INTRODUCTION
Anal fissure is a common anorectal condition. Both genders are equally afflicted, with a slight predilection towards males. It may also affect children.1 Symptoms of disease include pain during defecation and per rectal bleeding.2 Spasm of the internal anal sphincter leading to reduced blood flow is now considered the mechanism behind the pathogenesis and is responsible for the clinical presentation.3 Anterior fissure, though less common are associated with occult sphincter injury rather than poor blood supply.4 Although the precise nature of anal fissure was not confirmed until the seventies, anal dilatation and lateral anal sphincterotomy was the mainstay of treatment. Sphincterotomy, however, has been associated with incontinence in up to 35 percent of patients.5 With a better understanding of the hypertonia-ischemia nature of chronic anal fissure, the nineties witnessed the evolution of many pharmaceutical agents that lower the resting anal tone resulting in healing of the fissure. Kennedy et al. presented their successful experience with topical glycerl trinitrate (GTN) in the management of chronic anal fissure in 1996.6 Chrysos and colleagues conducted the first clinical study of the role of calcium antagonists on anal canal pressure using sublingual nifedipine and found a substantial decrease in the resting anal pressure.7 Since then, many treatments including diltiazem, botulinum toxin and sildenafil have been tested to manage chronic anal fissure.8-10 Each reduces the resting anal pressure without any risk of incontinence and hence can cause a state called medical or chemical sphincterotomy. Due to this major advantage over surgical modalities, these agents are now the first line of treatment in the management of patients with chronic anal fissure, with surgery reserved for either refractory cases or those with intolerable side effects of drugs.

This study was conducted to assess and compare the effectiveness of topical 0.2% glyceryl trinitrate (GTN) and topical 2% diltiazem (DTZ), in the management of chronic anal fissure.

METHODOLOGY
This study was conducted at the outpatient department of SU-IV, Liaquat University Hospital, Jamshoro/ Hyderabad. It included patients presenting with chronic anal fissure from September 2004 to August 2005. All...
patients, irrespective of age and gender, with the diagnosis of chronic anal fissure were included in this study. The criteria for chronicity of fissure were pain during defecation (with or without bleeding, pruritis and/or discharge) of more than 3 months duration, presence of sentinel pile, and/or exposed horizontal fibres of the internal anal sphincter. Patients with a symptom duration of less than three months or having systemic co-morbidities like hypertension, ischemic heart diseases and migraine and those preferring surgery were excluded from the study.

A sample size of 100 patients (50 in each group) was selected at the beginning of the study, based on the records of outpatient clinic, suggesting of 7-10 cases of chronic anal fissure reporting per month. For the sake of convenience, the first 50 patients were prescribed 0.2% GTN for topical application (initial five and half months). By the end of one year, it was possible to prescribe 2% DTZ in only 47 patients. They were asked to apply the cream (roughly the size of a pea, taken on fingertip) topically at the peri-anal area three times a day for 8 weeks.

Data was recorded on a proforma, designed specially for this study. The study variables included age, gender, treatment prescribed, side effects, compliance of the patients, symptoms scoring, healing of the fissure at the end of treatment and recurrence for a follow-up period of one year.

The research participants were completely informed about the purpose and methodology of study. They were counselled about the possible side effects and were allowed to withdraw from the trial at any time without stating a reason.

One consultant (not the researchers), unaware of the assigned treatment was requested to help in evaluating of effectiveness of treatment at fortnightly intervals, for 8 weeks. Healing was defined as complete absence of ulcer crater and tenderness.

After completion of study, the data was analyzed using SPSS version 10 for statistical analysis. For quantitative data, descriptive statistics were calculated (mean, mode, median and standard deviation). The association between treatment given and symptomatic relief, along with healing of fissure, was examined using $X^2$ test. The same test was also applied to examine the relation between treatment given and side effects and treatment with recurrence rates. The association was considered significant if p-values were less than 0.05.

**RESULTS**

A total of 97 patients were included in this study. There were 53 females and 44 males with a female: male ratio of 1.2:1. Group A (0.2% GTN) included 50 patients with 27 females while group B (2% DTZ) had 47 patients with 26 females. The age of the patients ranged from 16 to 75 years with a mean age of 30 years.

All the patients presented with severe pain during defecation with a mean pain score of 9 (range 8-10) on verbal rating scale (VRS). Bleeding per rectum was reported by 40 patients and clinical evaluation revealed the presence of sentinel tag in 60 patients and exposed fibres of internal anal sphincter in 18 patients. Table I depicts the clinical profile of the patients.

### Table I: Clinical profile of the patients.

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding per rectum</td>
<td>40</td>
<td>41%</td>
</tr>
<tr>
<td>Pain during defecation</td>
<td>97</td>
<td>100%</td>
</tr>
<tr>
<td>Sentinel tag</td>
<td>60</td>
<td>62%</td>
</tr>
<tr>
<td>Exposed fibres of IAS</td>
<td>18</td>
<td>18%</td>
</tr>
</tbody>
</table>

IAS= internal anal sphincter

After 6-8 weeks of treatment, 73% of the study population showed excellent/substantial response in their symptoms. The mean pain score dropped from 9 to 2 in patients who were prescribed 2% DTZ whereas amongst those who applied 0.2% GTN, it fell from 9 to 3. Out of 50 patients in group A, 35% showed complete improvement in their symptoms whereas in group B, 37% patients showed relief of their symptoms. This difference though was not statistically significant. (df=1, Pearson chi-square=0.891, p=0.345). Twenty seven percent of patients showed no response to either treatment. Out of 47 patients in group B, 61% showed complete healing at the end of treatment. Seventeen and 21 percent of fissures remained partially or not healed at all. Among the patients in group A, 52% were completely healed at the end of treatment, 40% showed partial healing and 8% did not heal at all. The difference in healing observed between the two groups was statistically significant (df=2, Pearson chi-square=7.793, p=0.02).

On the basis of previous studies, the proportion of participants expected to experience headaches was 44-55% for 0.2% GTN and 10% for 2% DTZ. By the end of the study, 26% of the patients in group A and 2% patients in group B complained of headaches (df=1, Pearson chi-Square 8.763 and p=0.003). Other side effects observed in the two groups are shown in Table II.

### Table II: Side-effects profile.

<table>
<thead>
<tr>
<th>Side-effects</th>
<th>GTN No Percentage</th>
<th>DTZ No Percentage</th>
<th>Chi-square</th>
<th>P-value (two tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postural hypotension</td>
<td>2 4%</td>
<td>5 11%</td>
<td>1.594</td>
<td>0.207</td>
</tr>
<tr>
<td>Pruritis</td>
<td>2 4%</td>
<td>1 2%</td>
<td>0.283</td>
<td>0.594</td>
</tr>
<tr>
<td>GI upsets**</td>
<td>3 6%</td>
<td>1 2%</td>
<td>0.919</td>
<td>0.338</td>
</tr>
<tr>
<td>Headaches</td>
<td>13 26%</td>
<td>2 4%</td>
<td>8.763</td>
<td>0.003</td>
</tr>
</tbody>
</table>

* Statistically significant; ** GI upsets = Nausea, vomiting, diarrhea

Following the completion of 8 weeks of treatment, patients were evaluated for recurrence of fissure. The minimum follow-up period was 8 months. Five patients...
(10.6%) in group B came back with recurrence of fissure. Thirty (64%) were symptom free by the end of one year and 12 (25%) did not report at all. Out of those patients who were prescribed topical GTN, 8 patients reported back with recurrence (16%). The outcome in patients on GTN (group A) is elaborated in detail in Figure 1. The difference observed between the two groups was statistically insignificant (df=2, Pearson chi-square=2.469, p=0.291).

In this study, out of 50, twenty six patients treated with 0.2% GTN showed complete healing of the anal fissure. This response of GTN is comparable to that reported by others showing a response rate of 54 to 62 percent. Others report a better response of up to 73 percent. Patients in the GTN group showed an over all improvement in their symptomatology, namely pain during defecation. The mean verbal pain score dropped from 8 to 3 in this group. This is comparable to Omar et al., and Kocher et al.

The treatment with GTN is not free of side effects. A different series reports a variety of undesirable effects, mainly headache. These headaches are usually self-limiting, occur within 15 minutes of application of the cream and subside with simple analgesics like acetaminophine. It was assumed that upto 55% of the study population will experience headache at some point during the trial. However, 26% of patients in the GTN group suffered from headache. This was mainly observed during the first two weeks of therapy and was usually self limiting. In case of intolerance, patients were advised to take simple analgesics. The incidence of headaches reported elsewhere was comparably higher (50-70%). In comparison to this, the incidence of headaches reported with topical DTZ remains low.

Fifty two percent patients prescribed 0.2% GTN, were disease free by the end of one year. In this study, 10% of the patients in this group returned with recurrence. This is comparable with 11% of Richard et al. but is less than that reported by Graziano et al.

Patients in group B who were treated with topical DTZ, showed better results vis-a-vis pain relief. Out of 47 patients, 36 (74%) showed a drop in verbal pain scale from 8 to 2. This was statistically insignificant as reported by Kocher et al. When healing rates were analyzed, 61% of fissures were completely healed after the application of DTZ. Jonas et al. have reported similar healing rates (65%). But, Omar et al., Gupta et al. and Knight et al. reported better rates varying from 75 to 82 percent.

Kocher et al. and Gupta et al. report no recurrence in their studies. Whereas Omar et al., Jonas et al. and Knight et al. reported recurrence levels of 6%, 4% and 11% respectively. This is comparable with the presently observed recurrence rate of four percent.

Until now, a strong correlation between anal tone and MARP was hypothesized but this is being opposed in recent work done at an international level. MARP

![Figure 1: Observed rates of recurrence.](image-url)
monitoring devices are not available in the study set up. Secondly, because of the fear of pain, most of the patients were reluctant to undergo digital rectal examination at the time of presentation. The study therefore, remains inconclusive about the reliability of this association.

Since these agents cause a “reversible sphincterotomy”, recurrence will presumably remain a problem with all methods of pharmacological sphincter relaxation, as the anal resting pressure may revert to pretreatment levels. Besides, each medicine has its own accompanying side effects. These issues will remain unresolved until an ideal pharmacological preparation is available for “chemical sphincterotomy.”

CONCLUSION

Both 0.2% GTN and 2% DTZ are equally effective in managing the chronic anal fissure, but DTZ has fewer side effects, a better healing response and low recurrence rates. Headache, though a frequent complication of both treatments, is reversible and manageable with simple analgesics.

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REFERENCES


