

EPIDEMIOLOGICAL SURVEY TO DESCRIBE THE IMPACT OF REFLUX DISEASE ON EVERYDAY LIFE IN GERD PATIENTS BEFORE AND AFTER 4 WEEKS TREATMENT

Abstract

Methods: This is a multi-center, non-intervene epidemiological survey using GERD Impact Scale (GIS) to compare the changes of frequency and impacts of symptoms on patient daily activities after 4-week treatments.

2,055 eligible GERD outpatients were enrolled for a 4-week treatment course.

Results: A total of 1,564 patients with sufficient data were analyzed. Generally, the disease is well controlled after 4 weeks of treatment. The rate of “very well controlled” increases by 10.9%, “very poorly controlled” decreases by 60.9%. The frequency of symptoms declines 62.7 – 70.7%. Treatments with PPIs, antacids, antiH2, pro-kinetics and life modification increase the rate of the controlled, of which the PPI (monotherapy and combination by antacids) is the most effective. Physician’s assessment on frequency and impacts of GERD symptoms is lower than that of patients.

Background and rationale

Gastroesophageal reflux disease (GERD) is one of the most prevalent gastrointestinal disorders with 10 to 20% of Western populations affected by at least weekly typical GERD symptoms (heartburn and/or regurgitation) (1-4). GERD symptoms are also a common reason for consulting in the primary care setting (5-9) and account for an increased workload in health care visits to primary care physicians (PCPs) and specialists (10). In addition to the typical symptoms of heartburn and regurgitation, GERD is associated with a range of extra-esophageal and atypical symptoms (11-18). A recent prospective survey has estimated the prevalence of asthma (4,8%), chronic cough (13%) and hoarseness (10,4%) in GERD patients (13). Around 40-50% of patients with GERD have also dyspeptic symptoms (15-18). Reflux esophagitis is significantly increasing in Asia countries with the prevalence of 3.9% in 1992 to 9.8% in 2001. A recent epidemiological survey in Hong Kong reveal that 631 out of 16,606 people interviewed (3.8%) have endoscopic esophagitis (19). The impact of these symptoms and the consequences on the everyday lives of patients with GERD are often overlooked (20).

Since symptoms occurring at least once a week adversely affect quality of life (HRQoL) (21) and because non-erosive reflux disease (NERD) is the most prevalent form of GERD (22), emphasis has been placed in the last decade on the relief of symptoms as the primary endpoint of therapy for the majority of patients. GERD, however, can also be associated with more severe lesions and complications (22).

In daily clinical practice, both the decision to treat and the type of treatment are determined by clinical judgment based generally on symptoms alone (23). However, there is a lack of agreement between doctors and patients in their relative assessment of the severity of reflux symptoms, with doctors most often underestimating symptom severity (24,25) and the impact of GERD on HRQoL (21). Because it is the doctor's assessment of the severity of disease that drives the choice of treatment, this may explain why many patients with heartburn are not effectively treated.

Given the impact of GERD on HRQoL, asking patients about the impact of their reflux symptoms may be useful during the diagnosis of GERD (21). Many patients are reluctant to

discuss the full impact of their symptoms on their everyday lives and, in the absence of appropriate questioning by the physician, an inadequate picture may emerge (25). This can hinder appropriate management and result in potentially sub-optimal treatment (26).

This has led to proposals for improving physician-patient communication and developing tools to better assess the symptoms (24-29). One of the tools is the GERD Impact Scale (GIS) (27-30). GIS is a single-sheet questionnaire asking patients with GERD about the impact of their symptoms and how these affect their daily life. The patients answer questions about the frequency of their reflux symptoms and about the effects on their work, sleep, diet and social life. It has been validated in a survey including 205 patients, that were recently or previously diagnosed with GERD, managed by PC physicians (29). In total, 77% of primary care physicians in the survey reported that the GIS was a source of information that was useful to adopt, in order to make therapeutic decisions (29).

Those are the reasons to conduct the survey in order to describe the change of the impact of reflux symptoms on the everyday life and the frequency of GERD symptoms perceived by patients before and after 4-weeks treatment by using the GIS in Vietnamese population.

METHODS

Patient selection:

Study subjects are outpatients aged 18 or older, already or recently diagnosed GERD by clinical symptoms, endoscopy. These patients are prescribed with PPIs, antacide, anti H2, pro-kinetics or a combination for 4 weeks at the first visit, then come back for the second visit after that.

Patients unable to read and understand the GIS or having a history or suspected symptoms of peptic ulcer, cancer, severe or malignant diseases (anorexia, weight loss, anemia, fever..) are excluded.

Sample size determined is 2,055 subjects to find out the 1% difference of the rate of symptoms between before and after a 4 week treatment with significant level of 0.05, power 90% and estimated rate of patient left the study of 20%.

Study design:

This is a multi-center, non-intervene epidemiological study. Data is collected at two visits 4 weeks apart. At each visit, patients were provided with the GIS for their filling in prior to doctor's clinical assessment.

Physician will complete the patient record form based on medical history obtained from patients and their clinical assessment, then in turns provide treatments for patients upon available information.

Patient assessment:

Study instruments are GERD Impact Scale (GIS) completed by patients and Patient Record Form (symptoms, diagnosis and treatment) completed by physicians.

Impact of GERD on everyday life of the patient based on GIS (GERD Impact Scale) is assessed as bellows:

- *Very well controlled* – all ticks in the “never” box
- *Fairly well controlled* – all but 3 ticks in the “never” box
- *Uncontrolled* –more than 3 ticks outside the “never” box
- *Poorly controlled* –more than 5 ticks outside the “never” box
- *Very poorly controlled* – no ticks in the “never” box

To quantify the severity of symptoms and impacts, their frequency is coded as follow.

Happen daily:	3 points
often:	2 points
sometimes:	1 point
never:	0 point

Statistic analysis:

The statistical analysis will be performed from two standpoints, a descriptive and comparative. In descriptive analysis for continuous variables, the arithmetic mean, standard deviation, median, minimum and maximum interquartile range will be provided. For categorical variables, absolute and relative frequencies will be provided. The frequency and severity of symptoms, medicine use will be analyzed using Chi squared test. The significant level is 0.05.

RESULTS

1. Subject characteristics:

Data of 1,564 patients (83.6%) is used for per protocol analysis, of which 710 male (45%), with age mean is 45 years and 854 female (55%) with age mean 43 years were included. 822 patients were tested for H. Pylori, of which 409 (47%) were positive. Mean BMI is 22.2 (72.5% lower 23, not overweight). There are 343 current smokers (22.1%) and 160 patients used to smoke (10.3%).

123 (7.9%) patients are already diagnosed GERD, time mean to diagnose is 13.1 months.

1441 (92.1%) patients are initially diagnosed GERD at this time by following methods:

Endoscopy:	740	(47.3%)
Clinical symptoms:	697	(44.6%)
Other:	4	(0.3%)

99 patients have alarming symptoms such as dysphagia, odynophagia, anemia, digestive bleeding, weight loss (12.9%)

At first visit, patients were treated with:

PPI	378	(24%)
Antacide	233	(15%)
Anti H2	131	(8%)
Pro-kinetics	116	(7%)
Combination (PPI, antacide)	403	(26%)
Life modification	303	(19%)

2. Changes of impact of reflux symptoms on the everyday life before and after 4 weeks

<i>Classification</i>	<i>Visit 1 (N, %)</i>	<i>Visit 2 (N, %)</i>	<i>p</i>
Very well	0	170 (10.9)	< 0.001
Fairly well	38 (2.4)	522 (33.4)	< 0.001
Uncontrolled	89 (5.7)	308 (19.7)	< 0.001
Poor	247 (15.8)	326 (20.8)	0.001
Very poor	1.190 (76.1)	238 (15.2)	< 0.001
Total	1.564	1.564	

Table 2. Comparison of the rate of "NEVER" of symptoms between before and after

treatment (%)			
Symptoms	Visit 1	Visit 1	p-value
Pain in the chest or behind the sternum	18.9	52.0	<0.0001
Feeling of burning in the chest or behind the sternum	12.2	46.9	<0.0001
Regurgitations or acid taste in the mouth	14.2	52.2	<0.0001
Pain or burning in the upper stomach	13.1	54.3	<0.0001
Sore throat or hoarseness related to heartburn or acid reflux	39.2	77.2	<0.0001
How often did you have problems to sleep well at night due to the symptoms?	21.1	63.2	<0.0001
How often did the symptoms prevent you from eating or drinking something you like?	27.0	42.6	<0.0001
How often did the symptoms prevent you from being completely productive at work or in your daily life activities?	18.6	61.0	<0.0001
How often did you take some additional medicine other than indicated by your doctor (such as Maalox ®, Phosphalugel®)?	60.7	86.6	<0.0001

	<i>Visit 1</i>	<i>Visit 2</i>	% decrease	<i>p</i>
GERD symptoms	1.5	0.56	62.7	< 0.001
Sleep disorders	1.7	0.61	64.1	< 0.001
Eating limitation	1.6	0.55	65.6	< 0.001
Work limitations	1.67	0.54	67.7	< 0.001
Additional medicine use	0.99	0.29	70.7	< 0.001

3. Change of impact of reflux symptoms on the everyday life after 4 weeks by treatments

Life modification	22 (7%)	P < 0.001
PPIs	45 (12%)	P < 0.001
Antacide	24 (10%)	P < 0.001
AntiH2	12 (9%)	P < 0.001
Pro-kinetics	11 (9%)	P < 0.001
Combination (PPI, antacide)	56 (14%)	P < 0.001

Generally compared, the rate of “very well controlled” is not significantly different between treatment groups ($p = 0.201$). However, in comparison with “life modification”, the rate of “very well controlled” among patients treated with PPIs (monotherapy and combination with antacide) is statistically significant different ($p = 0.002$ and $p = 0.014$ in sequence).

Treatments with antacide, anti H2 and pro-kinetics give no significant difference to life modification.

Table 5. Comparison of the rate of “very well controlled” among patients treated with medicines with that of patients with life modification

	OR	CI	P
Combination (PPI, antacide)	1.9	1.1 – 3.4	0.01 *
PPI	1.6	0.9 – 2.9	0.05 *
Antacide	1.4	0.7 – 2.7	0.25
Anti H2	1.3	0.6 – 2.7	0.53
Pro-kinetics	1.3	0.6 – 2.9	0.49

4. Frequency of GERD symptoms by treatments

Table 6. Comparison of change in rate of “NEVER” of symptoms after 4 week treatment by treatment (%)

Symptoms	Combination (PPI, antacide)	PPI	Antacide	Anti H2	Pro-kinetics	Life modification
Pain in the chest or behind the sternum	34.3	30.8	24.1	18.4	25	18
Feeling of burning in the chest or behind the sternum	35.1	31.2	27.7	31.5	19.5	20.2
Regurgitations or acid taste in the mouth	36.2	34.7	25.6	15.8	28.5	16.3
Pain or burning in the upper stomach	34.5	37.7	25.9	23.7	26.7	22.4
Sore throat or hoarseness related to heartburn or acid reflux	38.6	37.3	32.7	34.3	28.8	27.6
How often did you have problems to sleep well at night due to the symptoms?	36.2	39.7	26.1	7.9	34	20.4
How often did the symptoms prevent you from eating or drinking something you like?	10.5	12.2	1.7	7.9	11.4	8.4
How often did the symptoms prevent you from being completely productive at work or in your daily life activities?	34.8	38.7	31	21	32.7	23.6
How often did you take some additional medicine other than indicated by your doctor (such as	30.7	26.6	25.2	26.3	22.1	20.1

Maalox ®, Phosphalugel®)?						
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The rate of patients “NEVER” having symptoms increases in all symptoms and all kind of treatments. However, treatments with PPIs (monotherapy or combined with antacide) give much better improvement.

5. Concordance in GERD symptom assessment between patients and physicians

Table 7. Comparison of rate of “daily” of symptoms between patients and physicians at visit 1 (%)

	Patients	Physicians	Difference (%)	p
Chest pain	21	18.6	- 2.4	0.02
Heart burn	31.3	20.7	- 10.6	< 0.001
Acid regurgitation	30.2	19.5	- 10.7	< 0.001
Sore throat or hoarseness	8.7	10.4	+ 1.7	0.01
Sleep disorders	16.3	9.7	- 6.6	< 0.001
visit 2 (%)				
Chest pain	0.8	1.3	+ 0.5	0.013
Heart burn	0.6	1	+ 0.4	0.02
Acid regurgitation	0.8	1.3	+ 0.5	0.013
Sore throat or hoarseness	0.6	1.7	+ 1.3	< 0.001
Sleep disorders	1.6	1.7	+ 0.1	0.376

DISCUSSION

1. Diagnosis methods

The Montreal Consensus recommends that gastroesophageal endoscopy should be applied for patients at age 50 or older or having alarm symptoms because of having no lesion evidence on gastroesophageal membrane on endoscopy in many cases. Therefore, history and clinical symptoms are main evidence to make diagnosis of GERD. In this study, while there was only 2.9% patients have alarm symptoms, 47.3% of GERD patients were diagnosed by gastroesophageal endoscopy was really high.

2. Treatment effectiveness

Similar to other studies, PPIs are the first-line medication for GERD patients in attack and maintenance phases as well. In this study, 4 week treatment of PPIs (monotherapy or combined with antacide) gives a good effectiveness. This result is similar to the recommendations of the Montreal Consensus on GERD diagnosis and treatment. However, among PPIs, no one was predominant in improving GERD symptoms. Similarly, there is no special combination model of PPIs and antacide that is exceed to others found in this study.

3. Concordance in GERD symptom assessment between patients and physicians

At the first visit, physicians recorded the frequency of symptoms much lower than that of patient’s statement.

Chest pain, sore throat and hoarseness were well noticed by clinicians that results in not significant difference between patient and physician assessment. Conversely, assessment of heart burn, acid regurgitation and sleep disorders was significantly different among those mentioned above.

Additionally, there was not much different in symptom assessment between patients and physicians at the second visit. One explanation could be that GIS may help physicians pay more attention to history, patient complains in finding symptoms and their impacts.

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