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Clinical features of gastroesophageal reflux disease which is combined with goiter

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Abstract

The study involved 40 patients with GERD in combination with goiter. This pathology was more frequently diagnosed in women as compared to men. The specific feature of clinical picture of GERD in combination with goiter was prevalence of other than esophageal symptoms and syndromes. Manifestations of esophago-cardiac syndrome in the form of tachyarrhythmia and extrasystole were diagnosed in 47,5% of cases, esophago-pulmonary in 65,2%, oropharyngeal in 72,5% of cases. Therefore, there were detected essential disorders of sleep quality and structure in patients of both groups. By endoscopic examination of the esophagus in case of combined pathology, the most frequently were detected injuries of the lower third of the esophagus of C and D degrees. Among peculiarities of the stomach motor-evacuation function disorder in patients with mentioned combined pathology - continuation of evacuation period of food from the stomach into duodenum with pH $3,12 \pm 0,15$ was $95,22 \pm 4,74$, it was prevalence of hypotonic variant

Keywords: gastroesophageal reflux disease, goiter, iodine deficiency conditions, thyroid

1. Introduction

Gastroesophageal reflux disease (GERD) is one of the most popular diseases in the XXI century. During the last two decades, when GERD was defined by symptoms of at least weekly heartburn and/or acid regurgitation it's prevalence in the western population generally ranges from 10 to 20% with a growing tendency whereas in Eastern countries its rates less than 5% [7]. A bit less (13% of the population) it is registered in China. Most clearly this dynamics is observed in the USA, where overweight and obesity are growing among population, which are GERD risk factors [1,10]. Unfortunately, this pathology is not well studied in Ukraine, and is rarely to be diagnosed as people suffering from this disease are not even aware of reflux and its treatment. During treatment patients get better, but after stop taking medication their condition is getting worse again and the lower esophageal sphincter is losing its elasticity and ability to close completely. Permanent acid and alkaline esophageal refluxes influence on peoples sleep and activity during the day, constant cough and scratchy throat cause discomfort [3, 6]. GERD can cause complications such as stricture of the esophagus, bleeding and Barrett's esophagus, which is considered to be a precancerous condition [2]. The reason for delayed diagnosis of GERD are extra esophageal masks, monosymptomatic course of the disease, lack of attention to this pathology by doctors.

It is known that major symptoms of GERD are heartburn, regurgitation, belching, chest pain, dysphagia, increased salivation. Extraesophageal symptoms such as feeling of dryness and scratchy throat, hoarseness, difficulty in swallowing are also important in the clinical picture of GERD [15]. There are oropharyngeal, respiratory, cardiac and pseudo cardiac masks of extra esophageal GERD symptoms and syndromes. However, these symptoms may be specific to patients with thyroid disorders [5, 8].

Comorbidity of GERD and iodine deficiency conditions is not limited by similar clinical symptoms. Pathological hormonal influence of the thyroid gland functioning on the background of iodine deficiency plays an important role in the regulatory mechanisms of the upper gastrointestinal tract motility [4, 9]. Combination of GERD with thyroid diseases is very interesting, especially in areas with high levels of iodine deficiency diseases [14]. According to the authors data it is detected in 9.3% of cases. The prevalence of iodine deficiency conditions in the world ranges from 1.3 to 10.3%. This pathology is growing every year among the population of Ukraine and is 170.4 cases per 100 thousand of population. That's why problem of studying the pathological mechanisms, clinical picture and new approaches to the treatment of such combined pathology becomes significant.

Therefore, combination of GERD with thyroid disorders needs extremely important clinical evaluation, non-invasive methods of diagnosis and rationale approach to its treatment.

Material and Methods

The study involved 40 patients with GERD in combination with goiter who were treated at the University Clinic of Ivano-Frankivsk National Medical University. The initial diagnosis of GERD was based on the patient's history or on the responses to a questionnaire, on the results of a detailed assessment of the clinical picture, endoscopic study of esophagus, stomach and duodenum using apparatus company "Olympus" GIF-XPE, 24-hour pH monitoring of the lower part of the esophagus by apparatus "ar-1rN-M", ultrasound of abdominal cavity organs by apparatus "MyLab™50", X-ray of the stomach.

By endoscopy, all the study subjects were diagnosed as reflux esophagitis (RE) (+) or RE(-) subjects according to the Los Angeles classification [11]. RE was defined as the presence of mucosal breaks: grade A, -B, -C, or -D based on the Los Angeles classification. For patients who had GERD symptoms more than 10 years Lugol chromoendoscopy was conducted [12]. When Lugol-unstained streaks were observed at chromoendoscopy, biopsy specimens were obtained from unstained streaks and from adjacent stained mucosa.

Goiter (GT) in patients with GERD was diagnosed and classified according to WHO recommendations, following the standards of diagnosis and treatment of thyroid dysfunction [16]. Goiter was confirmed on the basis of anamnesis of the disease, palpation, ultrasound examination of the thyroid gland and the determination of the thyroid hormonal status.

The diagnosis of GERD was confirmed by the results of a detailed evaluation of the clinical picture using the Re Quest questionnaire. This system evaluates the frequency and severity of clinical symptoms, as well as the effectiveness of treatment. It helped to divide clinical symptoms to 6 groups: 1) acid complaints, 2) symptoms associated with the upper gastrointestinal tract (epigastric sense of overcrowding, etc.), 3) symptoms associated with the lower gastrointestinal tract (constipation, flatulence, and others.), 4) nausea, 5) sleep disorders, 6) general health violations. We also determined extra-esophageal symptoms (cardiac, bronchopulmonary, laryngopharyngeal, dental). Patients described the severity of complaints assessing the intensity of symptoms ranging from 0 to 4 points (0 - absence of particular symptom, 1 - slightly expressed, 2 - moderately expressed, 3 - expressed, 4 - aggressively expressed). The assessment of general well-being could vary from "excellent" (0) to "very bad" (4).

Quality of patients life was determined by the nature of sleep evaluation by using Pittsburg Sleep Quality Index (PSQI). Which was developed and patented by the scientists of the University of Pittsburgh in 1989 [13].

The Data were collected and entered into the personal computer. Statistical analysis were done using Windows software program Microsoft Excel 2010, Statistica 8. Arithmetic mean, standard deviation for categorized parameters, chi-square test was used while for numerical data, t-test was used to compare two groups. The level of significance was 0.05. Also to determine the reliability of the data was used Spearman's correlation test.

Results and Discussion

GERD in combination with goiter is in fact more frequently diagnosed in women (82, 5%) as compared to men (17, 5%).

The age of patients varied from 19 to 73 years and average age was (51,23±1,96) years. The patients were divided into different age groups based on the standard quality age periods recommended by WHO expert committee: young age (16-29 years), middle age (30-44 years), mature age (45-59 years) and senior age (60-74 years). According to the data of Table 2.2., GERD in combination with goiter (GERD+GT) was observed in 35% of middle age patients and 37,5% of mature age patients. The proportion of women with GERD+GT in the age group of 45-54 prevailed essentially and was 32,5%. In 65% of patients with GERD+GT the duration of diseases was from 5 to 10 years and mean duration was (8,19±1,12) years. The most frequently GERD+GT was diagnosed in patients of middle age group and lasted 5-10 years. Frequently enough, such combined pathology would lead to hospitalization of patients of mature (37,5%) and senior (12,5%) age.

Thus, GERD in combination with goiter is observed more frequently in persons of middle and senior age which is a problem of not only working age, but also a social problem.

Clinical characteristics of GERD+GT are presented in Table 1.

Permanent heartburn during the day time disturbed only 10% of patients with GERD on the background of GT. However, prevalence of symptom during the night time took place in 30% of patients. The origin of this symptom more than twice per week was recorded in 27, 7% of patients. But, in 42, 5% of patients with development of GERD+GT the heartburn was not a principal clinical symptom. In case of GERD+GT, there was observed a tendency towards reduction of heartburn frequency with aging of patients: young age – 66, 67%, middle age – 57, 17%, mature age – 20% (and complete absence in persons of senior age (after 60 years of age). Therefore, in case of GERD+GT combination, the classical pathognomic complain - heartburn in a part of patients, especially those of senior age and in case of durable course of the disease, was not a steady symptom that would complicate diagnostics and contribute to tardy and inefficient treatment of patients.

Pain in the lower third of the posterior sternum zone more than twice per week used to disturb one third of patients. Only 15% of patients pinpointed the episodes of painful sensation during the night time that would combine with heartburn. In patients with GERD+GT, absence of pain syndrome was more frequent than in one third of the examined patients.

Among other typical symptoms, more frequent were complains of dysphagia (77, 5%), odynophagia (62, 5%), regurgitation and belching (47, 5%), nausea (30%).

Clinical characteristics of extraesophageal manifestations of GERD + GT are presented in the table. 2

We have not observed specific clinical signs in some patients, however, there took place another complains that were analyzed as other than esophageal symptoms caused by GERD. Atypical complains (cardialgia, tachycardia, extra systole, difficult swallowing, hoarseness, throat irritation, coughing and dry cough attacks in the morning, episodes of night apnea and snoring and so on) were dominant in the clinical picture of GERD+GT. In particular, almost half of patients had manifestations of the cardiac syndrome – 47, 5%. The most frequently the patients were disturbed by "cardialgia" which they erroneously would consider as angina attacks and cardiac dysfunction, especially during the night time. The mentioned symptoms would also appear in case of heartburn aggravation and other complains typical for GERD. Normally, the patients of this group would present complains of cough, dry morning cough – 72,5% and short breath and

snoring while sleeping – 62,5%. In the clinical picture of patients with combined GERD+GT an important place was taken by oropharyngeal syndrome. Most of patients would point to hoarseness – 77, 5%, and throat irritation – 70%. More than half (60%) of patients emphasized the need of frequent dentist visits. The pathological changes of oral cavity included equally frequently both dental and soft tissues injuries (red ring around lips, mucous membrane of oral cavity, tongue, parodontium). The patients visited dentist for the reason of caries accompanied by halitosis, dental erosions, ulcerative stomatitis.

Thus, in case of combined GERD+GT, the clinical picture was covert with atypical complaints that in series.

Characteristics of sleep disorders in patients with gastroesophageal reflux disease in combination with goiter is presented in Table 3

The sleep is an integrative indicator of patient’s condition, reflection of numerous exogenic and endogenic factors (age, sex, individual peculiarities, condition of vegetative nervous and endocrine systems and so on). Normally, presence of diseases may significantly influence the sleep quality, and affirm evaluation of health condition and life quality. 57, 5% of patients with GERD+GT noted difficulties in falling asleep (more than 30 minutes). Only one third of them (25%) had a good sleep and would not wake up at night time during the week. The patients named heartburn and pain as a reason of waking up at night. Half of patients (50%) complained of snoring or other signs of sleep apnea (52, 5%), and 77,5% of patients evaluated the sleep quality during the last week as bad or unsatisfactory. As a rule, the reason of sleep disorder was pain in the lower third of the posterior sternum and epigastrium, often in combination with night heartburn, feeling of heat posterior the sternum. In order to reduce the night symptoms, 72, 5% of the examined patients had to take a forced position, slept semi-sitting or on the high pillows. Some patients used to consume food, drink water and use baking soda for reduction of sleep disorder. According to PSQI questionnaire data, the average daily time of falling asleep was two hours (from 22⁰⁰ to 24⁰⁰), patients used to spend average of 78, 94±7,740 minutes (from 15 minutes to 4,5 hours), time of morning waking up was 5,04±0,48 hours (from 03⁰⁰ to 07⁰⁰), total quantity of real sleep per night was 4,45±0,29 hours (from 2,4 to 7 hours per night).

Therefore, there were detected essential disorders of sleep quality and structure in patients with isolated GERD and GERD+GT. In case of combined GERD+GT pathology, typical for GERD complains quite frequently were hidden behind the clinical manifestations of the thyroid disease.

The final confirmation of GERD should be based on satisfactory objective criteria that would complement the results of clinical symptoms and syndromes evaluation, and one of such methods is esophagogastroduodenoscopy. All the supervised patients underwent the procedures of endoscopy of the upper part of gastrointestinal tract and chromoendoscopy using Lugol’s solution as a coloring agent that confirmed changes of mucous membrane of the esophagus. They manifested through focal or diffuse erythema and erosive defects located on the folders’ top. According to Los-Angeles endoscopic GERD classification, the reflux-esophagitis of A degree was diagnosed in 7,5% in case of combination of main disease with GT. Injury of mucous membrane of the esophagus of B degree was detected in 22,5% patients, the reflux-esophagitis of C degree – in 47,5% and of D degree – in 22,5% of patients.

Comparison of reflux origin with subjective feelings of patients based on evaluation of symptoms index after G.J. Weiner *et al.* is also of clinical significance. Symptom index is quantity of symptoms in percentage, and reflects the ratio of symptoms that originate during the periods of gastroesophageal reflux (during 5 minutes after refluxate falling into esophagus) to total quantity of symptoms per day. One of faults of endoscopic method of GERD diagnostics is existence of endoscopically negative form and impossibility of evaluation of frequency, duration and nature of physiological and pathological refluxes into the esophagus. Daily measurement of pH of the lower third of the esophagus can evaluate the indicated reflux parameters and is considered as a “gold standard”. We used the DeMeester scale for evaluation of results of daily measurement of pH. We have taken into account the main characteristics of intensity of refluxes and esophageal clearance for the period of 24 hours (number of reflux episodes, their duration, connection with the periods of the day, position of the body). As a result of realized daily measurement of pH, it has been established that in case of GERD+GT combination 70% had mixed, and only 30% had acid refluxes.

In patients with GERD+GT, the tolerance of symptoms (<25%) to the episodes of gastroesophageal reflux was related only to the pathological conditions of oral cavity (24,82±1,07)%. Clinically valid was dependency of nausea (76,64±5,52)%, dyssomnia (79,58±5,54)%, cough and other manifestations of bronchopulmonary (73,48±5,53)% and oropharyngeal (92,72±6,14)% syndromes on refluxes with alkaline content. Increase of dependency between emergence of mixed refluxes and other than esophageal symptoms of GERD, causes hypodiagnostics and incorrect strategy of patient management.

Study of the condition of motor-evacuation function of the stomach was performed using 13C-octane acid breath test, calculation of the period of stomach solid food elimination half-time (T ½) and evacuation coefficient (GEC). In case of GERD+GT combination, there took place stomach motor-evacuation function disorder with prevalence of mixed refluxes – T ½ (95,22±4,74) min, and GEC index (3,12±0,1).

Table 1: Clinical characteristics of patients with gastroesophageal reflux disease which is combined with goiter

	Patients with GERD + GT n=40	
	n	%
Heartburn worries :		
– no	9	22,50
– 1-2 times a week	16	40
– > 2 times a week	11	27,7
– always during a day	4	10
– always at night	12	30
Pain worries :		
– no	14	35
– 1-2 times a week	12	30
– > 2 times a week	12	30
– always during a day	2	5
– at night	6	15
Regurgitation, vomiting	19	47,5
Heartburn of the tongue	3	7,5
Dysphagia	31	77,5
Nausea	12	30
Hypersalivation	5	12,5
Odinophagia	25	62,5

Table 2: Characteristics of extraesophageal manifestations of gastroesophageal reflux disease in the examined patients in combination with goiter

	Patients with GERD + GT n=40	
	n	%
Tachycardia, extrasystole, cardialgia (cardiac syndrome)	19	47,5
Morning cough, bronchospasm attacks, breathlessness	29	72,5
Night dyspnea (bronchopulmonary syndrome)	25	62,5
Hoarseness of voice	31	77,5
Sore throat, foreign body sensation (Oropharyngeal syndrome)	28	70
Caries, periodontal disease, frequent dental visits (dental syndrome)	24	60

Table 3: Sleep disorders in patients with gastroesophageal reflux disease in combination with goiter using questionnaire PSQI (n=40)

Formulation	Not observed		Less than 1 t / week		1-2 t / week		3 and > t / week	
	n	%	n	%	n	%	n	%
Sleep > 30 min	2	5	8	20	18	45	12	12,5
Awakening at night	6	15	8	20	16	40	10	25
The need for a toilet at night	7	17,5	6	15	15	37,5	12	12,5
Cough or snore	6	15	6	15	16	40	12	12,5
Feeling cold	8	20	21	52,5	6	15	5	12,5
Feeling hot	16	40	16	40	5	12,5	3	7,5
Bad dreams	5	12,5	5	12,5	14	35	16	40
Pain under the sternum	15	37,5	7	17,5	10	25	8	20
Sleep quality for the last week	good		not bad		bad		unsatisfactory	
	5	12,5	4	10	17	42,5	14	35

Table 4: Symptomatic index (%) based on the results of a comparison of daily pH monitoring of the esophagus in patients with gastroesophageal reflux disease and gastroesophageal reflux disease combined with goiter

Symptom	Patients with GERD+GT (n=40)
Pain in the lower part of the esophagus	52,85±2,36
Regurgitation	59,48±3,27
Heartburn of the tongue	52,80±3,85
Dysphagia	59,57±4,27
Nausea	76,64±5,52
Hypersalivation	39,78±2,18
Sleep disorders	79,58±5,54
Cardiac syndrome	86,48±4,72
Bronchopulmonary syndrome	73,48±5,53
Oropharyngeal syndrome	92,72±6,14
Dental syndrome	24,82±1,07

Conclusions

1. The specific feature of clinical picture of gastroesophageal reflux disease in combination with goiter is prevalence of other than esophageal symptoms and syndromes. Manifestations of esophago-cardiac syndrome in the form of tachyarrhythmia and extrasystole were diagnosed in 47,5% of cases, esophago-pulmonary (dry cough, predominantly during morning hours, short breath attacks, snoring during the sleep) – in 65,2%, oropharyngeal (hoarseness, throat irritation) – in 72,5% of cases. Heartburn, as a pathognomic symptom of gastroesophageal reflux disease was reported only by 46,15% of patients, and pain of different intensity in the lower third of the sternum was reported by 75% of patients with combined pathology.
2. Based on the results of endoscopic examination of the esophagus in case of GERD+GT combined pathology, the most frequently were detected injuries of the lower third of the esophagus of C and D degrees in 47,5% and 22,5% of patients respectively.
3. Patients with GERD+GT had average pH value of the

lower third of the esophagus 3,12±0,08 based on the data of 24 hours monitoring, time of its maintenance below 4,0 was 58,85±2,29 minutes, and average quantity of episodes of durable acid regurgitation was in 15,17±0,14 cases. The episodes of alkaline refluxes (pH>7,0) were 68,28±0,38 minutes. Among peculiarities of the stomach motor-evacuation function disorder in patients with mentioned combined pathology - continuation of evacuation period of food from the stomach into duodenum, respectively with pH 3,12±0,15 (in healthy people – 3,97±0,03) and T ½ - 95,22±4,74 (in healthy people – 64,69±2,17), that is prevalence of hypotonic variant.

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