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Running head: Symptoms of posterior laryngitis

Posterior laryngitis: A Study of Persisting Symptoms and Health-Related Quality of Life

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Abstract

Objectives. Posterior laryngitis is a common cause of chronic cough, hoarseness, voice fatigue and throat pain. The aim of the present study was to examine how patients with posterior laryngitis have been examined, treated and followed up, and to assess their present health-related quality of life (HRQOL).

Methods. Patients treated for posterior laryngitis at consultation at the Ear-, Nose- and Throat (ENT) clinic during 2000-2008 were contacted by mail. The letter contained questionnaires addressing the current symptoms and medication, and the HRQOL 36-item short-form questionnaire (SF-36). Medical records were scrutinized. One hundred and twenty-two patients with verified signs and symptoms of posterior laryngitis were included.

Results. Forty percent of the patients had been treated for acid-related symptoms prior to consultation. The most common symptoms at the time of consultation were the sensation of hoarseness (women 40%, men 37%), globus (women 35%, men 33%) and cough (women 33%, men 26%). The most frequent diagnosis was gastro oesophageal reflux disease (GORD). Ninety percent of the women and 92% of the men were treated with proton pump inhibitors (PPIs). At the time of study, 63% of the patients still had symptoms. The results of the SF-36 questionnaire showed significantly lower HRQOL for women.

Conclusions. Patients with posterior laryngitis present varying symptoms, and are often not adequately treated or followed up. When PPI treatment fails, other aetiologies of their complaints, such as visceral hypersensitivity, weakly gaseous acid reflux or non-acid reflux are not considered. Symptoms from posterior laryngitis have a negative impact on the HRQOL for women.

Key words: posterior laryngitis, health-related quality of life

Introduction

Posterior laryngitis is an inflammation involving the interarytenoid area in the larynx [1, 2]. There are several factors that can cause inflammation in this region, e.g. virus- or bacterial infections, smoking, alcohol abuse, allergy, postnasal dripping, chronic sinusitis and voice abuse. Posterior laryngitis causes symptoms such as chronic coughing, hoarseness, a sensation of having a lump in the throat (globus), excessive throat clearing, voice fatigue and throat pain [2]. The results of previous studies indicate that 4-10% of the patients who visit an Ear-, Nose- and Throat (ENT) specialist have reflux-related complaints in the pharynx and larynx [2]. Other studies suggest that as many as 50-55% of patients who suffer from hoarseness have reflux of gastric content to the hypopharynx, laryngo-pharyngeal reflux (LPR)[2, 1].

The diagnosis of LPR is controversial. Patients with non-specific symptoms, and findings of posterior laryngitis are believed to be over-diagnosed as having acid reflux, and consequently an inappropriate use of PPIs are prescribed to patients with findings and symptoms unrelated to reflux [3]. A critical analysis of the literature in the field concerning gastro oesophageal reflux disease (GORD) and its extra-oesophageal manifestations shows, lack of an ideal method of registering LPR [4]. Many signs in the larynx attributed to LPR are non-specific and are found in normal subjects without symptoms of posterior laryngitis [4, 5].

The primary aim of the present study was to investigate how a group of patients diagnosed as suffering from posterior laryngitis were examined, treated and followed up. Secondary aims were to determine whether follow-up is needed, whether the patients still had symptoms arising from their posterior laryngitis after treatment with proton pump inhibitors (PPIs), and to register their current health-related quality of life (HRQOL).

Subjects and methods

This study was performed according to the Helsinki declaration, and was approved by the Regional Ethics Review Board at Lund University. Informed written consent was obtained from the participants.

Study design

Two hundred and forty-five patients, 143 women and 102 men, treated at the ENT clinic, Skåne University Hospital, over the period 2000-2008 were retrospectively identified, and were contacted by mail in September 2009. As the ICD-10 classification does not have a specific code for posterior laryngitis, all the patients treated

during this period with the following diagnoses were contacted: GORD with/without oesophagitis (K210, K219), chronic laryngitis (J370), laryngeal spasm (J385), other diseases of the vocal cords (J383), pain in the throat (R070), dysphagia (R139) and dysphonia (R490). The letter gave information on the reasons for the study, a questionnaire addressing the patients' current symptoms of posterior laryngitis and anti-reflux medication (the gastro oesophageal reflux disease impact scale (GIS)), modified for the diagnosis of posterior laryngitis, the 36-item short-form HRQOL questionnaire (SF-36) and a consent form.

A second letter was sent to those who had not responded. The overall response rate was 69% (169 patients), 94 women and 75 men. Forty-three of the responding patients (25%) chose not to participate in the study. The medical records for the patients agreeing to participate were scrutinized for findings and symptoms typical of posterior laryngitis. The inclusion criteria were a thickening and/or oedema of the posterior part of the glottic region by fibre laryngoscopy in combination with one or several of the following symptoms: hoarseness, voice fatigue, throat pain, globus, coughing, excessive throat clearing and heartburn/regurgitation [1]. Four patients were excluded, as they did not have the signs and symptoms of posterior laryngitis. In total, 76 women and 46 men were included (Figure 1).

Information such as age at the first time of the first visit to the ENT-clinic, previous treatment for acid-related symptoms, symptoms, medication and tobacco- and alcohol habits was collected from the medical records. Examination procedures and results, final diagnosis and choice of treatment (kind of drug, dosage and duration of treatment) were noted when available. The extent of relief of symptoms and mode of follow-up were also recorded.

Questionnaires

mGIS questionnaire

The questionnaire consisted of a part of a modified questionnaire concerning the scale of impact of gastroesophageal reflux disease (gastro oesophageal reflux disease impact scale (denoted mGIS)). GIS is a validated instrument used to aid patient-physician communication concerning the symptoms of GORD and the treatment in a primary care setting [6]. The mGIS form contained modified questions more suited for symptoms experienced by patients with posterior laryngitis than GORD. Background data (age, gender, tobacco- and alcohol habits, voice-demanding profession), current symptoms and anti-reflux medication were noted. It was also ascertained whether any of the patients had had reflux-associated symptoms during the previous two weeks despite taking medication, whether any of the patients considered it possible to manage without medication, and how often patients increased their medication. The last nine questions are designed to determine how often during the previous two weeks patients had experienced specific symptoms of posterior laryngitis, and how these symptoms had affected their daily life. The possible responses to the questions are: "always", giving a score of 1; "sometimes", a score of 2; "seldom" a score of 3; and "never", a score of 4. Thus, a high score indicates that the patient has few symptoms and a low score indicates more symptoms.

The 36-item short-form questionnaire

SF-36 is an extensively used HRQOL instrument, which provides reproducible, reliable data on large populations, and has been shown to be useful as a global health monitor in clinical practice [7]. It is available in Swedish, and Swedish reference data are available for many different conditions [8, 9]. The SF-36 questionnaire is divided into eight subscales of general health, ordered according to the degree to which they measure physical versus mental health. These subscales are physical functioning (PF), role functioning-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role functioning-emotional (RE), and mental health (MH). Two additional dimensions can be calculated, physical (PCS) and emotional health (MCS), by on weighting the importance of the other eight subscales. The raw data were recorded after analysis; the maximum score is 100, the higher the score, the better the HRQOL.

Statistical analyses

Statistical calculations were performed on the information collected from the medical records, the mGIS questionnaire and the data from the SF-36 questionnaire. Results are given as means and standard deviation (SD). Fisher's exact test was used to compare different groups concerning the data from the medical records and the mGIS questionnaire. The one-sample t-test was used to compare the data from the SF-36 questionnaire with the Swedish reference values. The Kruskal-Wallis test was used to compare the SF-36 values of patients who had answered questions on the frequency of specific symptoms of posterior laryngitis and their impact on daily life. The level of statistical significance was set to $p \leq 0.050$. The data were analysed using the statistical software package SPSS for Windows (Release 19.0, IBM).

Results

Patient characteristics

Two hundred and forty-five patients with posterior laryngitis were identified. Seventy-six women (76/143, 53%) and 46 men (46/102, 45%) were finally included in the study with a diagnosis, as verified by their medical journal, of posterior laryngitis by fibre laryngoscopy (Figure 1). The mean age of the 122 participants was 58 and 59 years for women and men, respectively, at the time of examination and diagnosis by an ENT specialist, and 62 years for women and 63 years for women and men, respectively, at the time of completing the questionnaires. Information about smoking- and drinking habits was lacking, as most patients did not answer these questions when completing the questionnaire. The information about smoking- and drinking habits was also missing in their medical journals. Twenty-five patients had voice-demanding professions (Table 1). No statistical difference between women and men was found.

Symptoms

The results from the medical records showed that the most common symptoms reported at the consultation at the ENT clinic were hoarseness (women 40%, men 37%), followed by globus (women 35%, men 33%) and cough (women 33%, men 26%) (Table 1). These symptoms dominated over heartburn and regurgitation at that time, but 41% of the women and 39% of the men had been treated for acid-related symptoms prior to the consultation at the ENT clinic. The diagnosis of hiatal hernia (women 9%, men 7%), dyspepsia (women 8%, men 2%) and gastric ulcer (women 4%, men 4%) were less common.

At the time of consultation most of the patients complained of more than one symptom related to posterior laryngitis. The most common combination of symptoms was hoarseness and coughing (8 women, 5 men). The second most common combination was hoarseness and reflux (3 women, 8 men), and in third place, equally frequent were hoarseness and heartburn (4 women, 6 men), globus and excess phlegm (8 women, 2 men), or globus and breathing problems (5 women, 5 men).

Examinations and diagnosis

Fibre laryngoscopy had been performed on all of the patients. Thirteen patients (11%) were referred to oesophagogastroduodenoscopy (OGD) in combination with a barium swallowing study. Twelve patients (10%) were examined by OGD and an equal number of patients underwent a barium swallowing study. Six (5%) and five (4%) patients were investigated by 24-h pH monitoring and by 24-h pH monitoring in combination with OGD, respectively. Thirty-one women (41%) and 17 men (37%) were not investigated at all for the presence of reflux.

The examination(s) performed depended on the patient's symptoms. Breathing problems in addition to other symptoms led to the largest number of different examinations, independent of gender. When checking for associations between a specific examination procedure and specific patient-reported symptoms, OGD was associated with hoarseness ($p=0.036$), breathing problems ($p=0.032$) and heartburn ($p=0.016$). The barium swallowing study was associated with breathing problems ($p=0.032$) and globus ($p=0.027$), while oesophageal manometry was associated with breathing problems ($p=0.040$) and heartburn ($p=0.010$).

The most common diagnosis set at the ENT clinic was GORD without oesophagitis (55%), and the second most common was chronic laryngitis (18%). Only 64% (49/76 women, 29/46 men) of the patients perceived that the specialist had given them a diagnosis after their examination.

Treatment and treatment results recorded in medical journals

The most common treatment prescribed was PPIs at a dose of 20 mg once daily for up to 4 weeks. About two thirds of the patients were treated for 12 weeks or less. Seven percent of the patients were treated for more than 12 weeks. Of the patients who had undergone investigational procedures, 90% of the women and 92% of the men were treated with PPIs. Of the 48 patients not investigated, 85% (28 of 31 women, 13 of 17 men) received treatment with PPIs.

Alternative treatment, concerning either the choice of drug or the dosage, was considered in only a minority of the patients in spite of the fact that in most cases the effect of PPIs was inadequate (Table 2).

Information on the effects of treatment was lacking for 32 women and 14 men. In the remaining patients, 16% of the women and 34% of the men were free from symptoms after treatment. The effect, when noted, was most commonly seen during the first two weeks of treatment. However, 84% of the women and 66% of the men reported persisting symptoms, despite treatment.

An appointment with their physician was the most common mode of follow-up (women 40%, men 48%), followed by a consultation by telephone (both women and men 33%, respectively). Twenty-five percent of the women and 20% of the men had no follow-up at all recorded in their medical journal.

Current symptoms and medication as stated in the mGIS questionnaire

The majority of patients, 63% (51 women, 26 men), still had symptoms at the time of completing the questionnaires, which was an average of four years after their first consultation with an ENT specialist. About one third of them always or sometimes experienced sore throat/hoarseness, excessive throat clearing and globus, all of which are symptoms related to posterior laryngitis. Further, many of the patients sometimes also experienced acid reflux and a sour taste in their mouth, as well as a burning sensation/chest pain (Figure 2).

When asked about current anti-reflux medication and how it was taken, the responses showed that 71% (56 women, 31 men) of the participants were still taking PPIs. Thus, although the ENT specialist prescribed PPIs for only a short period, and no follow-up was reported in many cases, patients were still taking PPIs at the time of completing the study questionnaires. Medication was either prescribed by their physician or bought over the counter. Regardless of treatment, 41% (30 women, 14 men) took medication daily, some only when they had symptoms, while others took their medication several times a day (Table 3). Almost 30% of the patients always or sometimes increased the dose of anti-reflux medication or used medication for their symptoms other than that prescribed by their physician (Figure 3).

The symptoms experienced by the patients often prevented them from eating and drinking, and 34% reported that the symptoms of their posterior laryngitis affected their daily activities, thus having a negative impact on their lives. Almost half of the participants (45%) reported that their symptoms always or sometimes affected their sleep (Figure 3). The only statistically significant difference between genders was that women experienced more sleeping problems than men due to symptoms from posterior laryngitis ($p=0.007$).

More women than men had completed the mGIS score. The analysis of the scores showed that 29% (20/70) of the women had low scores (i.e. scores below 18). None of the men had scores below 18, which indicates more symptoms from posterior laryngitis in the women (highest attainable score is 36).

The 36-item short-form questionnaire

The values for each of the eight subscales were analysed for women and men separately (76 women and 46 men), and for the whole group ($n=122$). Gender- and age (49 to 75 years) corrections were performed. Values for women and men with posterior laryngitis were compared with the norm values of the general and the female and male Swedish population [9]. The women had significantly lower scores ($p=0.000$) for all subscales compared to the general and female Swedish population, except for the subscale PF that did not differ compared to the female Swedish population ($p=0.148$). The women also had significantly lower scores on all subscales compared to the men participating in the study (Figure 4). In men, the only subscales to differ from those of the general Swedish population were PF ($p=0.015$), which was higher and GH ($p=0.010$), which was lower (Figure 4). No difference was noted compared to the general male Swedish population (data not shown). This indicates that the HRQOL of men is not affected to the same extent by posterior laryngitis as that of women. Patients who frequently felt they had a lump in their throat had lower scores in the PF subscale than those who reported seldom having this problem ($p=0.043$).

Discussion

We found that patients with posterior laryngitis are not treated and followed up adequately. Sixty-three percent of the patients still had symptoms at the time of completing the questionnaire, and 71% still used PPIs, approximately four years after their first visit to the ENT clinic. The women, but not the men, except for the subscales GH, had significantly lower subscale scores than the general Swedish population and accordingly registered a lower HRQOL.

The symptom of breathing problems was found to be the most alarming symptom, and these patients underwent more investigational procedures than those not reporting this symptom. Physicians appeared to take this symptom more seriously than symptoms such as hoarseness and excess phlegm. Men were diagnosed as having GORD with oesophagitis more often than women (22% versus 4%). On the other hand, women were diagnosed as having GORD without oesophagitis more frequently than men (59% versus 48%). The predominance of women in this study, as has also been reported previously [10], does not necessarily mean that more women suffer from posterior laryngitis. It may reflect the propensity of women to complain about their symptoms, which may explain the more benign diagnostic findings in women, their lower reflux scores and lower HRQOL [11-13]. Their lower HRQOL could not be explained by inferior examination or treatment compared to men. According to Sataloff et al. [14] epidemiological studies to determine the prevalence of posterior laryngitis are still lacking.

Thirty-nine percent of the patients did not undergo to any investigation but nevertheless the physician chose to treat their symptoms of posterior laryngitis as if it were an acid-related illness, prescribing PPIs to more than 85 % of them. No investigational algorithm was used to methodically investigate the patients, and thus exclude or confirm the specific aetiology of their posterior laryngitis they were suffering from. Twenty-five percent of the women and 20% of the men appeared not to have been followed up, even though they had a prolonged history of symptoms, and were being treated with PPIs. This goes against the recommendations for the use of this kind of expensive and widely prescribed medication [15, 16].

None of the patients in our study reported that their symptoms became worse when treated with PPIs, but 63% (51 women, 26 men) still had symptoms of posterior laryngitis in spite of the fact that the majority were on acid-reducing therapy. This may have been due to an incorrect initial diagnosis.

Laryngo-pharyngeal inflammation can be caused by mechanisms other than acidic reflux, e.g. virus infections, allergy, voice disorders, alcohol and smoking [17]. Data concerning smoking- and alcohol habits were missing from the medical records, indicating that the ENT-specialist had not thought about smoking and alcohol abuse as the aetiology of posterior laryngitis, but had focused solely on acidity being the cause of the patients' complaints. The patients' use of alcohol and tobacco was also missing on the mGIS questionnaire. It is likely the patients wanted to avoid disclosing this kind of sensitive information.

Patients suffering from functional oesophageal disease are known to display typical reflux symptoms (heartburn/regurgitations) in spite of having a normal acid exposure time and a normal oesophageal mucosa as seen by endoscopy. This is thought to be due to visceral hypersensitivity, i.e. an enhanced perception of normal physiological signals arising from the oesophagus. These patients also have a poorer response to acid suppressive therapy [17, 18]. This line of thought is applicable to the results in our study, and the same mechanism of visceral hypersensitivity in the hypopharynx could explain why our group of patients still had symptoms in spite of being on PPI therapy. PPIs reduces the acidity of the gastric juice, but it does not affect the number or the duration of the reflux episodes, leaving a possibility for weakly acid, gaseous or non-acid reflux as being other possible mechanisms behind posterior laryngitis, thus explaining our current results [19, 20]. Disturbances in motilin concentrations and antibodies against the hormone gonadotropin-releasing hormone (GnRH) are other factors discussed in the pathogenesis of oesophageal dysfunction that can lead to reflux [21, 22].

Our study revealed that only 11% of the patients were diagnosed as having GORD with oesophagitis. This is comparable to the previously reported prevalence of GORD with oesophagitis in 11% [23] and 12% [24] of patients with posterior laryngitis, which is lower than the prevalence of oesophagitis in patients with GORD but without posterior laryngitis [25].

The majority of the patients in our study were treated for their symptoms of posterior laryngitis as if it were an acid-related illness, but only 40 % of the patients in the study underwent an OGD. In order to confirm or exclude the diagnosis GORD and to assist in the investigation of the diagnosis visceral hypersensitivity as a cause of PL, we recommend, as a routine, that this group of patients undergo OGD. This is especially important when the treatment with PPIs fail to improve the patients' symptoms.

The women participating in this study had lower HRQOL scores than the general population. The scores in our study were in the same range as found in previous studies describing patients suffering from posterior laryngitis, and confirm that these patients have a reduced HRQOL [26-28]. The new finding in the present study is that the reduced scores apply to the female population and not to the male population. The participants in our study were also found to have lower scores in all domains than Swedish patients with ulcerative colitis and Crohn's disease, except for the domain of vitality, in which patients with Crohn's disease scored lower [8]. This is in agreement with the results of the mGIS questionnaire, indicating that symptoms from posterior laryngitis affected their daily lives.

One limitation of this study is that only half of the identified patients participated, and it may indicate that patients with more severe symptoms were more inclined to participate. An additional limitation is that the information from the medical journals was collected in a retrospective manner.

Conclusions

This study indicates that patients suffering from posterior laryngitis still suffer from symptoms several years after diagnosis. The HRQOL of women is affected and the patients record lower scores than Swedish patients with ulcerative colitis and Crohn's disease. Patients with posterior laryngitis are treated with PPIs even though

no improvement of their symptoms is noted after using acid suppressing agents and when there is little evidence of acid reflux into the laryngo-pharynx. Other aetiologies for their complaints are not considered. We believe that patients not responding to PPI medication should be evaluated with regard to other causes of their symptoms, e.g. visceral hypersensitivity, non-acid reflux or weakly gaseous acid reflux. Furthermore, in order to confirm or reject GORD and assist in investigating the diagnosis visceral hypersensitivity, all patients with PL should undergo OGD. It is also of great importance to insistently ask about and record the patients' use of alcohol and tobacco, as these two factors are important for the development of PL. Further research is required to investigate the pathophysiology underlying their symptoms. Improvement is also called for concerning the frequency of follow-up to ameliorate the quality of medical care given to this group.

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Conflict of interest:

The authors declare that they have no conflict of interest.

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Table 1. Age at first visit and acid-related complaints leading to treatment. Information from medical records

	Women n=76	Men n=46
Mean age at first visit, years ^a	58±12	59±13
Voice-demanding profession, n (%)	17	8
Symptoms from medical records, n (%) ^b		
Hoarseness	30 (40)	17 (37)
Globus	27 (35)	15 (33)
Cough	25 (33)	12 (26)
Reflux	16 (21)	11 (24)
Excessive phlegm	15 (20)	7 (15)
Heartburn	11 (15)	11 (24)
Excessive throat clearing	7 (9)	6 (13)
Voice fatigue	4 (5)	4 (9)
Breathing difficulties	9 (12)	10 (22)
Feeling of cramp in the throat	3 (4)	5 (11)

^aAge values are given as mean±standard deviation (SD). ^bMore than one symptom for each patient was registered. There was no statistical difference between women and men.

**Table 2. Medical treatment and results of treatment.
Information from medical records**

	Women n=76 n (%)	Men (n=46) n (%)
Medical treatment^{ab}		
Proton pump inhibitor	61 (90)	37 (92)
Alginic acid	5 (7)	1 (2)
Histamine receptor blocker	1 (1)	1 (2)
Aluminumdihydroxide	0 (0)	1 (2)
Relief of symptoms^c		
Complete lack of symptoms	7 (16)	11 (34)
Improved	31 (70)	17 (53)
No change	6 (14)	4 (13)
Worse	0 (0)	0 (0)

^a Some patients were treated with more than one drug. ^b No information from 8 women and 6 men. ^c No information from 32 women and 14 men. There was no statistical difference between women and men.

**Table 3. Current anti-reflux medication and the patients' use of it.
Information from the mGIS questionnaire**

	Women n=76	Men n=46
Mean age, years ^a	62±13	63±14
Medication, n (%) ^b		
Proton pump inhibitor	56 (74)	31 (67)
Alginic acid/Aluminumdihydroxide	18 (24)	9 (20)
Bicarbonate	5 (7)	4 (9)
Histamine receptor blocker	6 (8)	0 (0)
Use of medication, n (%) ^c		
Every day	30 (45)	14 (35)
When symptoms arise	21 (31)	20 (50)
Several times a day	7 (10)	5 (13)
Defined period (e.g. 4 weeks)	5 (8)	0 (0)
Not used	4 (6)	1 (2)

^a Age values are given as mean±standard deviation (SD). ^b Some patients were treated with two different drugs concurrently. ^c No information from 9 women and 6 men. There was no statistical difference between women and men.

Figure legends

Figure 1. Flow-chart illustrating the selection process for the patients included in the study

Figure 2. The symptoms experienced by the patients during the 2 weeks prior to completing the mGIS questionnaire. Values are shown as percentage of participants answering the questionnaire

Figure 3. How often daily activities are affected by posterior laryngitis and how prescribed medication is taken. Values are shown as percentages of the participants answering the mGIS questionnaire

Figure 4. Analysis of SF-36 in the population of women and men with posterior laryngitis and the general Swedish population. Gender- and age- matched values are presented as mean values

Fig. 1

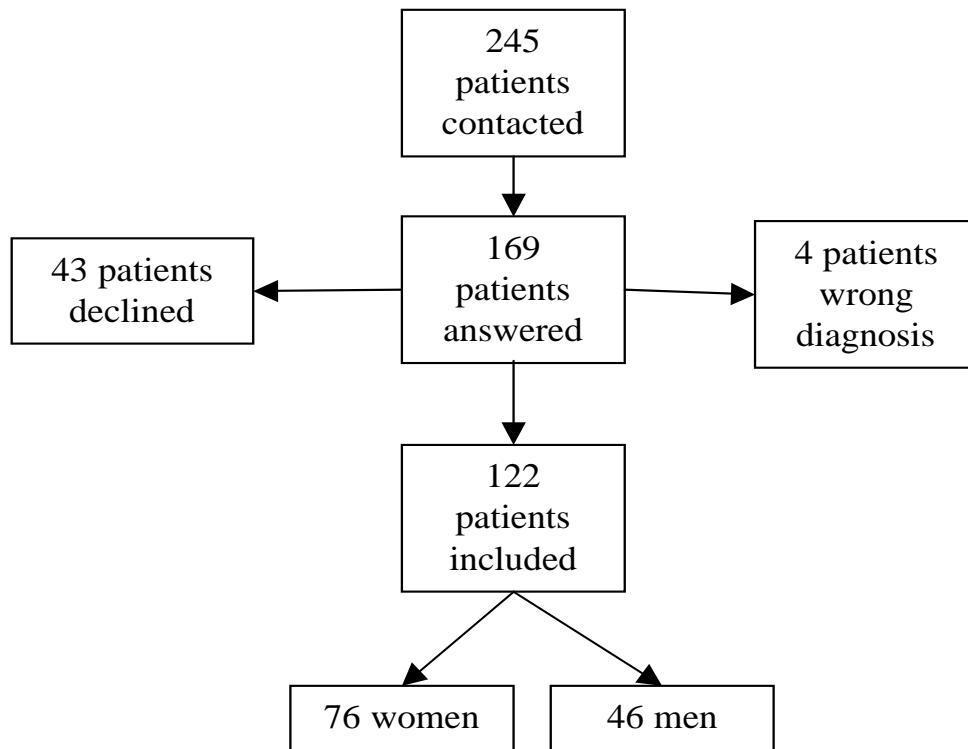


Fig. 2

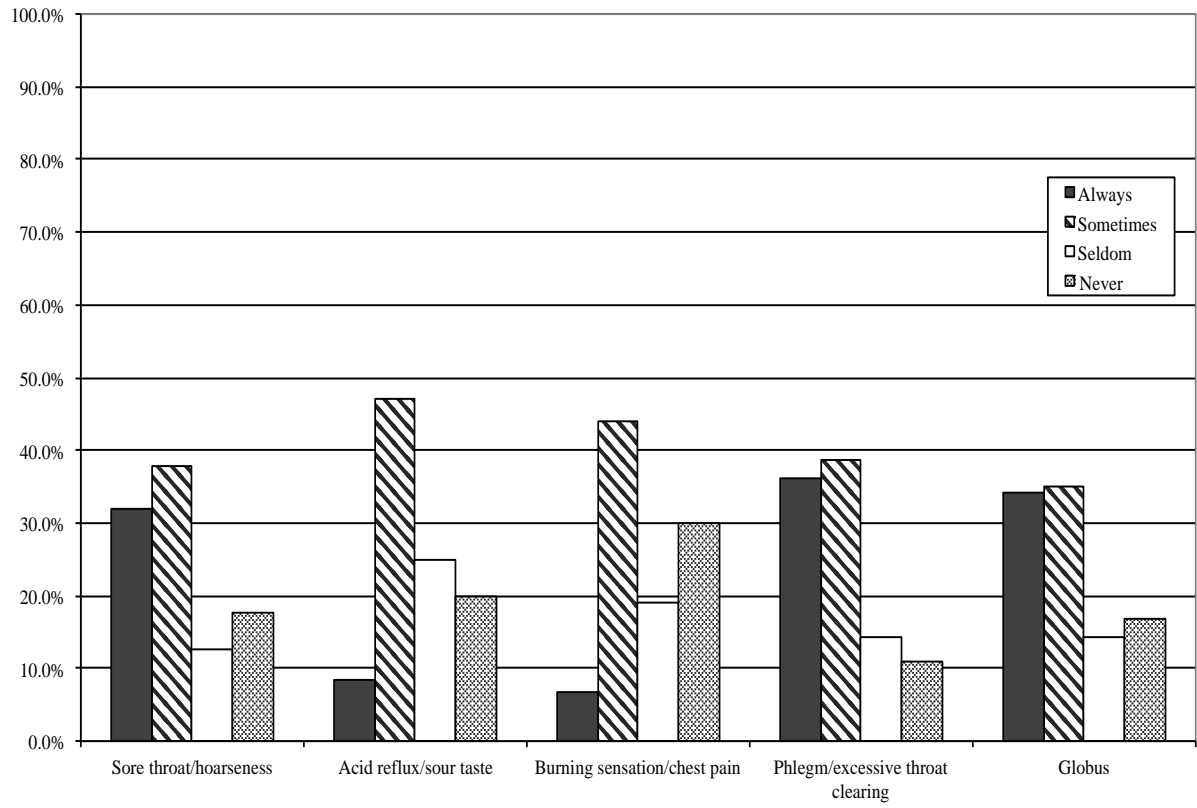


Fig. 3

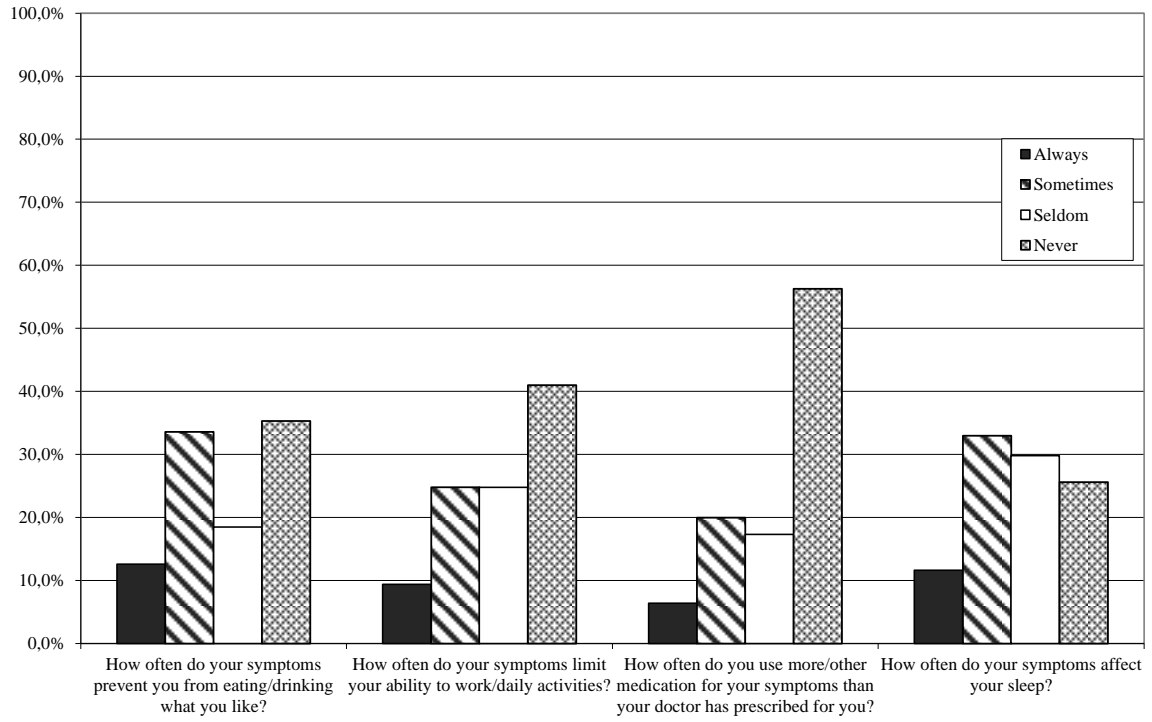


Fig. 4

