Prevalence of gastro-oesophageal reflux symptoms in patients with COPD

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ABSTRACT

Objective: To assess whether there is an increase in prevalence of gastro-esophageal reflux disease (GERD) in patients with chronic obstructive pulmonary disease (COPD), and the influence of reflux on the respiratory symptoms of these patients.

Methods: A case control study that was conducted at the outpatient clinic of Ibn Sina Teaching Hospital in Mosul, and two private clinics, during the years 2002-2003. Sixty six patients with COPD and 50 sex- and age- matched controls were questioned about experiencing GERD symptoms, utilizing a modified questionnaire originally developed by Mayo clinic. COPD patients were asked whether they noticed an association between experiencing reflux episodes and worsening respiratory symptoms, and whether smoking a cigarette is associated with GERD symptoms.

Results: COPD patients showed a significantly increased prevalence of GERD symptoms as compared with the control group (29(43.9%)vs. 11(22%), respectively), (p=0.014). COPD patients more frequently reported significant heartburn (43.9%vs. 20%; p=0.007), and regurgitation (25.8%vs. 6%; p=0.005).

COPD patients who were still smoking were not statistically significant from those who have stopped smoking regarding experiencing GERD symptoms (46.7%vs. 30.8%; p=0.08). Fifty one percent (51.7%) of COPD patients noticed that their respiratory symptoms are worsened during episodes of heartburn or regurgitation.

Conclusion: GER symptoms are more prevalent in patients with COPD, compared to control subjects.

Keywords: COPD, gastro-oesophagael reflux disease.

الخلاصـــة

السياق: هنالك علاقة وثيقة بين الكثير من الأمراض التنفسية وخاصة الربو مع داء الجزر المعدي المريئي.

الهدف: للبحث في نسبة الإصابة بداء الجزر المعدي المريئي عند المرضى المصابين بالداء الرئوي المسد المزمن، وتأثير أعراض الجزر على الأعراض التنفسية عند هؤلاء المرضى.

التصميم: دراسة مقارنة.

مكان و زمان أجراء الدراسة: العيادة الخارجية في مستشفى أبن سينا في الموصل وعيادتان خاصتان خلال السنوات 2002-2003.

المشاركون وطرق العمل: ستة وستون (66) مريضا مصابين بالداء الرئوي المسد المزمن و50 شخصا مكافئون لهم في العمر والجنس، خضعوا لأستبيان عن اعراض الجزر المعدي المريئي (محور من نموذج مبتكر من عيادة مايو). وقد سئل مرضى الداء الرئوي المسد المزمن عن أية ملاحظة لوجود علاقة بين حصول أعراض الجزر وازدياد الأعراض التنفسية لديهم، وهل أن التدخين يزيد من شعورهم بأعراض الجزر أم لا.

النتائج: مرضى الداء الرئوي المسد المزمن كانوا أكثر شعورا بأعراض الجزر من المجموعة المقارنة (43.9 % مقابل 22%)، (ب = 0.014). يشعر 43.9% منهم بحرقة الفؤاد مقارنة ب 20% (ب = 0.007) كما يشعر 25.8% منهم بالقلس مقارنة ب 6% من مجموعة المقارنة، (ب = 0.005)

مرضى الداء الرئوي المسد المزمن المستمرون على التدخين لم يختلفوا إحصائيا في نسبة الإصابة بأعراض الجزر عن الذين تركوا التدخين (46.7% مقابل 30.8%)، (ب = 0.08). 51.7% من مرضى الداء الرئوي المسد المزمن أحسوا بوضوح أن نوبات أعراض الجزر يصاحبها ازدياد في الأعراض التنفسية لمرضهم.
الاستنتاج: أعراض داء الجزر المعدي المريئي أكثر حصولا عند مرضى الداء الرئوي المسد المزمن من غيرهم.

An association between gastro-oesophageal reflux disease (GERD) and many respiratory diseases has been reported[1,2]; the strongest was the association between GERD and asthma[3-7]. GER symptoms were estimated to occur daily in 7% of the general population, and weekly in 14 -28 %[8-11], while 39-70 % of patients with asthma report at least weekly GERD symptoms[4-6]. Episodes of reflux were associated with exacerbation of asthma symptoms and GERD was shown to contribute to poor asthma control[2,7].

This study is to evaluate whether there is a similar increase in prevalence of GER symptoms in patients with chronic obstructive pulmonary disease (COPD) in comparison with age and sex matched controls, and to study the association of reflux episodes with worsening respiratory symptoms.

Patients and methods

Sixty six patients with a diagnosis of COPD were enrolled in the study. They were attending an outpatient clinic in Ibn-Sina teaching hospital in Mosul and private clinics of two general physicians with a special interest in respiratory medicine during the years 2002-2003. The diagnosis of COPD was defined according to the American Thoracic Society (ATS) standards [12]. Inclusion criteria included 1- Age more than 30 years. 2- Abnormal findings of pulmonary function tests; demonstrating nonreversible airway obstruction based on ATS criteria (< 200 ml and 12% improvement in FEV_1 or FVC after inhaling salbutamol) [13]. Exclusion criteria included: 1- Respiratory symptoms rather than COPD. 2- Reversible airway obstruction after bronchodilator therapy 3- Known oesophageal disease such as cancer, achalasia or stricture.

The control group consisted of 50 patients attending the same clinics for other medical problems, who denied respiratory symptoms like dyspnoea, or chronic sputum production, nor having previous diagnosis of respiratory diseases. The control group was matched with the study group in respect to age and sex.

Both COPD patients and the study group completed a modified version of a previously validated questionnaire developed by Locke and associates at the Mayo clinic [14]. The questionnaire included assessment of the smoking history (including the number of pack year), and a detailed questioning of the presence of symptoms like heartburn, acid regurgitation, dysphagia, odynophagia, and sore throat. Each positive answer is followed by addressing the duration, frequency and severity of that symptom. Only those experiencing at least weekly symptoms were included. Patients self assessment of any relation between reflux symptoms and smoking was sought, and patients with COPD were questioned if they have noticed any temporal relation between episodes of reflux and worsening respiratory symptoms. Any previous diagnosis of GERD or the use of over-the-counter antacids and prescription of acid suppressive medication were included in the questionnaire.

Data were statistically evaluated using Z test and Fisher Exact test.

Table (1): *Demographics of the patients with COPD and the control subjects.*

COPD (66 patients)	Control (50 patients)
Males 53 (80.5%) Females 13 (19 %) Age range: 31-85 years Mean ± (SD) (58.75 ± 11.85) Smoking : Non smokers 0 (0%) Smokers 40 (61%) X-smokers 26 (39%)	Males 37 (74%) Females 13 (26%) Age range: 30-75 years Mean ± (SD) (54.06 ± 10.57) Smoking : Non smokers 16 (32%) Smokers 26 (52%) X-smokers 8 (16%)

Table (2): *Association of GERD symptoms in patients with COPD compared with control subjects*

Symptoms	COPD(*66 patients*)	Control(*50 subjects*)	P Value
Any GERD Symptom	29(43.9%)	11(22%)	0.014(S)
Heartburn	29(43.9%)	10(22%)	0.007(S)
Regurgitation	17(25%)	3(6%)	0.005(S)
Dysphagia	0(0%)	2(4%)	0.18(NS)
Sore Throat	2(3%)	0(0%)	0.32(NS)
Use of Acid Suppressive Drugs	11(16.7%)	6(12%)	0.45(NS)

Table (3): *Prevalence of GERD symptoms in current smokers with COPD compared with previous smokers.*

Symptoms	Current Smokers *(40 patients)*	Previous Smokers *(26 patients)*	P Value
Any GERD Symptom	21(46.7%)	08(30.8%)	0.08(NS)
Heartburn	21(46.7%)	08(30.8%)	0.08(NS)
Regurgitation	12(13.0%)	05(19.2%)	0.33(NS)
Sore Throat	01(02.5%)	01(03.8%)	0.64(NS)

Results

The characteristics of the 66 patients with COPD and the 50 control subjects are presented in table 1. The majority of participants were males; 53(80.3%) of the study group and 37 (74%) of the control group ($p > 0.05$). Patients in the COPD group were slightly older (mean ± SD: 58.75 ± 11.76 years vs. 54.06 ± 10.57 years, respectively; $p= 0.027$). As expected; a greater proportion of the COPD group were current smokers (40 (60.6%)), compared with 26 (52%) of the control group. All the remaining 26(39.4%) patients with COPD were previous smokers; while 16 subjects of the control group (32%) have never smoked and 8(16%) were x-smokers.

COPD patients have significantly increased prevalence of GERD symptoms compared with the control group (29(43.9%) vs. 11(22%), respectively), ($p = 0.014$). COPD patients more frequently reported significant heartburn (43.9% vs. 20%; $p = 0.007$), regurgitation (25.8% vs. 6%; $p = 0.005$), and persistent sore throat (3% vs. 0%), (but the latter was not significantly different; $p = 0.32$). Patients with COPD more commonly used antacids, H_2 blockers, or proton pump inhibitors to treat reflux symptoms than the control group (16.7% vs.12%), although this difference did not reach statistical significance (Table 2).

Within the study group, patients who are still smoking were not significantly different regarding experiencing GERD symptoms than those who have stopped smoking (46.7% vs. 30.8%; $p = 0.08$) (table 3). Only 3 (10.3%) of the patients in the COPD group who have reported GERD symptoms noticed an association of these symptoms with smoking. On the other hand, 15 (51.7%) of them clearly reported that their respiratory symptoms (dyspnoea, cough, or wheezing) are worsened during episodes of heartburn or regurgitation.

Discussion

The results of this study suggest a significant association between GER symptoms and COPD; an association that parallels similar findings in asthmatic patients

The diagnosis of GERD was based on a questionnaire that was shown by its founders at the Mayo clinic to accurately reflect the presence of reflux [14], depending on the fact that heartburn and regurgitation are specific symptoms of GERD [15].

Twenty two percent (22%) of the control group reported at least weekly GER symptoms, a prevalence similar to what was reported by other population based surveys (14-28 %) [8-11].

Three other recently published studies have all shown similar association; two of them were also questionnaire based [16, 17], while the third included an oesophageal pH monitoring [18]. The latter besides proving the same increase in prevalence of GERD in COPD patients, has shown that 52% of patients who were diagnosed on pH monitoring did not report any GERD symptoms, indicating that the true prevalence is even higher.

The effect of smoking on GERD is controversial [19, 20], and in one study; smoking or abstaining from smoking did not modify the results of oesophageal pH monitoring [21]. However, the question whether smoking contributes to the increased prevalence of GERD in COPD patients was considered, and a subgroup analysis to compare current and previous smokers did not show a significant difference in the prevalence of reflux symptoms, suggesting that cigarette smoking is not responsible for the increase

of GERD in COPD patients. Furthermore, only a minority of the current smokers noticed an association between smoking a cigarette and experiencing GER symptoms. Drugs like β_2 agonists, anticholinergics, and theophylline may increase GER by lowering oesophageal sphincter pressure[22,23]. However, results of several studies have questioned the association between reflux and these medications[24-26].

A significant proportion of COPD patients have noticed a temporal relation between GER and respiratory symptoms (51%). This may suggest a possible contribution of GERD to COPD exacerbation, similar to what was noticed in asthma. This is supported by the findings of Casanova *et al*; who noticed that oxygen desaturation coincides with episodes of increased oesophageal acidity in 40% of COPD patients with GERD[18].

There are several mechanisms by which GER can induce symptoms in patients with COPD and asthma. One mechanism suggests that reflux can induce micro aspiration, whereas other studies suggest that acid reflux causes reflex broncho-constriction[27,28]. Severe hyperinflation and vigorous coughing may increase intra-abdominal pressure and change the relationship between the diaphragm and lower oesophageal sphincter, decreasing diaphragmatic contribution to sphincter tone and thereby promoting gastro-oesophageal reflux[4,27,29-31].

Treatment of associated GERD in asthma which is difficult to control has been shown to improve pulmonary function[32,33]. Directing therapy toward the associated reflux in COPD patients may help in the management of this disease that is even more difficult to treat than asthma.

Our study supports the assumption that GERD is more frequent in COPD patients than the general population, but the real impact of this association on the severity or exacerbation of COPD, and whether its treatment could help in improving COPD symptoms require further study.

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