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Preclinical trial of a modified gastroscope that performs a true anterior fundoplication for the endoluminal treatment of gastroesophageal reflux disease

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Abstract
Background Laparoscopic fundoplication provides good reflux control, but side-effects due to the surgical procedure are known. Different endoluminal techniques have been introduced, but all with disappointing results.
Objective Evaluation of the feasibility and safety of a new device, which enables a totally endoluminal anterior fundoplication for the treatment of gastroesophageal reflux disease (GERD).
Material The device is a modified video gastroscope, which incorporates a surgical stapler (using standard 4.8 B-shaped surgical staples) and an ultrasonic sight. The cartridge is mounted on the shaft and the anvil is at the tip. This enables accurate stapling of the fundus to the esophagus, using the ultrasonic sight to guide distance and alignment of the anvil and the cartridge.
Method Sixteen female swine of mixed breed were used in the study; 12 underwent the endoscopic procedure, and 4 were used a controls to monitor weight gain. The 12 study animals were sacrificed at 2, 4, and 8 weeks (4 pigs each time) and visually inspected for complications, healing, and fundoplication. The study was sponsored by MediGus Ltd. and monitored for compliance with good laboratory practice (GLP) regulations by an external company (Econ Inc.), which is GLP certified by the German Federal Government. It was conducted at the animal testing facility of the Charité Virchow Clinic in Berlin.
Results The procedure went smoothly in all pigs; median procedure time was 12 min (range 9–35 min). At sacrifice, the stapled area had healed well, all animals had a satisfactory 180° anterolateral fundoplication, and there were no procedure-related complications.
Conclusions Creating a satisfactory anterior fundoplication with the new device is feasible, easy, and safe. Proof of efficacy must await clinical trials, which are underway.

Keywords Reflux · Endoscopic fundoplication

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Several endoluminal methods of treating gastroesophageal reflux disease (GERD) have either been approved, or are under investigation and development. While feasibility and short-term efficacy in improving subjective outcome parameters [reflux symptoms, heartburn-related quality of life, proton pump inhibitor (PPI) requirement] could be shown, the effects on objective outcome criteria [esophageal acid exposure and manometric characteristics of the lower esophageal sphincter (LES)] are less convincing

[1–5]. Endoscopic full-thickness plication could reduce GERD symptoms and medication use for at least 3 years postoperative, but no manometric data are available [3]. The EsophyX procedure was safe and cured GERD in 56% of patients based on symptom reduction and PPI discontinuation [4].

The new techniques aim to compete with standard treatment modalities: proton pump inhibitors and laparoscopic fundoplication. The anticipated advantage over antisecretory drugs is that, instead of merely altering the acidic content of the refluxate, the new endoscopic technologies intend to restore the compromised barrier function of the esophagogastric junction and thereby eliminate/reduce reflux. By using a totally endoluminal route, the new methods, if successful, will have advantage over laparoscopic surgery by avoiding the perceived risks and economical burden of formal operations. To date, reported results with endoscopic methods have been disappointing. The main reason is that each tried unproven method to reinforce the reflux barrier.

The new device presented herein is designed to create an 180° anterior fundoplication, restoring the gastroesophageal flap valve to normal. It is therefore expected to have clinical results similar to those of surgically created partial fundoplication.

Randomized controlled clinical trials have demonstrated that 180° anterior fundoplication is as effective as Nissen fundoplication, but is associated with fewer complications and improved ability to belch. Therefore a new device, called the SRS (produced by MediGus), to endoscopically create anterior 180° fundoplication, has been introduced [6]. In this study we present the first animal data with this device.

Methods

SRS endoscope

The device combines a two-way flexible video gastroscope with a stapler mechanism and ultrasonic sights (Fig. 1). The ultrasonic sights ensure accurate alignment of the anvil at the tip of the device with the stapler cartridge on the shaft. Once proper alignment is obtained, the anvil and cartridge are locked by means of two pins that penetrate across the walls of the stomach and esophagus, and a quintuplet of staples arranged horizontally is fired. The staples are standard 4.8-mm B-shaped (when closed) surgical staples, the same as used for gastroesophageal anastomosis in open surgery. During the procedure, the operator inserts the device to the gastroesophageal (GE) junction, marks its location, and then advances the device gradually into the stomach with retroflexion. The top of the fundus is caught and brought against the shaft of the device, which contains the stapler cartridge that is fired. The device is then partially withdrawn, rotated 120°, and the procedure is repeated. The result is a tent of the anterior wall of the stomach that is about 180° at the GE junction (Fig. 2). In ex vivo experiments, this tent is as effective as Nissen or Toupet fundoplication in preventing reflux. Surgical experiments show that two quintuplets hold the anterior fundoplication in place 7 months after placement.

Fig. 1 Two-way flexible video gastroscope with a stapler mechanism and ultrasonic sights

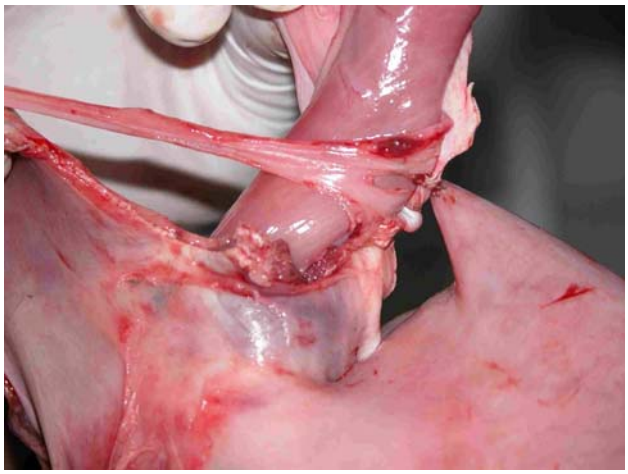

Fig. 2 After the procedure is completed, the result is a tent of the anterior wall of the stomach that is about 180° at the GE junction

Animal study

The study was sponsored by MediGus Ltd. and monitored for compliance with GLP regulations by an external

company (Econ Inc.), which is GLP certified by the German Federal Government. It was conducted at the animal testing facility of the Charité Virchow Clinic in Berlin.

Sixteen female swine of mixed breed were used in the study; 12 underwent the endoscopic procedure, and 4 underwent a sham procedure and were used as controls to monitor weight gain.

All examinations were performed under general anesthesia and with the animal intubated and breathing spontaneously. The animals were kept on a liquid diet for 24 h prior to endoscopy.

After all animals had undergone endoscopy using an Olympius OM-10 endoscope, to exclude any abnormalities in the upper gastrointestinal (GI) tract, an overtube (external diameter 1.5 cm) was inserted to facilitate passage of the SRS endoscope. In the four control animals the SRS endoscope was inserted and withdrawn without performing the procedure. In all other animals the procedure was performed as described above.

The 12 study animals were sacrificed at 2, 4, and 6 weeks (4 pigs each time) and visually inspected for complications, healing, and fundoplication.

Results

All animals tolerated the procedure well without evidence of complications, and all procedures could be completed satisfactorily. All animals exhibited normal health parameters for the duration of the experiment. Median procedure time was 12 min with a range of 9–35 min.

In the postoperative course no procedure-related complications or adverse events occurred, but two pigs developed enzootic pneumonia, which healed without further treatment.

All animals maintained their weight and appeared to eat and swallow normally, and there was no difference between the control and the study animals.

After the animals were sacrificed, all autopsy examinations confirmed satisfactory fundoplications. After 2, 4, and 6 weeks the two quintuplets hold the anterior fundoplication in place (Fig. 2).

Discussion

The novel endoscopic technologies for treatment of reflux attempt to "burn, tie, stuff or otherwise manipulate the hiatus" [7]. This study shows that creating a satisfactory anterior fundoplication in animals with the SRS endoscope is feasible, easy, and safe.

The major problem with endoscopic gastroplication methods is the durability of the created plication when utilizing endoscopic suturing. To overcome this problem the SRS endoscope utilizes a stapler mechanism with ultrasonic sights. The ultrasonic sight ensures accurate alignment, and the quintuplet of staples, as used for gastroesophageal anastomosis in open surgery, ensures durability. After the animals were sacrificed, all autopsy examinations confirmed satisfactory fundoplications. After 2, 4, and 6 weeks the two quintuplets hold the anterior fundoplication in place.

The risk of upper gastrointestinal endoscopy is increased when large overtubes are used. In the trial reported on the gatekeeper system, in which an overtube had been used, one case of pharyngeal perforation due to insertion of the overtube and one case of persistent nausea have been reported [8]. In this animal study we did use an overtube since regular endoscopy was performed in all animals prior to the fundoplication procedure and intubation of the animal's esophagus sometimes appeared to be bothersome. It is not planned to use an overtube in human patients.

In this animal study all examinations were performed under general anesthesia and with the animal intubated and breathing spontaneously. As reported in other studies on endoscopic reflux devices the procedure can be performed as an outpatient procedure under analgosedation. There were no procedure-related complications in the animals and we do not expect any when the procedure is performed on human patients.

Median procedure time was 12 min, which is shorter than reported in all other endoscopic reflux procedures [9].

An approach for restoring the esophagogastric junction has previously been described by DeMeester [10]. The microinvasive gastric stapler valvuloplasty is a combined endoscopic–laparoscopic technique, which has only been tested on baboons so far. The technique is similar to the technique we used. The valvuloplasty is performed with staplers, which are introduced into the lumen of the GI tract through transgastric route. The authors could show greater competency of the lower esophageal sphincter by an increase in median yield pressure from 12.75 mmHg in the control group to 22.87 mmHg in the valvuloplasty group, and an increase in median yield volume from 825 to 1525 mL, respectively. Both measurements were significantly at the $P < 0.01$ level [11]. We expect similar results with the SRS endoscope.

Endoscopic full-thickness plication was performed in 29 patients. Reduction of GERD symptoms and medication use was stable from 1 to 3 years, but a significant limitation in the design of this study was the lack of a sham group with which to compare the results [3]. Patient data is also available for the EsophyX device. Twelve-month results showed that the device was safe and effective in improving quality of life and reducing symptoms, PPI use, hiatal hernia, and esophagitis, as well as increasing LES pressure

and normalizing esophageal pH and cardia circumference in chronic GERD patients [4].

We believe that anterior fundoplication by totally endoluminal route can fill the gap between PPI and laparoscopic fundoplication and could show that creating a satisfactory anterior fundoplication with the new device is feasible, easy, and safe. Proof of efficacy must await clinical trials, which are underway.

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