

## **The Frequency of Gastroesophageal Reflux Disease in Nutcracker Esophagus and the Effect of Acid-Reduction Therapy on the Motor Abnormality**

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**Aim:** The purpose of this prospective study is to estimate the frequency of gastroesophageal reflux disease (GERD) among patients with nutcracker esophagus and to assess the effect on the motility after acid-reducing treatment. The study was performed at King Khalid University Hospital, Riyadh, Saudi Arabia between January 1995 and December 1996.

**Methods:** Patients were included in the study if 1) esophageal manometry showed nutcracker esophagus tracing, 2) ages between 16-75 years, and 3) no prior use of acid suppressing agents or drugs that change esophageal motility a week before. Initially, all patients underwent upper gastrointestinal endoscopy and 24-hour esophageal pH monitoring.

**Results:** Eleven patients: seven females and four males, mean  $\pm$  (SD) age was 35 (11) years. Mean  $\pm$  (SD) amplitude of the distal esophageal contraction for the whole group before and after treatment were  $205 \pm (33.7)$  and  $145.7 \pm (40.5)$  mmHg respectively ( $P < 0.001$ ). Gastroesophageal reflux disease was present in eight (72.7%) patients- six females and two males. Esophageal motor abnormalities returned to normal in the majority of patients (85.7%) after 12 weeks of aggressive acid suppressing therapy.

**Conclusion:** Gastroesophageal reflux disease is frequent among nutcracker patients. High acid suppressing treatment can reverse the motor abnormalities.

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The most common esophageal motor disorder detected in patients presenting with noncardiac chest pain is the "nutcracker esophagus"<sup>1,2</sup>. This is a motor disorder of the distal esophageal body characterized manometrically by high amplitude contractions<sup>3,4</sup>. In addition to chest pain, patients with nutcracker esophagus may present with heartburn, dysphagia and regurgitation<sup>2</sup>. DeMeester et al was the first to demonstrate the presence of reflux in a group of patients presenting with non-cardiac chest pain<sup>5</sup>. Furthermore, Achem et al, found gastroesophageal reflux disease (GERD) in 65% of nutcracker esophagus patients studied by prolong ambulatory 24-hour pH monitoring<sup>6</sup>. Moreover, the majority of treated patients obtained a significant improvement in terms of frequency of chest pain episodes and the severity of pain<sup>6</sup>.

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The objective of this prospective study is to find the frequency of gastroesophageal reflux disease (GERD) in patients diagnosed to have nutcracker esophagus at King Khalid Hospital, Riyadh, Kingdom of Saudi Arabia and to study the effect of acid-reducing therapy on the motor abnormality.

## **METHODS**

Esophageal manometry was performed at King Khalid Hospital, Riyadh, Saudi Arabia, in 191 patients over a two-year period (January 1995 to December 1996). Eleven patients (seven females and four males) fulfilled the criteria of nutcracker esophagus; normally propagating high amplitude contractions in excess of 180 mmHg at 2 and/or 7 cm above the level of the lower esophageal sphincter. The main indications for esophageal manometry were heartburn, regurgitation, chest pain and dysphagia. Before esophageal manometry, all patients underwent an upper esophagogastroscopy and a 24-hour pH monitoring.

### **Esophageal Motility Study**

The study was performed in fasting patients. Acid suppressing agents and medication which might affect motility were discontinued at least seven days before the procedure. The study was performed in supine position using eight-lumen polyvinyl catheter (outer diameter is 4.5 mm; internal diameter is 0.8 mm; ESM 3R, Arndorfer Medical Specialties). The distal four openings were spaced 1 cm apart at 90° angle, while the proximal four openings were spaced at 5 cm distance at 90° angle. The catheter was connected to external pressure transducers (Novadome MX 860 medex Rossenda, England). The catheter was continuously perfused with distilled water at a rate of 0.5 ml/min by a low-compliance pneumohydraulic capillary infusion system (Arndorfer Medical Specialties). The catheter assembly was passed through the nose until all recording orifices were in the stomach.

The station pull-through of the lower esophageal sphincter (LES) was performed at 1 cm intervals. The LES pressure recorded for each patient represented the calculated average of four individual pressures (distal ports), measured at end-expiratory variation to the mean gastric baseline pressure. Esophageal body recordings were performed by positioning the four proximal ports 2, 7, 12 and 17 cm above the LES. At least 10 wet swallows (10 ml water each) were administered, each separated by 30 seconds period. The amplitude of pressure wave was measured from the mean intraesophageal baseline pressure to the peak of the wave. Nutcracker esophagus was diagnosed when the mean distal esophageal contraction amplitude was greater than 180 mmHg at 2 and/or 7 cm above LES. This was seen in all patients diagnosed to have nutcracker esophagus 2 cm above LES and in further three patients 7 cm above LES. The mean amplitude presented in this study is that recorded 2 cm above LES. Amplitude of the distal esophagus is expressed as a mean  $\pm$  (SD) of ten wet swallows in mmHg.

### **Ambulatory 24-Hour pH Monitoring**

In an overnight fasting patient, an antimony pH probe with an outer diameter of 2.1 mm, was positioned 5 cm above the upper border of the LES and a reference electrode was attached to the anterior chest wall. Both electrodes were connected to a recording device (Synectics Medical, Inc., Irving Tx) pH electrode was calibrated using buffers of pH 1 and 7. Patients were instructed to keep record of their upright and supine positions and they had been told to

discontinue all medications that might affect pH recording seven days prior to the test. The pH tracings were analyzed by a commercial computer software program and reviewed by the

author. Reflux disease was considered pathological if any of the following criteria were exceeded: 1) % total time pH < 4 (normal < 5.5%); 2) % upright with pH < 4 (normal < 8.2%); 3) % supine with pH < 4 (normal < 3 %) <sup>7</sup>. Once gastroesophageal reflux was documented by upper gastrointestinal endoscopy and 24 hour pH monitoring, the patient either received proton pump inhibitor (n=7) or underwent surgery (n=1). Fundoplication procedure was performed in this patient due to several reasons: i) patient's symptoms had failed to respond to prolong H<sub>2</sub> blocker and antireflux measures before enrollment in the study, ii) endoscopically grade II reflux esophagitis was seen inspite of patient taking acid suppressing medicine, iii) pH study results were one of the highest among all patients tested. Esophageal manometry and pH monitoring were repeated in seven and six patients, respectively, after 12 weeks while on omeprazole.

**StatisticalAnalysis:** We used student t-test to compare amplitude values before and after treatment. P value less than 0.05 was considered significant.

## RESULTS

This study included 11 patients (seven females and four males, mean age ± [SD] 35 [11] years) diagnosed manometrically to have nutcracker esophagus. Heartburn, regurgitation, chest pain and dysphagia were the main presenting symptoms in 73%, 55%, 36% and 36% of patients respectively. Table 1 shows esophageal manometry and 24 hour pH monitoring before treatment. Patient number four was 28 week pregnant when first seen and took prescribed acid suppressant medication intermittently.

Table 1. **Esophageal manometry and pH study before treatment**

Pt's No	Age	Sex	Mean amplitude (SD)mmHg	pH study		
				% upright	% Supine	Total
1	38	F	213(35.7)	11.3	0	5.6
2	45	F	233.7(98)	2	2.9	1.5
3	37	F	200 (20)	12	7.2	9.6
4	27	F	189(14)	11	42.6	19.8
5	16	M	183(12.6)	1.7	1	1.5
6	43	M	224(22)	21.7	22.8	22.1
7	36	M	196.5(30.8)	6.8	1.3	3
8	29	M	207(41.4)	23.1	3.8	19.5
9	32	F	216(26)	2.3	10.8	3.7
10	60	F	196(10)	7.7	5.4	7.1
11	25	F	195.5(38)	8.2	5.4	1.8

Upper gastrointestinal endoscopy showed grade II reflux esophagitis in three patients. Mean amplitude  $\pm$  (SD) of the distal esophageal contraction before treatment for the whole group was  $205 \pm (33.7)$  mmHg. Twenty four hour pH monitoring showed gastroesophageal reflux disease in eight patients (72.7%). pH tracing of five patients demonstrated reflux in both supine and upright positions, whereas supine reflux was present in three patients. Patients diagnosed to have gastroesophageal reflux disease received either acid suppressing drugs (seven patients) or underwent fundoplication (patient number six). Esophageal manometry and pH monitoring was repeated in seven and six patients, respectively (Table 2). Contraction amplitude reduced to normal level in six patients, while the remaining patients (the pregnant patient) maintained her nutcracker esophagus tracing. Mean  $\pm$  (SD) contraction amplitude of the distal esophagus after 12 weeks of treatment was  $145.7 (40.5)$  mmHg. The pH monitoring normalized in five patients and improved in one (the pregnant patient).

**Table 2. Esophageal manometry and pH monitoring after treatment**

Pt's No	Age	Sex	Mean amplitude (SD)mmHg	pH study		
				% upright	% Supine	Total % pH<
1	38	F	71.7(9.6)	2.8	1.3	1.2
3	37	F	121 (13.6)	1.7	0.5	1.3
4	27	F	190(21)	15.7	15.5	15.9
6	43	M	164(24)	0.6	0	0.3
8	29	M	149 (37)	5.3	2.2	4.1
9	32	F	*ND	0	1.4	0.8
10	60	F	153 (20.6)	*ND	*ND	*ND
11	25	F	128(25.6)	*ND	*ND	*ND

\*ND – not done

Table 3 compares esophageal manometry and 24 hour pH monitoring before and after treatment. Mean esophageal contraction amplitude before and after therapy were  $205 (33.7)$  and  $45.7 (40.5)$  mm Hg. The difference was highly significant ( $P<0.001$ ).

**Table 3. Patient's demographic data. Esophageal manometry and pH monitoring before and after treatment.**

Pt's No.	Age	Sex	AMP/mmHg Mean (SD)		pH Study B/A			ECG
			B	A	% Upright	% Supine	Total % pH<4	
1	38	F	213 (35.7)	717 (.6)	11.3/2.8	0/1.3	5.6/1.2	N
2	45	F	233.7 (98)	*ND	2*ND	2.9*ND	1.5*ND	N
3	37	F	200 (20)	121(13.6)	12/1.7	7.2/0.5	9.6/1.3	N
4	27	F	189 (14)	190(21)	11/15.7	42.6/15.5	19.8/15.9	R <sub>2</sub>
5	16	M	183 (12.6)	*ND	1.7/*ND	1/*ND	1.5/*ND	N
6	43	M	224 (22)	164 (24)	21.7/0.6	22.8/0	22.1/0.3	R <sub>2</sub>

7	36	M	196.5 (30.8)	*ND	6.8/*ND	1.3/*ND	3/*ND	N
8	29	M	207 (41.4)	149 (37)	23.1/5.3	3.8/2.2	19.5/4.1	R <sub>2</sub>
9	32	F	216 (26)	*ND	2.3/0	10.8/1.4	3.7/0.8	N
10	60	F	196 (10)	153 (20.6)	7.7*ND	5.4/*ND	7.1/*ND	N
11	25	F	195.5 (38)	128 (25.6)	8.2/*ND	5.4/*ND	1.8/*ND	N

*Amp = Amplitude*

*B = Before treatment*

*A = After*

*N = Normal*

*pH B/A = pH before/after treatment*

*\*ND = not done*

*R<sub>2</sub> = Reflux esophagitis Grade II*

*EGD = Esophagogastro duodenoscopy*

## DISCUSSION

Nutcracker esophagus is the most common manometric abnormality detected in patients presenting with non-cardiac chest pain<sup>1,8</sup>. The term nutcracker was first used by Benjamin et al<sup>9</sup>. This is characterized by normally propagating high amplitude contractions (in excess of 180 mmHg) in the distal esophagus. The recognition of gastroesophageal reflux disease in patients with non-cardiac chest pain was first investigated by DeMeester who demonstrated gastroesophageal reflux disease in almost half of his patients with non-cardiac chest pain<sup>5</sup>.

This study demonstrated high frequency rate of gastroesophageal reflux disease (72.7%) among patients with nutcracker esophagus. This is slightly higher than that reported by Achem et al<sup>6</sup> who evaluated 20 patients with nutcracker esophagus using prolong ambulatory pH monitoring and found gastroesophageal reflux disease in 65% of the investigated patients. The difference, although small, may be explained by the high frequency of heartburn (73%) in our study population.

Furthermore, Triadafilopoulos and Castillo studied 35 consecutive patients with spontaneous, repetitive, non-propulsive esophageal contractions detected on esophagography<sup>10</sup>. Gastroesophageal reflux disease was noted in 20 patients (58%). Moreover, esophageal manometry showed nutcracker esophagus in eight patients. Five (62.5%) of them suffered from gastroesophageal reflux disease<sup>10</sup>. However, manometry and pH monitoring was not repeated after a period of treatment.

Our study demonstrated normalization of esophageal contraction amplitude in six (85.7%) patients after 12 weeks of antireflux management. This is in contrast to Achem et al<sup>7</sup> who repeated the manometric test after eight weeks of antireflux therapy in 11 patients while on treatment. Seven (63.6%) out of 11 patients in Achem's study showed a change in manometric diagnoses; four had a non-specific esophageal motor disorder, one had diffuse esophageal spasm and two had a normal tracing while the remaining four patients maintained their nutcracker esophagus tracing. This difference could be partly explained by longer period of therapy (12 weeks versus 8 weeks) before repeating manometry in our study. Of interest is the persistence of nutcracker esophagus pattern in the pregnant patient who ingested her medication intermittently and repeated pH monitoring revealed abnormal reflux.

## CONCLUSION

**This study demonstrates the high frequency rate of gastroesophageal reflux disease among patients with nutcracker esophagus reported by Achem et al. Moreover, this**

**study shows that antireflux therapy successfully normalized the manometric feature in the majority of patients. However, a double-blind placebo controlled trial should be carried out to confirm the observations in this study.**

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