



Modified retention enema, possible cure for solitary rectal ulcer

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Abstract

Since ancient times, enemas have been used in various clinical scenarios. It was used as a way to relieve constipation, administration of analgesia and anesthesia in children, pre-operative bowel preparation, control of fever and seizures, post-operative analgesia, and the treatment of acute pancreatitis, hepatic encephalopathy and hyperkalemia.

We believe clinical application of this modified retention enema can benefit patients suffering from solitary rectal ulcer syndrome (SRUS).

Our hypothesis is to prove superiority of combination therapy to conventional therapies for Mucosal Prolapse Solitary Rectal Ulcer Syndrome (MPSRUS). Our modified retention enema has active components that improve inflammation, protects mucosa and explained method of administration will also improve mucosal blood perfusion. This will result in clinical and histological healing of the SRUS.

Keywords

Solitary rectal ulcer, Enema, Sucralfate

Introduction and history

Enema is the procedure of introducing liquids into the rectum and colon via the anus for medical reasons; the history of using enema goes back to 1500 B.C, when an Egyptian, Ebers Papyrus has mentioned it (1).

Evidence has shown that in ancient times, enema was very much common for some serious problems. Egyptians believed that all diseases were caused by superfluities of the food, which now most people believe to be true, and enema can relieve patients from their accumulation.

In pre-revolutionary France, adapted enemas were used on a daily basis after dinner and for beauty purposes. Even Louis XIV had used enema

about 2000 times in his whole lifetime. This practice was considered as a good therapy for many diseases.

Nowadays, the application of enema becomes very limited and many have forgotten about the benefits this therapy can provide.

Solitary Rectal Ulcer (SRU)

As the name implies, solitary rectal ulcer syndrome is a condition in which, typically but not always a single ulcer occurs in the rectum; although this is a very rare condition but it can produce significant pain, bleeding and discomfort for the patients (2,3). Diagnosis of this condition goes back to the first description by Cruveilhier in 1830 (4) and since

then our understanding of this disease have improved so much.

Pathophysiology

Solitary Rectal Ulcer is now commonly referred to as mucosal prolapse or mucosal prolapse solitary rectal ulcer syndrome (MPSRUS).

The underlying etiology of this condition is poorly understood, theories involves ischemia and direct trauma. As this condition is usually accompanies conditions such as chronic constipation, straining during bowel movements, rectal prolapse, and digital stool evacuation we could assume that both of these theories play a role in development of this disorder (3).

Other suggested hypothesis are congenital malformation such as hamartomas (5), poor relaxation of puborectalis muscles, inflammation (6), localized bowel ischemia, and rectal prolapse (7-9). Among these various hypotheses rectal prolapse has received the largest attention.

Therefore, the goal of any treatment, whatever surgical or conservative management, would be to "improve defecation dysfunction".

Sucralfate

Sucralfate is a sucrose sulfate-aluminum complex and had been approved by food and drug administration (FDA) in 1981 for duodenal ulcer (10).

Since then sucralfate has been used for a wide range of indications such as upper gastrointestinal bleeding (11), stress ulcer (12) and radiation or ulcerative colitis induced proctitis (13-17) and gastro-oesophageal reflux disease (18,19).

One study have shown that Sucralfate retention enemas 2 grams twice a day for 6 weeks shows both clinical improvement by 2 weeks and endoscopic healing by 4-6 weeks of treatment (20). This latter study by Zargar and colleagues demonstrates the potential benefits of the sucralfate retention enema but very few number of patients (6 patients), and lack of proper histological improvement in the study clearly shows necessity of placebo controlled larger clinical trial with a modified protocol (20).

Other components

Steroid retention enemas and 5-aminosalicylic acid have long history of use as enema in chronic ulcerative disorders of colon and rectum for example a meta-analysis reviewing 17 randomized, double-blind controlled trials concluded that topical mesalamine is useful for treatment and maintenance of remission in left-sided ulcerative colitis and proctitis (21) similar results are reported with steroids (22)

Antibiotics role have also been emphasized in treatment and reduction of inflammation in colon and rectal ulcers by several studies (23,24). However, none of these chemicals have long lasting or satisfactory results in treatment of MPSRUS.

Safety

As more than 90% of orally used sucralfate excreted unchanged in the feces it produces very little side effects (10). Large scale clinical studies have also confirmed the safety of sucralfate usage and the most common side effect was constipation (25).

Enema can also produce complications both due to the mechanical trauma and by the fluid and electrolyte imbalances. However, this technique is far safer in comparison to current conventional therapies and complications can be easily avoided by proper solution preparation with normal osmolarity and by education

Hypothesis

We believe that combination therapy is superior to other therapies for MPSRUS. Our modified retention enema has active components that improve inflammation, protects mucosa. Method of administration will also improve mucosal blood perfusion. In addition, sucralfate, as mechanical barrier, prevents further trauma and improves blood flow to the lower rectum by a decrease in sphincteric pressure. This multi aspect therapy has been used in a very limited number of patients and has had dramatic results. Antibiotics used in the composition will also prevent bacterial overgrowth and further inflammation and results in long lasting results.

Modified retention enema protocol

Composition

- 120 gram sucralfate
- 78 Iodoquinol
- 30 gram tetracycline
- 30 gram metronidazole
- 60 gram sulfasalazine
- 23.5 gram Bismuth
- 1 gram Hydrocortisone

One table spoon of the above combination (15 g) is being dissolved in 50 ml of saline.

Administration

A sterile disposable squeeze bottle is used. The rectal tube is pre-lubricated with petroleum jelly or other suitable lubricant. The squeeze bottle is meant to be discarded after using it only once. The rectal tube is then inserted into the rectum by the usual known method and approximately 50 ml of

prepared compound in saline liquid are introduced into the lower intestinal tract of the patient via the rectum by manually squeezing the plastic squeeze bottle. The bottle is then discarded. The fluid will stay in the bowel for at least an hour.

Patients will receive the above compound daily, up to 2 months and in case the clinical symptoms or histological symptoms persists therapy may be extend to 6 months.

Major outcome of interest

Inclusion criteria for this study would be all cases of diagnosed MPSRUS. The diagnosis will be made by endoscopic (ulcerative, polypoid, and flat types) (26) and presence of histological features of SRUS (ie. fibromuscular obliteration of the lamina propria with upward extension from hypertrophic and splayed muscularis mucosa and glandular crypt abnormalities).

Manometric and histological measurements beside clinical improvement in sign and symptoms of these patients should be recorded. Three months of follow-up is the minimum required time for conclusion. Efficacy assessment of the above compound needs a double blind study with sufficient number of study subjects.

Objectives are histological evidence for ulcer healing, improvement in clinical symptoms (bleeding, passage of mucus, and rectal pain or tenesmus). Secondary outcome of interest for this study is relapse rate during the follow-up, treatment failure and number of cases who finally undergo surgery.

Design

A double blind placebo controlled clinical trial is needed. In the proposed study, the modified retention enema will be compared to placebo (normal saline with neutral dyes mimicking the active compound). All the patients in this study should receive the concurrent medical care (diet modification, fibers, and bowel training).

Discussion

Many studies have shown that current treatment for SRU is sub-optimal (27-31). For example one study showed only 19% symptomatic improvement in their study with bulk laxatives and bowel retraining (29). There is also a disjunction between histological and symptomatic results among patients (29,31).

Why combination therapy?

Combination therapy refers to the simultaneous administration of two or more medications to treat a single disease. Combination therapies are being

used for cancers, tuberculosis, HIV and AIDS and malaria. All of these conditions have the following characteristics in common, all of them are chronic conditions and none of them have a definitive therapy. By combination therapy, the disease is being suppressed by different pathways in disease mechanism. The same rules are implied here for MPSRUS, it is a chronic disease with no definite or efficient therapy. We believe by the postulated therapy we can spare a larger number of patients from going to the operation room and we can provide our patients with an efficient therapeutic option. This will finally results in lower failure rates and a more cost benefit treatment.

Study limitations

The greatest barrier for this study would be very few numbers of cases available. We can overcome this problem by doing multicenter clinical trials. Next concern would be problem with controls the few number of patients will make examining different dosage of the therapy very difficult, we may also need extra trial arms to examine each of the active components for example we might have an extra arm with all the active components in the enema except the sucralfate. This problem might be overcome with comparison of the cases to retrospective cases that had other combination of drugs for enema.

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