Clinical Study Review

Study Name
Multi-Center, Non-Randomized, Prospective Study of the Reza Band® UES Assist Device for the Treatment of Esophagopharyngeal Reflux

In Short
Determine the safety and effectiveness of the Reza Band using the validated Reflux Symptom Index (RSI)

Objective or Subjective (Patient Centric)
Subjective

Physicians Involved
Stacey Silvers, MD – Madison ENT – New York City
Michael Vaezi, MD – Vanderbilt University – Nashville, TN
Nimish Vakil, MD – Aurora Healthcare – Milwaukee, WI
Alan Raymond, MD – NYU Gastroenterology Associates – New York City
Michael Schmalz, MD – GI Associates – Milwaukee, WI

Study Objective
Assess the safety and effectiveness of the Reza Band when worn by patients that had been clinically diagnosed with laryngopharyngeal reflux (LPR).

Methods Utilized
Testing Method

- The subjects wore the device while sleeping. The effectiveness of the Reza Band was determined with the Reflux Symptom Index (RSI), comparing the baseline to week 4. In addition, subject and physician satisfaction questionnaires and subject diaries were completed and returned. Subject diaries were used to capture data in between study visits.
- The safety of the Reza Band was evaluated by assessing the incidence, type, duration and severity of adverse events observed in all subjects.
- The primary effectiveness endpoint was defined as the percentage change in RSI from baseline (week 0, visit 1) to the end of the study (week 4, visit 3). Effectiveness was also measured at the midway (week 2, visit 2).

Subject Group Size/Demographic, Single or Multi-Centered

- 95 subjects. 89 finished the study and were included in the population. The 6 excluded did not return for visit 2 or 3.
- Non-randomized, prospective, open label trial. If subjects were taking medication, they were instructed to continue to do so.
- 5 Sites (Multi-centered)
- Subjects had been diagnosed with LPR and met the study inclusion and exclusion criteria
- Mean age – 48.8 years; Mean BMI – 25.5; Females – 69.5%; Race – Caucasian 81.1%, Hispanic 8.4%, African American 4.2%

Timeline
4 weeks

Results
Effectiveness
Baseline – Mean RSI: 26
Week 2 – Mean RSI: 14
Week 4 – Mean RSI: 12

Safety

- Adverse events reported during study were generally mind and short in duration. The majority of those events were not related to the device. The events related to the device were also generally mild and short in duration.
- Device related adverse events did not result in reduced outcomes of the RSI score from baseline to visit 3 (week 4), and were consistent with the overall population.
- There were no deaths, unexpected adverse events or subject withdrawals due to adverse events.

Conclusions

- The Reza Band is a safe and effective therapy for physicians and their extraesophageal reflux patients, in that it's a non-invasive therapy that provides symptom relief within the first two weeks, and this benefit is maintained and improved at four weeks.
- There is no indication that there is any residual or cumulative risk with the use of the device.

Key Terms and Definitions

Double Blinded Study – When both the doctor and the patient do not know if they are getting the study treatment or a placebo

Single Blinded Study – When only the doctor knows if the patient is getting the study treatment or the placebo

Dyspepsia – Indigestion

Dysphagia – Difficulty or discomfort swallowing

Esophagoscopy – Procedure in which a flexible endoscope is inserted through the month and into the esophagus. Used with a device to display magnified images on a video screen

Impedance pH Monitoring – Technique used in the diagnosis of gastroesophageal reflux disease, by monitoring both impedance and pH

Laryngospasm – Brief spasm of the vocal cords that temporarily makes it difficult to speak or breathe

Mean – Average

Non-Randomized – To be randomized means people being studied are randomly selected to the study treatment or placebo. Non-randomized, means this wasn't done

Odynophagia – Pain when swallowing

Open Label Study – Both the researchers and subjects know if getting study treatment or placebo

Placebo – Looks like study treatment but provides no benefit (like a sugar pill in a drug study)

Prospective Study – Study in which the subjects are followed real-time for effects of a study treatment.

p-Value – A statistical number that shows if 2 groups being compared are really different or not. A p-Value of <0.05 means that there is a difference. >0.05 means there is no difference.

Retrospective Study – Looking back at records to see if a study treatment had an effect.

Reflux Symptom Index (RSI) – Validated nine-item patient-administered outcome questionnaire designed to document the symptoms and severity of LPR. Patients rate themselves on how the nine symptoms affected them on a scale of 0 (no problem) to 5 (severe problem), with a max score of 45.

Study Treatment – The device that is being studied

Customer Summary

- The Reza Band is a safe and effective method for treatment of reflux symptoms into the throat and lungs. 86% of subjects had a successful outcome with a significant reduction in symptoms after two weeks. Physicians reported being satisfied with the Reza Band 92% of the time and subjects were satisfied 78% of the time, with 59% being very satisfied.
- Adverse effects are short and generally mild
- High subject acclimation and satisfaction without any safety risk

FAQ

Why not double blind study?

With the Reza Band, it's impossible to perform a double-blind study, as both the subject and the investigator know whether or not the subject is using the device.

What about the placebo effect?
The success criterion of 25% improvement was based on the average placebo response of placebo-controlled trials using the RSI in the literature.

How did you come to the trial size/why not more subjects? Assuming the Reza Band has a 35% reduction in RSI and using power of 80%, and a one-sided significance level of 0.05, it was determined that 85 subjects were required for the study. The 35% was based on the 25% seen in the literature.

How were the subjects diagnosed with LPR? It was determined by the patient's history of office visits, medical management and various in- and out-patient testing.

Why only 4 weeks? It has been shown that improvement occurs quickly when extraesophageal tissues are no longer exposed to gastric contents. The clinical study confirmed this by demonstrating a significant improvement within 2 weeks. There is no anatomical or physiological reason that the effect of the Reza Band would decrease after 4 weeks. If tissues are healed as the Reza Band keeps working, then the effect is constant. The amount of pressure being placed on the hard cricoid cartilage will not cause any changes or damage. Studies have shown that when a cricoid is exposed to 800 mmHg of trauma, there still isn't any damage.

What were the Reza Band problems? There have been a few reports that a magnet has come out. The design of the Reza Band changed to address the problem.

What was the External Manometer problem? Thought that the External Manometer was not correct, as subject noted that Reza Band felt too tight after being fit. The External Manometer was returned and found to function correctly.

Physician / Subject Satisfaction – All subjects completed a 12 question satisfaction questionnaire and rated each question from "extremely dissatisfied" to "extremely satisfied". For every subject, investigators filled out their satisfaction, using the same 12 questions and same ratings. The investigators were more satisfied than subjects, as they were evaluating from a patient care perspective.

If 86% of the subjects had successful outcomes, why were only 59% very satisfied? Subjects may have been complete cure without taking any medications, etc. Therefore, some were not "ecstatic" but were still satisfied with their improvement.

With the 5 physicians that participated, how could they be satisfied with the device 92% of the time? Investigators were asked to rate satisfaction for every subject. While the vast majority of subjects had significantly improved outcomes, some did not do as well as hoped.

Why not more objective testing? The typical diagnostic tools commonly employed for reflux such as esophagoscopy, pH or impedance monitoring suffer from lack of sensitivity and specificity in patients with extraesophageal symptoms. Use of pH and impedance in this anatomical area is still controversial and it was determined, with the investigators, that this study would not solve that controversy. The RSI is a validated, well accepted, symptom based method, and it provides clinically relevant outcome measures for this patient population.

Additional Commentary
- Presented at DDW 2014, AAO-HNSF 2014, DDW 2015, Submitted for publication July 2015 (Under review)
- Study documentation utilizes terms extraesophageal, laryngopharyngeal reflux (LPR), and esophago-pharyngeal reflux interchangeably. All terms are common and familiar to the call points.