Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Short Communication

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Fariborz Eshghi
Department of General Surgery,
Imam Komeini Hospital,
Faculty of Medicine,
Mazandaran University of
Medical Sciences,
Sari, Iran

Fax: +98-151-2228213
Tel: +98-151-2225764

J. Med. Sci., 7 (3): 481-484
1st April, 2007

The Efficacy of L-arginine Gel for Treatment of Chronic Anal Fissure Compared to Surgical Sphincterotomy

Fariborz Eshghi

Aim of the present study was to compare the effect of L-arginine (chemical sphinctrotomy) with lateral internal sphinctrotomy (surgical sphinctrotomy) in treatment of chronic anal fissure. This clinical trial study was preformed on 60 patients referring to hospital complaining of chronic anal fissure diseases. They were randomized two groups of equal number patients undergoing internal sphinctrotomy (control) and treatment of topical L-arginine gel (case). All of the patients were assessed for pain, bleeding and wound healing for three months. The results obtained from case group showed that rectal bleeding discontinued and pain controlled in 70% while wound healing occurred in only 26.7%. In the control group treated with surgical method, had not any pain and bleeding after treatment and wound healing occurred in 56.7%. Local application of L-arginine cannot use instead to surgical internal sphinctrotomy, but can be used when patient is not candidate for surgery and predisposing complication.

Key words: Anal fissure, medical treatment, L-arginine gel

ANSInet
Asian Network for Scientific Information

Department of General Surgery, Imam Komeini Hospital,
Faculty of Medicine, Mazandaran University of Medical Sciences,
Sari, Iran

INTRODUCTION

Anal fissure is a common anorectal problem. Characteristic symptoms are severe pain with defecation and rectal bleeding with as small amount of bright red bleeding. An acute fissure is a superficial tear of distal anorectum. The pathogenesis is uncertain, but it seems to be caused by passage of hard stool during a period of constipation. Chronic fissures develop ulceration heaped-up edge with the white fibers of internal anal sphincter visible at the base of the ulcer. There is associated between external skin tag and a hypertrophied anal papilla internally this fissure is more challenging to treat (Schwartz, 2005).

Acute fissures treated with medical management. Fissures that have failed medical therapy or lasting more than 6 weeks with features of chronics need to be healed by surgery. Surgical lateral internal sphincterotomy is the gold standard treatment for chronic anal fissure, which has a risk of transient or permanent fecal and flatus incontinence (0-30%), in addition to expected complications after any surgery (Lindsey *et al*., 2004). Studies have shown that in patients with anal fissure, internal anal sphincter has a higher resting pressure than healthy persons. Recent studies have been focused on efficacy of muscle relaxant drugs in treatment or prevention of chronic anal fissure (McCallion and Gardinor, 2001; Griffin *et al*., 2002; Simms *et al*., 2004). Local application of some drugs used in treatment of anal fissure such as glyceril trinitrate and injection of botulinum toxin have side effects like headache, especially in younger age and they don't have complete efficacy on healing (Simms *et al*., 2004; Carapeti *et al*., 1999). So studies are doing on drugs to find more effective and with less side effects. Local application of L-arginine gel has been shown to be an effective drug in healing fissures by reducing anal resting pressure (Griffin *et al*., 2002; Acheson *et al*., 2003; Gosselink *et al*., 2005). Even in patients with anal fissure who had failed medical therapy, local application of L-arginine gel was a successful treatment (Griffin *et al*., 2002). There were not any studies to show in comparison between L-arginine gel and surgical internal sphincterotomy for healing chronic anal fissures. The present study evaluates efficacy of local application of L-arginine in healing chronic anal fissures and compares it with gold standard treatment (surgical internal sphictrotomy).

MATERIALS AND METHODS

After obtaining permission from medical ethics committee of the university and patient's agreement, this sequential trial was conducted in Imam Hospital in Mazandaran University of Medical Sciences, Sari, Iran on 60 patients between 2004 and 2005. This prospective randomized clinical trial was studied patients with chronic fissure who referred to the surgical outpatient clinic of Imam hospital in Sari. All of the patients suffered from anal pain and bleeding. A surgeon did anal examination. Patients randomized in case (n = 30) and control (n = 30) groups, treated by local application of 5% L-arginine gel and surgery, respectively.

Patients with fissure due to an underlying identifiable pathology such as Crohn's disease, tuberculosis, anal cancer or HIV and patients with history of diabetes were excluded. L-arginine gel 5% was prepared faculty of pharmacy. Patients educated to use gel for his or her anal application.

L-arginine was applied twice daily for 3 months. One surgeon in control group performed lateral internal sphincterotomy. All of the patients were evaluated at 1, 2, 4 and 12 weeks after treatment. Each evaluation included examination of anus, assessment of any side effects, pain severity, bleeding rate and experienced on defecation. A Visual Analog Scale (VAS) was used to assess fissure related pain. The bleeding rate was asked from each patient.

Bleeding rate was assessed and registered as one of these terms: 1- No bleeding; the patient has no bleeding on or after defecation. 2- Reduce bleeding rate; bleeding rate is reduce after beginning of the treatment. 3- No change in bleeding rate; the patient has bleeding rate after treatment as the same as before treatment.

Fissure healing was visually assessed and registered as one of these terms: 1- Complete healing; no ulcer is seen. 2- Partial healing; a linear tearing with epithelialization in the base of it. 3- Not healing; no change in ulcer. 4- Complicated healing; more severe ulcer (an abscess or fistula is added). Data were recorded in checklist and then analyzed by Chi-square test. p-value of less than 0.05 was considered statistically significant.

RESULTS

Case group was 23 (77%) female and 7 (23%) male (mean age 36.2±11 years). Control group consisted 18 (60%) female and 12 (40%) male (mean age 34.4±14 years).

At the end of follow up, stoppage of bleeding and pain reduction occurred in all of the patients treated surgically. There were 21(70%) patients with pain relief in L-arginine group compared with the patients treated surgically and were significantly lower within one, two, 4 and 12 weeks after treatment ($p = 0.001$) (Table 1).

There were reduce bleeding and no change in bleeding rate in case group compared with control group that were no bleeding in all patients (Table 1).

Table 1: Percentage of pain relief and bleeding rate in patients treated with L-arginine gel (case) and surgery (control)

	Treatment group	
Parameters	Control N (%)	Case N (%)
Pain relief	30 (100)	21 (70)
No change in severity of pain	-	9 (30)
No bleeding	30 (100)	21 (70)
Reduce bleeding rate	-	7 (23.3)
No change in bleeding rate	-	2 (6.7)

Table 2: Percentage of healing in ulcer in patients treated with L-arginine gel (case) and surgery (control)

	Treatment group	
Parameters	Control N (%)	Case N (%)
Complete healing	17 (56.7)	8 (26.4)
Partial healing	13 (43.3)	7 (23.3)
No healing	-	14 (46.7)
Complicated healing	-	1 (3.3)

At the end of follow up, healing of ulcer was not complete in both groups, but there were significantly differences between complete healing and partial healing in the two groups. No healing and Complicated-healing rate was not observed in control group (Table 2).

All of the patients attended for follow-up. No side effect was observed in surgery group and only one patient in L-arginine group developed headache and dizziness.

DISCUSSION

Different medical treatments have been shown to be effective for patients with chronic anal fissure (Lindsey *et al*., 2004; McCallion and Gardinor, 2001), but there are fewer studies about the efficacy of topical L-arginine in the healing of chronic anal fissure.

Gosselink *et al.* demonstrated that local application of L-arginine reduced the maximum resting anal pressure significantly and 62% of patients in that study showed complete healing of fissure 18 weeks after local application of L-arginine (Gosselink *et al*., 2005), it has been shown that L-arginine gel is effective in healing of anal fissure by reducing of internal anal sphincter spasm which is mediated through the action of nitric oxide synthesize.

Griffin *et al*. (2002) by measuring internal anal sphincter pressure after local application of L-arginine gel demonstrated that it caused a significant pressure drop in comparison with placebo. Previous studies showed that glyceryl trinitrate ointment, as a nitric oxide donor, can reduce internal anal sphincter pressure which results in fissure healing, since headache as a side effect of glycerine trintrate, is shown to be a major contributing factor to noncompliance.

According to this and previous studies, frequency of side effects, specially headache, after local application of L-arginine is very lower than other chemical agents such as, glyceryl trinitrate (Griffin *et al*., 2002; Acheson *et al*., 2003; Carapeti *et al*., 1999; Bacher *et al*., 1997; Dorfman and Levitt Platell, 1999). Also in studies with oral arginine has been given to patients in the evaluation of esophageal and gallbladder physiology, no headaches were reported (Luking *et al*., 1998; Smith *et al*., 1997). L-arginine is going to be an alternative treatment for anal fissure, but further evaluation is needed before it can be used as a possible alternative treatment for chronic anal fissure (Griffin *et al*., 2002; Lund and Scholefield, 1997a, b).

Present study showed that surgical internal sphincterotomy is more effective than topical application of 5% L-arginine gel in healing chronic anal fissure. It means that surgical sphincterotomy cannot be used instead to local application of 5% L-arginine gel as the first therapeutic approach in patients with chronic anal fissure. Since no side effect after repeated doses with topical L-arginine were reported (Griffin *et al*., 2002), we recommend it as an effective temporary or alternative medical treatment when there is a counter indication to surgery in chronic anal fissure.

REFERENCES

Acheson, A.G., N. Griffin and J.H. Scholefield, 2003. L-arginine-induced relaxation of the internal anal sphincter is not mediated by nitric oxide. Br. J. Surg., 90: 1155-1162.

Bacher, H., H.J. Mischinger and G. Werkgartner, 1997. Local nitroglycerin for treatment of anal fissure: An alternative to lateral sphincterotomy? Dis. Colon Rectum, 40: 840-845.

Carapeti, E.A., M.A. Kamm and P.J. McDonnlad, 1999. Randomised controlled trial shows that glyceryl trinitrate heals anal fissures, higher doses are not more effective and there is a high recurrence rate. Gut, 44: 727-730.

Dorfman, G. and C. Levitt Platell, 1999. Treatment of chronic anal fissure with topical glyceryl trinitrate. Dis. Colon Rectum, 42: 1007-1010.

Gosselink, M.P., M. Darby and D.D.E. Zimmerman, 2005. Treatment of chronic anal fissure by application of L-arginine gel: A phase II study in 15 patients. Dis. Colon Rectum, 48: 832-837.

Griffin, N., D.D.E. Zimmerman and J.W. Briel, 2002. Topical L-arginine gel lowers resting anal pressure. Possible treatment for anal fissure. Dis. Colon Rectum, 45: 1332-1336.

Lindsey, I., O.M. Jones, C. Cunningham and M.C.C. Mortensen, 2004. Chronic anal Fissure. Br. J. Sur., 91: 270-279.

Luking, J.C., B.L. Weusten and P. Portincasa, 1998. Effects of long term oral L-arginine on esophageal mortality and gallbladder dynamics in healthy humans. Am. J. Physiol., 274: G984-991.

Lund, J.N. and J.H. Scholefield, 1997a. A randomized prospective double blind, placebo-controlled trial of glyceryl trinitrate ointment in treatment of anal fissure. Lancet, 349: 11-14.

Lund, J.N. and J.H. Scholefield, 1997b. Glyceryl trinitrate is an effective treatment for anal fissure. Dis. Colon Rectum, 40: 468-470.

McCallion, K. and K.R. Gardinor, 2001. Progress in the understanding and treatment of chronic anal fissure. Postgrad. Med. J., 77: 753-758.

Schwartz, 2005. Principle Surgery, 2005. Anal Fissure. 8th Edn., pp: 1103-1104.

Simms, H.N., N. McCallion and W. Wallace, 2004. Efficacy of botulinum toxin in chronic anal fissure. Ir. J. Med. Sci., 173: 188-190.

Smith, S.D., M.A. Wheeler and H.E. Faster, 1997. Improvement in interstitial cystitis syndrome scores during treatment with oral L-arginine. J. Urol., 158: 703-708.