ABSTRACT

Objective: The aim of this study is to review available treatment options and to review current opinions in the management of patients with chronic gastroesophageal reflux disease (GERD).

Materials and methods: This is a review article. Articles for the literature review were collected by using Google Search Scholar Engine. Literature search included relevant original and review articles addressing issues like medical treatment for GERD, surgical treatment for GERD, studies comparing surgical and medical treatment for GERD.

GERD is a common and chronic syndrome. Patients affected with syndrome experience symptoms which affect their quality of life.

The goals of treatment in this condition is to control symptoms, heal injured esophageal mucosa and to prevent complications. Both proton pump inhibitor (PPI) therapy and antireflux surgery are equally effective in controlling symptoms and in healing esophageal mucosal injury. In the recent years, laparoscopic surgery is increasingly been offered to patients with GERD. However, there is still controversy over best approach to management of GERD. This study attempted to review current opinions of this issue.

Conclusion: PPIs is an option for initial management of GERD. However, this condition been a chronic condition, relapse is common while on therapy with medications or following discontinuation of therapy. Hence, a treatment option which provides effective control of symptoms and prevents or minimizes complications has to be offered to patients. Medical therapy with PPI and laparoscopic antireflux surgery, both can achieve these therapeutic goals. Hence, in the light of this literature review it is recommended to individualize the treatment offered to the patient with GERD, in consultation with the patient himself or herself.

Keywords: Acid suppression therapy, Long-term safety of PPIs, Side-effects of PPIs, Surgical management of GERD, Clinical outcomes, PPIs vs laparoscopic fundoplication.


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INTRODUCTION

Montreal consensus defines gastroesophageal reflux disease (GERD) as ‘a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications’. Symptoms are considered to be ‘troublesome’ if they affect the individual’s well being.1 GERD is one of the most common upper gastrointestinal diseases in the Western countries and is reported to have a prevalence of 10 to 20%. GERD has been recognized as a clinical entity since 1930s.2-5 From a surgical perspective GERD is viewed as a mechanical disorder resulting from failure of antireflux barrier between the esophagus and the stomach. However, the exact nature of the antireflux barrier is not well-established but the lower esophageal sphincter, the diaphragmatic crura and phrenoesophageal ligament are considered as crucial elements of the antireflux barrier. Failure of this barrier results in reflux of gastric contents into the esophagus. Mechanical causes of failure causing GERD include: Defective lower esophageal sphincter, gastric emptying disorder or failure of esophageal peristalsis. The result of failure of antireflux barrier ranges from symptoms like ‘heartburn’ to structural damage to esophagus with or without further complications.6,7 GERD manifestations can be grouped into esophageal and extraesophageal syndromes. The esophageal syndromes include the typical reflux syndrome, the reflux chest pain syndrome and the syndromes with esophageal injury. The esophageal injury may range from reflux esophagitis; reflux esophageal stricture, Barrett’s esophagus to esophageal adenocarcinoma, and the extraesophageal syndrome include chronic cough, asthma, otitis media and laryngitis. The extraesophageal manifestations are thought to be due to reflux of gastric contents into the respiratory tract.8

GERD is a chronic disease and, hence, the approach to its management aims at controlling the symptoms and to prevent relapse. Symptomatic relief and relapse control can be reasonably achieved with proton pump inhibitors (PPIs) and has been the main stay of treatment for GERD but this approach fails to correct the motor abnormalities of the upper gastrointestinal tract that are associated with GERD.9 Alternative to PPI drug therapy is surgery. It was Nissen in 1951, who had first performed fundoplication and first laparoscopic fundoplication was reported in 1991 and the latter has rapidly replaced conventional Nissen fundoplication as the surgical therapy for GERD.10 It is also been reported that laparoscopic fundoplication is increasingly been offered for GERD patients as an alternative to long-term medical management. This is
because various studies has shown that laparoscopic fundoplication is safe in experienced hands, is effective for symptomatic relief and controlling recurrence, improves quality life, reduce hospital stay and also, following laparoscopic fundoplication patients can return to work earlier as compared to conventional Nissen fundoplication.11,12 In this review, an attempt will be made to compare the pros and cons of medical and surgical management of GERD based on the available literature and recommend a management approach for patient with GERD.

AVAILABLE TREATMENT OPTIONS FOR GERD

Nonsurgical Treatment Approaches

First-line treatment for GERD has been lifestyle modifications, supplemented by different medical formulations ranging from antacids to PPIs. Lifestyle and dietary modifications that appear to decrease gastric acid exposure of lower end of esophagus include; reducing dietary fat intake, reducing weight, cessation of smoking, elevation of the head end of the bed and avoiding recumbency for 3 hours postprandial.13

ACID SUPPRESSION THERAPY FOR GERD

Histamine 2 receptor antagonists (H2RAs) have been in use since 1970s, for symptomatic relief in the patients with GERD symptoms. H2RAs are effective in decreasing gastric acid secretion and have a longer duration of action compared to antacids. Drawbacks of H2RAs included relapse while on standard dose and also fails to heal severe esophagitis.14,15

Another group of drugs that emerged into the market because various studies has shown that laparoscopic fundoplication is safe in experienced hands, is effective for symptomatic relief and controlling recurrence, improves quality life, reduce hospital stay and also, following laparoscopic fundoplication patients can return to work earlier as compared to conventional Nissen fundoplication.11,12 In this review, an attempt will be made to compare the pros and cons of medical and surgical management of GERD based on the available literature and recommend a management approach for patient with GERD.

Another group of drugs that has been used in conjunction with PPIs were prokinetic drugs. One representative drug from this group is cisapride, but it was withdrawn from the market because it is associated with fatal arrhythmias. Cisapride is a selective agonist of 5-HT4 receptor and it could be modulated. Baclofen is a GABA B agonist and it blockage is one of the mechanisms through which TLESRs could be modulated. Baclofen is known to have frequent side effects and hence, it is recommended to start with a low dose and gradually increase as tolerated. Visceral pain modulators like trazodone (tricyclic antidepressant) and selective serotonin reuptake inhibitors when used in nonmood altering doses are useful in GERD patients who are found to have negative esophageal impedance monitoring. These drugs act in the central nervous system to produce visceral analgesia.19,20

Another group of drugs that has been used in conjunction with PPIs were prokinetic drugs. One representative drug from this group is cisapride, but it was withdrawn from the market because it is associated with fatal arrhythmias. Cisapride is a selective agonist of 5-HT4 receptor and it could significantly reduce TLESRs during sleep and hence, used to be combined with PPIs for the treatment of nocturnal reflux. Newer 5-HT4 partial agonists are promising and in a recent study it was shown that tegaserod (selective 5-HT4 receptor partial agonist) reduced postprandial esophageal acid reflux episodes without an apparent effect on lower esophageal pressure.19

MAINTENANCE THERAPY

As noted earlier GERD is a chronic disorder and large proportion of GERD sufferers would require prolonged
maintenance therapy, in order to maintain a reasonable quality of life. Both endoscopy-positive and-negative GERD patients experience relapse. Studies have shown that PPIs are the most effective pharmaceutical agents in the management of GERD for maintenance therapy and they are effective in reverting esophageal inflammation and providing symptomatic relief.\(^{21,22}\)

**CONCERNS IN THE LONG-TERM USE OF PPIs**

PPIs are not free from potential side effects, especially in prolonged use. Though risk of developing carcinoid tumors due to atrophic gastritis and or hypergastrinemia is remote but is a significant concern. Other problems associated with prolonged use of PPIs are the potential for development of clostridium difficile colitis and bacterial gastroenteritis.\(^{23,24}\)

Other concerns that have been raised against long-term use of PPIs include; concerns regarding vitamin \(B_{12}\) absorption, interference with iron absorption and interference in calcium absorption. Increased risk of gastric and colon cancer is also another concern that has been raised against prolonged use of PPIs.\(^{23}\)

Several studies have studied the association between vitamin \(B_{12}\) absorption and prolonged PPI use but they have failed to substantiate the claim that prolonged PPI use interferes with vitamin \(B_{12}\) absorption. On theoretical grounds it is assumed that prolonged use of PPIs can interfere with iron absorption and again the available data is not sufficient to conclude that prolonged PPI use could cause iron deficiency.\(^{23}\)

Several studies have linked potential for development of osteoporosis and consequent increased risk for fractures in patients on long-term PPI. However, there are no sufficient grounds to recommend discontinuation of PPI therapy for patients on PPI with recommended dose for proper indications.\(^{23}\)

Though, theoretically there is increased risk of developing gastric and colonic cancers in patients on long-term PPIs, this has not been validated in prospective randomized trials.\(^{23}\)

**SURGICAL TREATMENT FOR GERD**

**Open Antireflux Surgery**

Open antireflux surgery was initiated in 1950s as a treatment for patients with hiatal hernia and was aimed at keeping the lower esophageal sphincter within the peritoneal cavity.\(^{25}\)

Subsequently with the recognition of low esophageal sphincter pressure as the cause of GERD, antireflux surgery was offered to patients with GERD to increase lower esophageal sphincter pressure. It was Nissen in 1956 who had introduced antireflux surgery following an incidental finding that a fundal patch performed to reinforce the esophageal suture line could also correct gastroesophageal reflux.\(^{23}\) Later Belsey and Toupet applied a modified fundal wrap where a partial wrap was performed for GERD. Over time the procedures has been refined and outcomes following the procedures in the immediate postoperative period and in the long-term has improved. With better understanding and insight into the pathogenesis of GERD, antireflux surgery aims at lengthening the intra-abdominal portion of lower esophageal sphincter and to prevent effacing of the lower esophageal sphincter that occurs as a consequence of postprandial stomach distension.\(^{23}\)

The long-term clinical outcome of antireflux surgery is now well established and several studies have shown that there is over 90% reflux control in the long-term following Nissen fundoplication.\(^{26}\) Following first documentation of successful laparoscopic cholecystectomy, minimally invasive surgery has revolutionized the way various surgical procedures are performed and laparoscopic fundoplication became a reality.

**Laparoscopic Antireflux Surgery**

It is Geagea from Canada and Dallenmagne from Belgium in 1991 who had first reported series of fundoplication for GERD.\(^{23}\) Since, then laparoscopic fundoplication has become the procedure of choice for patients with GERD. It is also interesting to note that the threshold in offering surgery for patients with GERD has been lowered following the introduction of laparoscopic fundoplication. This is because of the advantages of minimally invasive surgery. Laparoscopic fundoplication is well-accepted both by the patients and the practitioners alike as it is a straightforward procedure and has an acceptable complication rate in the hands of surgeons experienced in the procedure. Though, laparoscopic fundoplication has been well-established as the procedure of choice for patients with GERD requiring surgical intervention,\(^{27}\) new approaches are been explored for the management of the same. One such approach is endoluminal surgery.

**ENDOLUMINAL ANTIREFLUX PROCEDURES**

Endoscopic approached like endoluminal gastroplication and another technique using a plicator device had been introduced in the recent past. Endoluminal gastroplication was the first endoscopic procedure to be proposed for the management of GERD.\(^{28}\) A commercially available suturing system called EndoCinch was used for endoluminal gastroplication. This procedure was reported to be safe and found to be effective in 60% of patients with GERD. Though the procedure was reported to be safe and relatively effective
it failed to normalize the acid reflux and had some serious complications.

Plicator device mimics the effects of conventional antireflux surgery by recreating the antireflux barrier, restoring the angle of his and by forming a one-way gastroesophageal valve. This procedure is free from serious complications and is reasonably tolerated.

Another novel endoluminal technique is the endoluminal fundoplication technique. This is an improvement over plicator technique and in this technique the gastroesophageal valve is recreated from within the stomach through oral route. It is claimed that this technique creates a robust and durable gastroesophageal valve that helps in reconstructing the altered antireflux barrier in patients with GERD. There is an ongoing multicenter study in Europe to assess the long-term efficacy of the endoluminal fundoplication technique.

**ADVANTAGES AND DISADVANTAGES OF ANTIREFLUX SURGERY**

Conventional Nissen fundoplication involves a complete fundal wrap and is associated with acceptable morbidity and mortality and has a success rate of 90% in the control of reflux in GERD patients who had undergone this surgery. However, it is associated persistent dysphagia, inability to belch and vomit. Other problems like epigastric fullness, postprandial pain and bloating, temporary swallowing discomfort and intense flatus also has been reported. On the other hand Toupet fundoplication is a partial wrap and, hence, basal lower esophageal sphincter tone is significantly lower than in Nissen fundoplication following this procedure. This procedure is reported to normalize lower esophageal sphincter tone, without impairing the ability of the lower esophageal sphincter to relax on proper stimulation. Toupet procedure used to be recommended for the patients with poor esophageal motility but randomized clinical trials fail to support this recommendation and certain modifications on Nissen procedure has minimized the side effects which used to follow Nissen fundoplication. Floppy Nissen with a short wrap is the preferred modification and it is reported to have a success rate of 90% with minimal morbidity and mortality.

Patients with Barrets esophagus usually have severe reflux and antireflux surgery, have the potential to restore lower esophageal sphincter pressure and prevent gastroesophageal reflux. However, complete regression of intestinal metaplasia does not occur but some regression of Barret’s epithelium is observed following antireflux surgery. It is also observed that progression to severe dysplasia or adenocarcinoma is also less compared to medical therapy in patients who had undergone antireflux surgery.

Clinical outcome of laparoscopic fundoplication is excellent, but still need for redosurgery is relatively high and ranges from 4 to 13%. Some long-term follow-up of laparoscopic fundoplication patients has shown 90% symptom control 10 years after the surgery while only 10% had to resume medications. Patients with dysphagia after Nissen fundoplication sometimes require revision of surgery and convert to a Toupet procedure or dilatation. Persistant dysphagia, wrap disruption, incorrect wrap placement and slippage are other causes which require revision of surgery. Revision of surgery after initial fundoplication is technically demanding but experienced surgeons are able to reproduce results comparable to initial correct surgery.

Studies comparing laparoscopic fundoplication with open surgery have demonstrated that laparoscopic fundoplication is as effective as open surgery in controlling symptoms of GERD. With the advantages of minimally invasive surgery and the procedures ability to effectively control GERD symptoms and improve quality of life even in patients with intractable GERD, laparoscopic fundoplication has replaced the open surgery in most of the centers world over.

**DISCUSSION**

Open antireflux surgery is effective management option for patients with GERD affecting quality of life, but this option used to be offered to patients with chronic complicated reflux who fail to respond to medication and lifestyle modification. This is because open reflux surgery is a major invasive procedure and is associated with peroperative and postoperative major complications. However, with the introduction of laparoscopic fundoplication there is a tendency to offer surgery for less complicated GERD. There are several reasons for this trend. One of the main reasons for this is that now the surgeons performing this surgery are more experienced in this procedure and techniques of the procedure are more refined and they are able to reproduce constant and reliable results. Since, laparoscopic fundoplication is less invasive and postoperative morbidity is much less, it has become more acceptable to patients as well.

On the other hand, modern medical treatments like PPIs are equally effective in the long-term management of GERD, but there are concerns over their safety in prolonged use. Some of these concerns include; interference with vitamin B12 absorption, iron absorption and calcium. However, these concerns have not been proved in large scale randomized control trials. More serious issues raised against prolonged use of PPIs include the theoretical risk of developing gastric carcinoid and colonic malignancies.
Again these theoretical possibilities has not established in the clinical settings.

GERD is a chronic condition and just like any other chronic syndrome patients with GERD also require prolonged medication. The consensus on pathophysiology of GERD is breakdown of antireflux barrier in patients with GERD, and PPIs or other medications effective in controlling GERD symptoms fail to address this primary cause of the disease. This is a major criticism leveled against prolonged use of PPIs by proponents of surgery for GERD. In addition there are several large studies which has shown that the clinical outcome of laparoscopic antireflux surgery is more favorable than that of long-term PPI therapy. Other studies also have demonstrated that laparoscopic Nissen fundoplication provides better physiological control of reflux and improved quality of life.

As noted earlier, GERD is syndyome which represents nonerosive reflux disease and erosive and ulcerative gastroesophageal disease. Hence, there are studies which have challenged the superiority of antireflux surgery in the treatment of esophagitis. These studies have demonstrated that recurrence rate of esophagitis between antireflux surgery and PPI are equal and healing of esophagitis is also similar. Similarly, controversy exists in the management of Barretts esophagus. In this regard, earlier studies have shown laparoscopic antireflux surgery to be the choice for patients with Barrets esophagus, as it reconstructs the antireflux barrier, and following surgery regression of intestinal metaplasia has been observed and it also appeared to reduce the risk of adenocarcinoma. But a recent meta-analysis has failed substantiate such a protective effect against development of esophageal cancer in patients with Barretts esophagus following antireflux surgery.

Endoluminal procedures have been recently evolving in an interesting and promising less invasive procedures than laparoscopic antireflux surgery. However, significant data is lacking about these procedures and there are no studies that have compared the efficacy of these procedures with either antireflux surgery or with medical treatments.

CONCLUSION

GERD is a syndrome resulting from breakdown of antireflux barrier at the lower end of esophagus. This breakdown of antireflux barrier results in reflux of gastric contents into the esophagus. Mechanisms for the antireflux barrier breakdown are thought to be due to TLESRs and hiatus hernia.

PPIs is an option for initial management of GERD. However, this condition been a chronic condition, relapse is common while on therapy with medications or following discontinuation of therapy. Hence, a treatment option which provides effective control of symptoms and prevents or minimizes complications has to be offered to patients. Medical therapy with PPI and laparoscopic antireflux surgery, both can achieve these therapeutic goals. Hence, in the light of this literature review it is recommended to individualize the treatment offered to the patient with GERD, in consultation with the patient himself or herself.

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