial Hospital and Burhani Medical Center, Rawalpindi during April 2003 and April 2005. The diagnosis was made on clinical finding of a split in the skin of anal margin and related symptoms of severe pain with defecation persisting afterwards. Those with associated disease like hemorrhoids or fistula were excluded.

**Fig 1. Age distribution of patients**
GTN 0.2% gel was used as a topical agent, applied thrice daily for ten days and first follow up of patients was recorded at tenth day of treatment. Analgesics were not prescribed to find out the true incidence and severity of headache due to GTN therapy. Severity of headache was recorded on verbal descriptor scale, with 0 denoting no pain and 10 denoting most severe pain. 0 was interpreted as no pain. 1-3 was interpreted as mild pain, 4-7 as moderate pain and 8-10 as severe pain. Degree of interference with routine daily activities due to headache was also assessed. Subjective acceptability was recorded regarding continuation of
treatment with the GTN Gel. The number of patients refusing to continue treatment due to intractable headache was recorded.

**RESULTS**

There were 13 (26%) females and 37 (74%) males in the study. Minimum age was 14 years and maximum 55 years (Fig 1). All patients reported varying degree of headache with the use of GTN Gel from the first day of its application. Eighteen patients had mild, 28 moderate and four had severe headache (fig 2).

**Fig 2. Severity Distribution of Headache.**
Mild headache = 1-3  Moderate headache = 4-7  Severe headache = 8-10

In four out of fifty (8%) patients it was very severe and treatment had to be abandoned due to intractable headache in 3 patients (6%). In 13 out of fifty (26%) patients, it caused significant disturbance with the normal daily routine. All these patients had sedentary occupation related to mental work. However, they continued treatment with GTN Gel attributed to the relief of anal symptoms.
DISCUSSION

Fissure in ano is an extremely painful condition and causes significant morbidity. Etiology of fissure in ano has been found to be intimately related to sphincter dynamics and spasm of anal sphincter has been associated with acute fissure in ano.\textsuperscript{5} This association has led to the reduction of sphincter tone as a therapeutic approach for the treatment of acute fissure in ano.\textsuperscript{6} It led to a search of pharmacologic agents capable of reducing anal sphincter tone. A number of such compounds have been discovered that have an action to reduce the tone of anal sphincter including nitroglycerin,\textsuperscript{3,4} botulinum toxin,\textsuperscript{7} and clove oil.\textsuperscript{8} Among them the action of nitroglycerin is related to the release of nitric oxide in the tissues. Organic nitrites release nitric oxide when applied topically to the anal area, an inhibitory neurotransmitter in the internal anal sphincter.\textsuperscript{9,10} It leads to the reduction in mean resting pressure of anal sphincter on local application.\textsuperscript{3} It also appears to increase the local blood flow after topical application.\textsuperscript{11} Topical GTN is one of the medical
treatments of choice for acute fissure in ano \(^{12}\) and carries the additional benefit of being easily repeatable in case of recurrence of fissure in ano.\(^{13}\) The use of nitroglycerin, however, is associated with throbbing headache due to its systemic vasodilator effect. The incidence of headache is high, though the intensity of this side effect is variable. In a certain proportion of cases, it is severe enough to make further treatment impossible and treatment has to be abandoned. The present study has documented a high frequency headache necessitating discontinuation of treatment in 6% of patients.

**REFERENCES**


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