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The Effects of Diaphragmatic Breathing and Omeprazole on Respiratory Indices and Diaphragmatic Excursion in Patients with Gastroesophageal Reflux Disease

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Abstract

Background: Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders that can disturb patients' respiratory indices. Proton pump inhibitors (PPIs) such as omeprazole are currently the most common treatment in the patients. PPI-refractory GERD is a clinical problem constituting around 30% of patients with GERD.
Objectives: The aim of this study was to investigate the effects of diaphragmatic breathing (DB) and omeprazole on respiratory indices (RI) and diaphragmatic excursion (DEX) in patients with GERD.
Methods: This is a clinical trial conducted for eight weeks among 40 patients with severe GERD in Tehran in 2018. The block randomization method was designed to randomize 40 patients into two groups (DB and control) that resulted in equal sample sizes. The control group received omeprazole 20 mg once daily, and the DB group, in addition to omeprazole, performed DB. Respiratory indices, including (Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV1), Peak Expiratory Flow (PEF)), and DEX were evaluated before, immediately, and six weeks after the end of intervention by spirometry and ultrasonography; respectively.
Results: There was no significant difference in the RI and DEX before the intervention between groups. FVC ($P = 0.04$) and PEF ($P = 0.02$) significantly changed in the control group, but FEV1 ($P = 0.001$), FVC ($P = 0.002$), PEF ($P = 0.001$) and DEX (0.001) significantly changed after DB. There was a significant difference in terms of RI between before and followed up in DB.
Conclusions: Diaphragmatic breathing with omeprazole had more effects on RI and DEX than omeprazole alone. The positive effects of DB remain at least six weeks after the end of the intervention.

Keywords: Diaphragmatic Excursion, Respiratory Indices, Reflux, Omeprazole, Ultrasonography, Spirometry

1. Background

Reflux is one of the most common digestive problems in the world, and there is still no complete treatment without complications (1). The prevalence of GERD in patients with asthma is about 80% (2). Microaspiration of gastric acid into airways is the most important cause of respiratory mechanism disturbance (3). Some studies demonstrated the correlation between pulmonary disease and reflux (4), so spirometry results may be abnormal in patients with reflux because of airway resistance (5). Pulmonary disease is associated with high mortality and a high economic burden in the countries (6).

The efficacy of proton pump inhibitors (PPIs) on respiratory indices (RI) in patients with GERD is controversial and has a lot of side effects (7, 8). Since DB activates the diaphragm muscles properly (9) and diaphragm muscle plays a key role in supporting the lower esophageal sphincter, we used DB to improve RI of the patients (10, 11).

2. Objectives

The aim of this study was to compare the effects of DB in combination with omeprazole and omeprazole alone on RI and diaphragmatic excursion (DEX) in patients with severe reflux.

3. Methods

3.1. Patient Selection

The study started when consecutive patients attending the Taleghani Hospital were invited to join after fulfilling the inclusion criteria. The study design was a randomized clinical trial with IRCT and ethics number IRCT20190619043949N1 and USWR.REC.1396.272, respectively. We included adult patients (18 to 50 years old) with severe GERD, according to the assessment of clinical severity by Kahrilas definition (12). Patients needed to have experienced heartburn or regurgitation more than twice per week (12). The exclusion criteria were alcohol and tobacco use, pregnancy, patients with extreme body mass index ($<$ 18 or $>$ 35). Informed consent was obtained from all participants, and the protocol was approved by the Singhealth Centralized Institutional Review Board before the start of the study. All participants were matched in terms of age, gender, and demographic characteristics. The block randomization method was designed to randomize 40 patients into two groups that resulted in equal sample sizes. In the control group, omeprazole (capsule 20 mg, KRKA, Slovenia) was used by the participants before breakfast and daily. In the DB group, in addition to omeprazole, DB was performed by the patients. The study was conducted for eight weeks, and also, patients were followed for six weeks after completing the study. Researchers called the patients either phone call-based or traditional face-to-face to follow the clinical program, and all patients completed the study (Figure 1).

3.2. Spirometry

Spirometry was conducted according to the criteria of the American Thoracic Society and the European Respiratory Society for standardization (13). Spirometer (BIONET SPM-300, South Korea) was used (14) to determine the changes of FEV1, FVC, and PEF. Spirometry was performed before, immediately, and after the follow up in the same condition. We asked patients to avoid vigorous exercise and eating a large meal within two hours of the start of the test. The patients used loose and comfortable clothing that did not restrict their breathing.

3.3. Diaphragmatic Excursion

Diaphragmatic excursion (DEX) was analyzed by M mode ultrasonography (E500) in the right hemidiaphragm (15). The DEX was measured with a 2 to 5 MHz US probe (M-Turbo, Fujiflm SonoSite Inc., Bothell, WA, USA) placed over one of the lower intercostal spaces in the right anterior axillary lines for the right hemidiaphragm. The DEX was measured on the vertical axis of the tracing, from the baseline to the point of maximum height of inspiration.

3.4. Diaphragmatic Breathing

Diaphragmatic breathing (DB) was performed five days a week and five sessions every day. Each session consisted of 75 respirations. The patient lying in the supine position and placing a pillow under his or her knees, putting one hand on his or her chest and placing the other on the abdomen, and maintaining his or her contact with the body. The patient throws a deep breath through his nose, as much as the abdominal hand reaches the highest point of the earth. Then, he/she takes out air through his/her mouth and returns to the first (Figure 2).

3.5. Statistical Analysis

The study was initially designed to compare the effects of DB and omeprazole on RI and DEX in patients with GERD. However, early in the study, it was noted that most patients recruited had severe reflux and the study protocol was amended with the new aim to compare RI and DEX of post-DB with omeprazole in all patients. All authors had access to the study data and reviewed and approved the final manuscript. Mauchly's Test of Sphericity showed the sphericity of the data. Kolmogorov-Smirnov test was used for the normal distribution of variables by IBM SPSS Statistics23 (IBM, Armonk, NY), and data are expressed as the mean $\pm$ standard deviation. Repeated measure [once between-subject factor (Groups: DB and Control) and once within-subject factor (Times: before, immediately and after 6 weeks follow-up)] was used to determine changes of RI and DEX between the two groups. The $P < 0.05$ was considered statistically significant.

4. Results

4.1. Patient Characteristics

Forty patients who fulfilled the inclusion criteria were randomly divided into two groups and completed the study, including the DB group (10 women (50%); mean age, 44.80 $\pm$ 6.59), and the control (10 women (50%); mean age, 38.00 $\pm$ 13.41) with 0.73 effect size. An initial 20 patients underwent DB immediately on enrolment (treatment groups), whereas the subsequent 20 subjects were considered the control group. There was no significant difference in terms of demographic characteristics between the groups (Table 1).

4.2. Respiratory Indices

There was no significant difference in the respiratory indices (RI) before the study between groups. The results of between-subjects are summarized in Table 2. The results of within-subjects showed that FEV1 is significantly different ($P = 0.001$). There was no change in FEV1 in the control

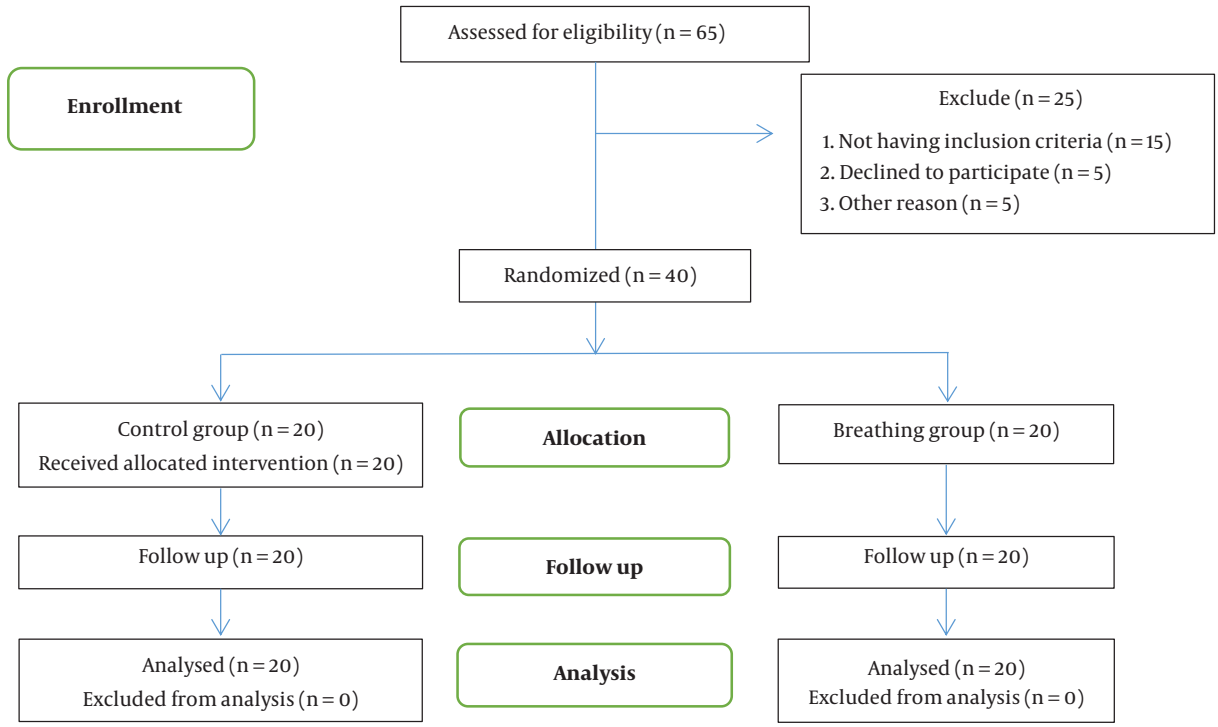

Figure 1. CONSORT flow diagram of the study

Table 1. Demographic Characteristics of the Subjects

Variables	Groups		P Value[a]
	Diaphragmatic Breathing	Control	
Age (years), Mean ± SD	44.80 ± 6.59	38.00 ± 13.41	0.06[a]
Weight (kg)	72.60 ± 13.04	69.20 ± 8.56	0.84[a]
Height (m)	1.71 ± 8.36	1.71 ± 0.45	0.33[a]
BMI (kg/m^2)	24.73 ± 3.51	23.50 ± 2.33	0.20[a]
Sex (female), No. (%)	10 (50%)	10 (50%)	0.10[b]

[a] Independent *t*-test
[b] Chi-square test

Figure 2. How to do diaphragmatic breathing exercises

group. The DB significantly increased FEV1, and there was a significant difference between before and follow up findings in the DB group (P = 0.001).

The results of within-subjects showed that FVC is significantly different (P = 0.001). There was a significant difference in FVC before and after the intervention in the DB and control groups (P = 0.002 and P = 0.04; respectively). The FVC was significantly different after follow up only in the DB group (P = 0.008). The tests of within-subjects showed that PEF is significantly different (P = 0.001). There was a significant difference in PEF before and after the intervention in the DB and control groups (P = 0.001 and P = 0.02,

Table 2. Comparison of Variables Between the Groups

Variables	Groups		P Value[a]
	Control	Diaphragmatic Breathing	
Forced expiratory volume in 1 second (L)			
Before	2.38 ± 0.48	2.73 ± 0.78	0.09
After	2.53 ± 0.49	3.97 ± 0.67	0.001
Follow up	2.44 ± 0.51	4.17 ± 0.59	0.001
Forced vital capacity (L)			
Before	2.58 ± 0.53	3.00 ± 0.87	0.07
After	2.85 ± 0.47	4.16 ± 0.88	0.001
Follow up	2.58 ± 0.56	3.75 ± 0.70	0.001
Peak expiratory flow (L/S)			
Before	4.20 ± 0.44	4.43 ± 0.78	0.26
After	3.96 ± 0.58	5.86 ± 1.0	0.001
Follow up	3.84 ± 0.52	5.71 ± 0.74	0.001
Diaphragmatic excursion (cm)			
Before	4.06 ± 0.39	3.72 ± 0.53	0.06
After	4.13 ± 0.55	5.92 ± 0.85	0.001
Follow up	4.25 ± 0.44	5.87 ± 0.86	0.001

[a] Repeated measures

respectively). The PEF after follow up was significantly different in DB (P = 0.001).

4.3. Diaphragmatic Excursion

The results of within-subjects showed that DEX is significantly different (P = 0.001). The DEX did not change in the control group but significantly increased in the DB group (P = 0.001). The DEX was not different between before and follow up in the DB group (P = 0.83).

5. Discussion

Reflux may decrease RI in patients and play an important role in the pathogenesis of respiratory diseases. Previous studies have reported that the incidence of GERD in patients with asthma and chronic cough is higher with various mechanisms being proposed, including microaspiration and bronchoconstriction reflexes (16-18). During the reflux, the stomach contents have reached the hypopharynx, and they may also reach the trachea. The GERD may also lead to bronchiectasis in adult populations. In a study by Sweet et al., patients with bronchiectasis were found to have severe reflux. The researchers also concluded that the probability of the occurrence of reflux is contributing to the pathogenesis of bronchiectasis (19). The aim of this study was to compare the effects of diaphragmatic breathing and omeprazole on RI and DEX in patients with severe GERD. As a result of this study, it was found that DB, in combination with omeprazole, can positively improve RI better than omeprazole alone. Furthermore, the effects of DB remain more than omeprazole after the end of the treatment.

In the present study, treatment with omeprazole has been shown to improve the FVC and PEF. According to previous studies, PPIs have been shown to improve RI. In a study by Harding et al., 30 patients with asthma after taking omeprazole for 1 month showed a 30% reduction in respiratory symptoms. Those who took omeprazole for 2 months showed a 43% decrease and those who took 3 months of use omeprazole showed a 57% reduction in asthma symptoms (20). Also, Giannikoulis et al. found no improvement in cardiopulmonary exercise test after 12 weeks of the treatment with a double dose of omeprazole (21). The different results may be due to the long usage and refractory period of omeprazole (22). In the present study, we used a single dose of omeprazole, just for eight weeks.

Furthermore, Sakurai et al. stated that the quality of life of patients improved just after a four-week treatment with omeprazole (23). Two studies have also examined the effect of PPIs on the RI and reported improvement in PEF after taking omeprazole. Previous studies have shown

that proper dosage and sufficient time to use PPI medications can improve RI in patients with asthma and reflux. Omeprazole did not increase the DEX of the patients of the present study; thus, researchers guess that decrement of airway tract resistance is the main mechanism of respiratory improvement by taking omeprazole. On the other hand, in a study by Sandur et al., the amount of exposure to esophageal acid was reduced with the use of omeprazole. Also, with increasing dosage, the rate of improvement in the reflux was increased (24).

The other results showed that DB, along with omeprazole improve FEV1, FVC, PEF, and diaphragmatic excursion in patients with reflux. The results of the study by Ford et al. indicated that the decrease in respiratory muscle activity, and in particular the diaphragm, mainly results in respiratory system impairment. Diaphragmatic dysfunction has several causes, one of the most common reasons for this is reflux. Various studies have suggested that laparoscopic abdominal surgery leads to reflux, which is the cause of the phrenic nerve pathway obstruction, leading to a reduction in respiratory depth and pulmonary ventilation (25). Our results are consistent with the results of Tahir et al. They showed that DB led to improved basal ventilation (26). Alaparthi et al. also showed that DB improved tidal volume and elimination of secretions (27). However, Manzano et al. showed that DB improved FVC in the patients. One of the reasons for improving FVC after DB is that patients with reflux can hardly breathe deeply. If they can breathe deeply through DB, this can improve FVC and FEV1, which keeps the lungs and closed alveoli open (28).

Furthermore, four weeks DB improve quality of life, and PPI usage in patients with reflux and follow up treatment group showed a decrease in PPI usage at 9 months (29). At six weeks, follow up of the present study showed significant effects of DB on RI as well. There are various possible reasons for improving RI in DB. Our study showed that DB increased the FEV1, FVC, PEF, and DEX, which is due to the diaphragmatic muscle strengthen. In the control group, only FVC and PEF improved after taking omeprazole. The physiological effects of DB are that breathing through the entire vital capacity and keeping it for 3 to 5 seconds causes the lungs to be completely opened; thus, alveoli with a small volume are kept open and the surfactant is produced in them. The DB also reduces the activity of the accessory muscles, which tends to bring the respiratory pattern closer to normal and reduces respiratory work (29-31). We suggest that future studies examine the effects of the potassium-competitive acid blockers (P-CAB) on reflux that may induce more important effects on RI than omeprazole (32).

5.1. Conclusion

Diaphragmatic breathing can improve respiratory indices and diaphragmatic excursion better than omeprazole in severe reflux patients. Also, the beneficial effects of diaphragmatic breathing remain at least six weeks after the end of the treatment.

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Footnotes

Authors' Contribution: Mehdi Ahmadi and Tahere Rezaeian participated in the design and data collection and writing of the manuscript. Iraj Abdollahi and Mohsen Amiri were Supervisors. Amir Mansoor Rezadoost prescribed the drugs and Enayatollah Bakhshi participated in the statistical analysis of the study. All authors read and approved the final manuscript.

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Conflict of Interests: The authors declare that they have no conflict of interest.

Ethical Approval: IR.USWR.REC.1396.272.

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Informed Consent: Informed consent was obtained from all participants, and the protocol was approved by the Singhealth Centralized Institutional Review Board before the start of the study.

References

1. Ness-Jensen E, Hveem K, El-Serag H, Lagergren J. Lifestyle intervention in gastroesophageal reflux disease. *Clinical gastroenterology and hepatology*. 2016;**14**(2):175–182. e3.
2. Bisaccioni C, Aun MV, Cajuela E, Kalil J, Agondi RC, Giavina-Bianchi P. Comorbidities in severe asthma: frequency of rhinitis, nasal polyposis, gastroesophageal reflux disease, vocal cord dysfunction and bronchiectasis. *Clinics*. 2009;**64**(8):769–73.
3. Nemzek JA, Kim J. Pulmonary inflammation and airway hyperresponsiveness in a mouse model of asthma complicated by acid aspiration. *Comp Med*. 2009;**59**(4):321–30. [PubMed: 19712571]. [PubMed Central: PMC2779206].
4. Cuttitta G, Cibella F, Visconti A, Scichilone N, Bellia V, Bonsignore G. Spontaneous gastroesophageal reflux and airway patency during the night in adult asthmatics. *American journal of respiratory and critical care medicine*. 2000;**161**(1):177–81.

5. Kanda S, Fujimoto K, Komatsu Y, Yasuo M, Hanaoka M, Kubo K. Evaluation of respiratory impedance in asthma and COPD by an impulse oscillation system. *Internal Medicine*. 2010;**49**(1):23–30.
6. Nielsen R, Johannessen A, Benediktsdottir B, Gislason T, Buist AS, Gulsvik A, et al. Present and future costs of COPD in Iceland and Norway: results from the BOLD study. *Eur Respir J*. 2009;**34**(4):850–7. doi: 10.1183/09031936.00166108. [PubMed: 19357148]. [PubMed Central: PMC3334277].
7. Matyasova Z, Novotna B, Matulova M, Dolina J, Kroupa R, Lanikova Z, et al. The relation of GERD, bronchial asthma and the upper respiratory tract. *Vnitrni lekarstvi*. 2005;**51**(12):1341–50.
8. Katz PO, Castell DO, Chen Y, Andersson T, Sostek MB. Intragastric acid suppression and pharmacokinetics of twice-daily esomeprazole: a randomized, three-way crossover study. *Alimentary pharmacology & therapeutics*. 2004;**20**(4):399–406.
9. Ong AM, Chua LT, Khor CJ, Asokkumar R, Wang Y. Diaphragmatic breathing reduces belching and proton pump inhibitor refractory gastroesophageal reflux symptoms. *Clinical Gastroenterology and Hepatology*. 2018;**16**(3):407–416. e2.
10. Sarwal A, Walker FO, Cartwright MS. Neuromuscular ultrasound for evaluation of the diaphragm. *Muscle Nerve*. 2013;**47**(3):319–29. doi: 10.1002/mus.23671. [PubMed: 23382111]. [PubMed Central: PMC3581727].
11. Kassem MM, Wallen JM. *Esophageal Perforation, Rupture, And Tears*. Treasure Island (FL): StatPearls Publishing; 2019.
12. Kahrilas PJ. Medical management of gastroesophageal reflux disease in adults. *UpToDate*. 2013.
13. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J*. 2005;**26**(2):319–38. doi: 10.1183/09031936.05.00034805. [PubMed: 16055882].
14. Moore VC. Spirometry: step by step. *Breathe*. 2012;**8**(3):232–40.
15. Cohen E, Mier A, Heywood P, Murphy K, Boultbee J, Guz A. Excursion-volume relation of the right hemidiaphragm measured by ultrasonography and respiratory airflow measurements. *Thorax*. 1994;**49**(9):885–9.
16. Lee AL, Goldstein RS. Gastroesophageal reflux disease in COPD: links and risks. *International journal of chronic obstructive pulmonary disease*. 2015;**10**:1935.
17. Özdemir P, Erdinç M, Vardar R, Veral A, Akyıldız S, Özdemir Ö, et al. The role of microaspiration in the pathogenesis of gastroesophageal reflux-related chronic cough. *Journal of neurogastroenterology and motility*. 2017;**23**(1):41.
18. Akyüz F, Mutluay Soyer Ö. Which diseases are risk factors for developing gastroesophageal reflux disease. *Turk J Gastroenterol*. 2017;**28**(Suppl 1):S44–7.
19. Sweet MP, Patti MG, Hoopes C, Hays SR, Golden JA. Gastro-oesophageal reflux and aspiration in patients with advanced lung disease. *Thorax*. 2009;**64**(2):167–73. doi: 10.1136/thx.2007.082719.
20. Harding SM, Guzzo MR, Schan CA, Alexander RW, Bradley LA, et al. Asthma and gastroesophageal reflux: Acidsuppressive therapy improves asthma outcome. *Am J Med*. 1996;(100):395–405.
21. Giannikoulis C, Karkoulias K, Thomopoulos K, Marangos M, Spiropoulos K, Nikolopoulou V. Patients with gastroesophageal reflux disease and respiratory manifestations do not present lung function disorders during cardiopulmonary exercise test. *Dis Esophagus*. 2011;**24**(3):189–93. doi: 10.1111/j.1442-2050.2010.01109.x. [PubMed: 21040148].
22. Takeuchi T, Oota K, Harada S, Edogawa S, Kojima Y, Sanomura M, et al. Characteristics of refractory gastroesophageal reflux disease (GERD) symptoms -is switching proton pump inhibitors based on the patient's CYP2C19 genotype an effective management strategy? *Intern Med*. 2015;**54**(2):97–105. doi: 10.2169/internalmedicine.54.3412. [PubMed: 25742999].
23. Sakurai K, Suda H, Fujie S, Takeichi T, Okuda A, Murao T, et al. Short-Term Symptomatic Relief in Gastroesophageal Reflux Disease: A Comparative Study of Esomeprazole and Vonoprazan. *Dig Dis Sci*. 2019;**64**(3):815–22. doi: 10.1007/s10620-018-5365-0. [PubMed: 30415407]. [PubMed Central: PMC6440932].
24. Sandur V, Murugesh M, Banait V, Rathi P, Bhatia S, Joshi J, et al. Prevalence of gastro-esophageal reflux disease in patients with difficult to control asthma and effect of proton pump inhibitor therapy on asthma symptoms, reflux symptoms, pulmonary function and requirement for asthma medications. *Journal of Postgraduate Medicine*. 2014;**60**(3):282–6. doi: 10.4103/0022-3859.138754.
25. Ford GA, Prior JS, Butland RJ, Wilkinson SP. Omeprazole in the treatment of asthmatics with nocturnal symptoms and gastro-oesophageal reflux: A placebo-controlled cross-over study. *Postgrad Med J*. 1994;(70):350–4.
26. Tahir AH, George RB, Weill H, Adriani J. Effects of abdominal surgery upon diaphragmatic function and regional ventilation. *International surgery*. 1973;**58**(5):337.
27. Alaparthi GK, Augustine AJ, Anand R, Mahale A. Comparison of diaphragmatic breathing exercise, volume and flow incentive spirometry, on diaphragm excursion and pulmonary function in patients undergoing laparoscopic surgery: a randomized controlled trial. *Minimally invasive surgery*. 2016;**2016**.
28. Manzano RM, Carvalho CRFD, Saraiva-Romanholo BM, Vieira JE. Chest physiotherapy during immediate postoperative period among patients undergoing upper abdominal surgery: randomized clinical trial. *Sao Paulo Medical Journal*. 2008;**126**(5):269–73.
29. Eherer AJ, Netolitzky F, Hogenauer C, Puschnig G, Hinterleitner TA, Scheidl S, et al. Positive effect of abdominal breathing exercise on gastroesophageal reflux disease: a randomized, controlled study. *Am J Gastroenterol*. 2012;**107**(3):372–8. doi: 10.1038/ajg.2011.420. [PubMed: 22146488].
30. Chitkara DK, Van Tilburg M, Whitehead WE, Talley NJ. Teaching diaphragmatic breathing for rumination syndrome. *The American journal of gastroenterology*. 2006;**101**(11):2449.
31. Halland M, Parthasarathy G, Bharucha AE, Katzka DA. Diaphragmatic breathing for rumination syndrome: efficacy and mechanisms of action. *Neurogastroenterology & Motility*. 2016;**28**(3):384–91.
32. Roman S, Mion F. Refractory GERD, beyond proton pump inhibitors. *Curr Opin Pharmacol*. 2018;**43**:99–103. doi: 10.1016/j.coph.2018.09.001. [PubMed: 30240968].