Study of voice disorders in patients with bronchial asthma and chronic obstructive pulmonary disease

Adel M. Saeed[a], Nermine M. Riad[a], Nehad M. Osman[a], Ahmed Nabil Khattab[b], Shymaa E. Mohammed[a]

Background Chronic obstructive pulmonary disease (COPD) and bronchial asthma are known to cause adverse effects on voice, which might affect the quality of life of an individual.

Aim The study was designed to study the voice disorders in patients with COPD and bronchial asthma and its relation to disease severity and medication.

Patients and methods Totally, 60 patients were recruited: 30 stable bronchial asthma patients and 30 stable COPD patients. All participants underwent spirometry and study of voice parameters using auditory perceptual assessment, videolaryngostroboscopy system, voice recording, and acoustic analysis.

Results Impaired voice quality and various grades of dysphonia were detected in the COPD group in 30% by means of auditory perceptual assessment; structural changes in the vocal folds (diffuse congestion, unhealthy mucosa, and edema) were detected in 36.6%. In the bronchial asthma group, impaired voice quality and various grades of dysphonia were detected in 16.7% and structural changes were detected in 20% of them, whereas acoustic analysis showed a highly significant increase in jitter and shimmer and decreased harmonic-to-noise ratio in 100% of patients of both groups. These changes were greater in metered dose inhaler users than in dry-powder inhaler users. In the bronchial asthma group, fluticasone propionate users had a significantly decreased harmonic-to-noise ratio compared with beclomethasone dipropionate and budesonide users, as well as the least pitch and highest shimmer and jitter. A significant statistical correlation was found between ipratropium inhalation usage and increased shimmer in the COPD group. There was a highly significant correlation between spirometric severity and both grade of dysphonia and character of voice in bronchial asthma patients.

Conclusion All COPD and bronchial asthma patients had dysphonia, either due to organic causes or due to functional causes. Voice changes were directly correlated with degree of severity and fluticasone propionate inhalation use in bronchial asthma patients, and with ipratropium bromide inhalation in the COPD group.

Egypt J Bronchol 2018 12:20–26

Egyptian Journal of Bronchology 2018 12:20–26

Keywords: bronchial asthma, COPD, voice changes

[a]Departments of Chest Diseases, [b]Phoniatrics, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to Shymaa E. Mohammed, MSc of Chest Diseases, Compound 17, Building 7, Apartment 23, El-Rehab City, New Cairo, Egypt
Tel: +20 100 748 7465;
e-mail: kareemattia198@gmail.com

Received 24 June 2017 **Accepted** 16 July 2017

Introduction

Voice problems in chronic obstructive pulmonary disease (COPD) and bronchial asthma patients were seldom investigated and increased attention was given to the assessment and treatment of the respiratory problem. These respiratory conditions are known to cause adverse effects on voice, which might further affect the quality of life of an individual [1].

COPD and bronchial asthma can affect vocal quality and production, both directly, associated with respiratory decline, and indirectly, as a side effect of medication and associated with concurrent symptoms [2].

The decreased lung volume associated with COPD and bronchial asthma and the effects of medications, including inhaled corticosteroids (ICS) and anticholinergic inhalers, all contribute to dysphonia [3–5]. Smoking is also a major risk factor that exerts a detrimental effect on vocal health [6].

Study objectives

The primary objective was to study the voice disorders (functional and organic) in patients with COPD and bronchial asthma, and the secondary objective was to study the relation of these voice disorders to disease severity and medication.

Patients and methods

A total of 60 patients who presented at the chest outpatient clinic at Ain Shams University hospitals were enrolled in this study. The study was approved by the institutional ethical committee.

Patients were classified into two groups: group A consisted of 30 randomly selected stable bronchial

 DOI: 10.4103/ejb.ejb_34_17

asthma patients defined according to GINA Guidelines, 2016 [7], and group B consisted of 30 randomly selected stable COPD patients according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, 2016 [8]. Oral consent was taken from all patients.

Exclusion criteria

Patients with any etiological factor that might affect the larynx and the vocal folds (e.g. voice abusers), patients suffering from repeated upper respiratory tract infection, patients who underwent any surgical interventions of the neck or the larynx, or patients refusing to participate in this study were excluded.

All patients in the present study were subjected to the following: Spirometry was carried out using a Viasys FlowScreen Spirometer (Viasys, Hoechberg, Germany), 2007. All techniques were performed according to the guidelines of American Thoracic Society/European Thoracic Society, 2005 [9]. Bronchodilator reversibility testing for bronchial asthma was carried out; positive bronchodilator reversibility is considered when the forced expiratory volume in the first second improves significantly after bronchodilator, and a change more than 12% and more than 200 ml occurs (GOLD, 2010).

Evaluation of voice dysfunction according to Kotby [10] using auditory perceptual assessment [based upon the modified grade, roughness, breathiness, asthenia, strain (GRBAS) scale], videolaryngostroboscopy system, high-fidelity voice recording, and acoustic analysis was carried out with the use of computerized speech laboratory (model 4300; Kay Elemetrics Corp., Lincoln Park, NJ, USA).

The following acoustic parameters were measured according to Kotby [10]:

(1) Average pitch.
(2) Jitter: (cycle-to-cycle variation in frequency), with mean normal jitter of 0.3154%.
(3) Shimmer: (cycle-to-cycle variation in amplitude), with mean normal shimmer of 0.5016 db.
(4) Harmonic-to-noise ratio (H/N), with mean normal H/N of 14.640 db.

The collected data were statistically analyzed using statistical package for the social sciences (2001, SPSS 15.0.1 for windows; SPSS Inc, Chicago, Illinois, USA).

Descriptive statistics: quantitative variables were presented as mean and SD. Analytical statistics: independent samples *t*-test, paired *t*-test, one-way analysis of variance, correlation analysis (using Pearson's method), and the χ^2-test were used.

The level of significance was set as follows: *P* value greater than 0.05 was considered as nonsignificantly statistical result; *P* value less than 0.05 was considered statistically significant result; and *P* value less than 0.01 was considered a highly statistically significant result.

Results

Demographic characteristics

In the COPD group, 28 (93.3%) cases were male and two (6.7%) female, with a mean age of 57.43 years with SD of 9.79. Twelve patients were current smokers, 16 were ex-smokers, and two were nonsmokers.

However, in the bronchial asthma group, there were only 13 male patients, representing 43.3%, and 17 female patients, representing 56.7%, with a mean age of 43.57 years with SD of 10.70. All bronchial asthma cases were nonsmokers.

All COPD patients had increased jitter, with a mean of 2.02±0.20%, increased shimmer, with a mean of 1.06 ±0.24 db, decreased H/N ratio, with a mean of 14.00 ±0.16, and pitch was within normal range for all of them, with a mean of 203.

In the bronchial asthma group, all cases showed increased jitter, with a mean of 0.97±0.13%, increased shimmer, with a mean of 0.90±0.14 db, decreased H/N ratio, with a mean of 11.29±1.03, and decreased pitch was found in 26.7%, with a mean of 198±12.82.

Spirometry in COPD cases showed that 50% had very severe obstructive pattern (GOLD 4), 26.7% had severe obstruction (GOLD 3), 20% had moderate obstruction (GOLD 2), and only 3.3% had mild degree (GOLD 1), and all of them had small airway affection.

Descriptive analysis among COPD and bronchial asthma groups is shown in Table 1.

Comparison between the asthma and the COPD group with the normal acoustic analysis values (according to Kotby) showed a highly significant difference (Table 2).

Video laryngostroboscopic examination in the bronchial asthma group showed that one (3.3%)

Table 1 Descriptive analysis among the chronic obstructive pulmonary disease and bronchial asthma groups

	Bronchial asthma (mean±SD)	COPD (mean±SD)	*t*-Test	*P* value
Age (years)	43.57±10.70	57.43±9.79	5.236	<0.001**
Pack-years (in current and ex-smokers)	0±0	44.11±33.44	2.150	0.001*
Duration of disease (years)	12.93±9.19	18.07±7.99	2.309	0.025*
Duration of ICS use (years)	3.69±4.71	6.62±6.40	1.818	0.076
FEV1/FVC	59.19±9.23	48.96±10.75	3.954	<0.001**
FEV1 (% of predicted)	58.50±22.34	36.43±18.18	4.198	<0.001**
FVC (% of predicted)	78.93±26.44	59.15±22.74	3.107	0.003*
MMEF (% of predicted)	27.41±14.70	15.52±9.24	3.752	<0.001**
H/N ratio	11.29±1.03	14.00±0.16	54.398	<0.001**
Shimmer (db)	0.90±0.14	1.06±0.24	0.969	0.336
Jitter (%)	0.97±0.13	2.02±0.20	23.771	<0.001**
Pitch	198±12.82	203±0.0	87.869	<0.001**

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; H/N, harmonic-to-noise ratio; MMEF, maximal midexpiratory flow. *Statistically significant. **Highly statistically significant.

Table 2 Comparison between the asthma and the chronic obstructive pulmonary disease group with the normal acoustic analysis values (according to Kotby [10]

	Bronchial asthma (mean±SD)	COPD (mean±SD)	Normal (mean±SD)	BA and normal		COPD and normal	
				t-Test	*P* value	*t*-Test	*P* value
H/N ratio	11.29±1.03	14.05±1.16	14.64±1.34	10.856	<0.001*	1.978	0.050*
Shimmer	0.95±0.12	1.06±0.24	0.52±0.26	8.225	<0.001*	8.359	<0.001*
Jitter	0.97±0.13	2.02±0.20	0.34±0.15	17.384	<0.001*	36.807	<0.001*
Pitch	208.29±12.82	2±0.0	185.56±14.49	6.435	<0.001*	69.384	<0.001*

BA, bronchial asthma; COPD, chronic obstructive pulmonary disease; H/N ratio, harmonic-to-noise ratio. *Statistically significant.

patient had diffuse congestion of both vocal cords, two (6.7%) patients had bilateral edema, three of them (10%) had increased vascularity, and one (3.3%) patient had unhealthy mucosal covering of the vocal folds. However, 6.7% suffered increased whitish, sticky, and viscid secretions and a 1 mm glottic gap. Two (6.7%) of the COPD patients showed diffuse vocal fold congestion, four (13.3%) patients had edema, three (10%) patients had unhealthy mucosal covering, and only one (3.3%) patient showed Reinke's edema of the vocal folds. Moreover, three (10%) cases had glottic gap, four (13.3%) cases had ventricular band hyperadduction, and five (16.7%) cases had viscid secretions.

Stroboscopy showed that three (10%) asthma patients had asymmetry in amplitude and phase and two (6.7%) had decreased amplitude and glottic gap. In COPD patients, five (16.7%) had asymmetry in phase, four (13.3%) had asymmetry in amplitude of both vocal folds, six (20%) cases had decreased amplitude, and three (10%) patients had glottic gap. All patients had normal glottic wave. There was no statistical significance between the two groups (P=0.448).

Auditory perceptual assessment (modified GRBAS scale) showed that five (16.7%) asthma patients suffered strained-leaky voice and four (13.3%) cases had grade 1 (mild) dysphonia and one (3.3%) had grade 2 (moderate) dysphonia. In the COPD group, seven (23.3%) patients had strained-leaky voice and two (6.7%) had irregular voice character; five (16.7%) patients had grade 1 dysphonia, whereas four (13.3%) had grade 2 dysphonia. There was no statistical significance between the two groups (P=0.323; NS).

Correlation between auditory perceptual assessment and spirometry in bronchial asthma patients showed a significant correlation (Table 3 and Fig. 1).

In the present study, although there was a positive correlation between pack-years and voice parameters (grade of dysphonia, ventricular band hyperadduction, decrease in amplitude, and both jitter and shimmer), there was no statistical significance (P=0.391; NS). There was no statistical significance between the effects of pressurized metered dose inhler (pMDI) and dry-powdered inhalers (DPI) use on voice in both groups (P=0.087; NS); however, pMDI users showed much more percentage of affection in all qualitative and quantitative voice parameters.

Treatment distribution among both groups for ICS and antimuscarinic inhalers is described in Table 4.

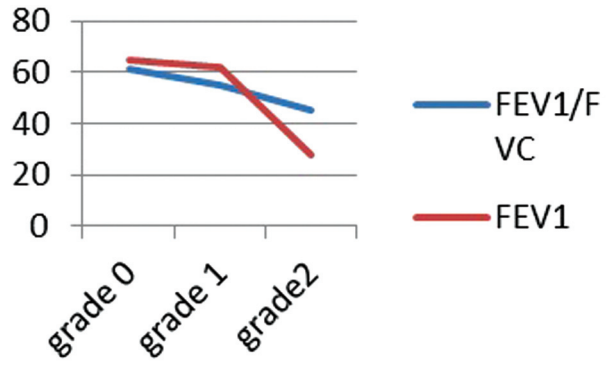
This study showed that, in the bronchial asthma group, fluticasone propionate (FP) users had the least H/N, with a significant statistical correlation, as well as least pitch and highest shimmer and jitter compared with beclomethasone dipropionate and budesonide users (P=0.024*; HS (Fig. 2). A significant statistical correlation (P=0.036*; HS) was found between ipratropium inhalation usage and increased shimmer in the COPD group in comparison with tiotropium bromide and glycopyrronium users, whereas in the asthma group there was no statistically significant correlation with type of antimuscarinic inhaler used; however, ipratropium users had higher shimmer, jitter, and less pitch.

Table 3 Correlation between auditory perceptual analysis and spirometry in bronchial asthma patients

Spirometry	Grade of dysphonia		Character of voice	
	T-test			
	T	*P* value	T	*P* value
FEV1/FVC	8.376	<0.001*	14.379	<0.001*
FEV1	3.804	0.035*	5.330	0.029
FVC	1.322	0.283	2.663	0.114
MMEF	3.419	0.047*	6.296	0.018*

EFV1, forced expiratory volume in the first second; FVC, forced vital capacity; MMEF, maximal midexpiratory flow. *Statistically significant.

Fig. 1



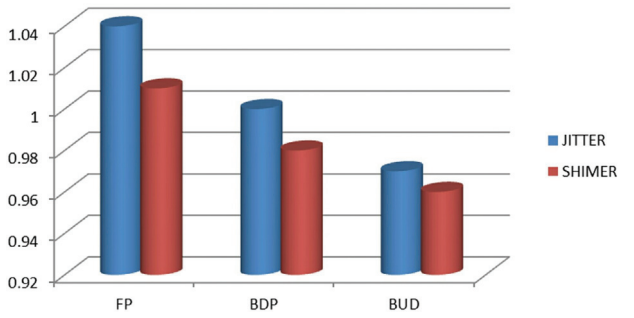
Correlation between grade of dysphonia and forced expiratory volume in the first second/forced vital capacity and forced expiratory volume in the first second

Discussion

In the present study, 30% of COPD patients showed variable grades of dysphonia (mild-to-moderate) and impaired voice quality, in the form of strained-leaky voice in 23.3% and irregular voice in 6.7% of patients. Laryngoscopic examination showed that 36.6% of patients had structural changes in the vocal folds – bilateral vocal fold edema, unhealthy mucosal covering, diffuse congestion of both vocal folds, and increased vascularity and telangiectasia.

These findings could be attributed to irritation of the laryngeal mucosa, or formation of deposits due to

Fig. 2



Comparison between types of inhaled corticosteroids used in asthma patients as regards jitter and shimmer

Table 4 Treatment distribution among both groups for inhaled corticosteroids and antimuscarinic inhalers

	Bronchial asthma [*n* (%)]	COPD [*n* (%)]	Total [*n* (%)]	χ^2	*P* value
Types of ICS inhaler					
None	6 (20.0)	5 (16.7)	11 (18.3)	11.175	0.011*
FP	6 (20.0)	4 (13.3)	10 (16.7)		
BUD	12 (40.0)	5 (16.7)	17 (28.3)		
BDP	6 (20.0)	16 (53.3)	22 (36.6)		
Types of ICS device					
pMDI	4 (16.7)	16 (64.0)	20 (40.8)	13.145	<0.001*
DPI	16 (66.7)	9 (36.0)	25 (51.0)		
Nebulized	4 (16.7)	0 (0.0)	4 (8.2)		
Antimuscarinic inhalers					
None	23 (76.7)	24 (80.0)	47 (78.3)	6.926	0.074
Ipratropium	6 (20.0)	1 (3.3)	7 (11.7)		
Tiotropium	1 (3.3)	2 (6.7)	3 (5.0)		
Glycopyrronium	0 (0)	3 (10.0)	3 (5.0)		

BDP, beclomethasone dipropionate; COPD, chronic obstructive pulmonary disease; BUD, budesonide; DPI, dry-powdered inhalers; FP, fluticasone propionate; ICS, inhaled corticosteroids; pMDI, pressurized metered dose inhalers. *Statistically significant.

inhalation of steroids or as an effect of changed gottal mechanism and laryngeal airflow. Moreover, smoking is a major risk factor for changes in the conformation of the vocal folds, producing mainly glottic edema [11].

Ventricular band hyperadduction was found in 13.3%, and glottic gap of 1 mm was found in 10%. The patients' trials to compensate for the small glottic gap by glottic and supraglottic hyperactivity could explain the appearance of strained quality, which is an analog to compensatory hyperfunctional elements. These led to a tense voice that was perceived as strained quality. Voice is also perceived as leaky in addition to strained when the strained voice with increased glottic and supraglottic activity is associated with air escape through glottal gap.

These results are in agreement with the study by Darweesh *et al.* [12] to detect the laryngeal findings in COPD and asthma patients, but slightly lower than the results of Jeffery [13], who detected laryngeal findings (swelling, congestion, and ventricular hypertrophy) in 60% of COPD patients.

The glottic gap found on stroboscopic examination in 10% of COPD patients in our study could be explained on the basis of muscle strain present due to faulty respiratory support, which would also account for the diminished amplitudes together with the asymmetries [14]. Pearson and Claverley [15] found that about 46% were divergent from ideal glottic closure in COPD patients, and 56% were detected in the study by Darweesh *et al.* [12], which were higher than the percentages reported in this study.

This discrepancy could be attributed to the different method of selection of the patients; in the previous studies patients enrolled complained of hoarseness, whereas our patients in this study were stable and did not have any voice complaints, although they had undetectable early voice affection upon examination.

Acoustic analysis showed a highly significantly decreased H/N ratio and increased jitter and shimmer for all patients of both groups (100%). It was reported by Kotby [16] that any subtle deviation in acoustic parameters may reflect the pathological changes in voice (dysphonia). The highly statistically significantly affected acoustic parameters could be attributed to the fact that the oscillating character and mechanical properties of the vibratory edges of the vocal folds are affected by the resultant pathological effects of COPD as irregularities in the free edge of vocal folds, congestion, and fusiform glottic gap [17]. This was similar to the results advocated by Acharya *et al.* [18] and Darweesh *et al.* [12], in which the acoustic analysis showed an overall statistically significant difference between the COPD group and the normal group.

The source of increased jitter and shimmer lies in a combination of anatomical and physiological changes in the vocal folds. An increase in the vocal fold mass and/or reduced stiffness of the cover are considered the most plausible causes of this change. Jitter is considered to reflect the stability of vocal fold vibration, whereas shimmer is thought to be related to the regularity of vocal fold contact. It is thus plausible that edema interferes with the adequacy and consistency of contact between the vocal fold edges during phonation, which would result in increased shimmer values in smokers. The values obtained for H/N ratio were attributed by Acharya *et al.* [18] to increased breathiness in the voice due to reduced subglottic pressure built up below the vocal folds of individuals with COPD, because of which presence of noise in the spectrum was higher in them.

Therefore, the dysphonia detected in 30% of the COPD patients was due to organic causes. Moreover, it was due to functional causes, in the form of signs of vocal abuse and compensatory ventricular hyperadduction.

In this study, there was a positive correlation between pack-years and voice changes, although not statistically significant. Similar to the present study, Weber [19], in their study to determine the influence of smoking on changes in vocal production in smokers, showed a direct correlation of the length of cigarette smoking with the degree of alteration, roughness, breathiness, vocal tension, and instability. The same was found by Damborenea TaJada *et al.* [20] and El-Maghraby and Mohamed [21].

In the present study, bronchial asthma patients showed that 16.7% of the patients had mild-to-moderate grade of dysphonia and changed character of voice in the form of strained-leaky voice. This was lower than that reported in the study by Darweesh *et al.* [12], who showed that 24% of bronchial asthma patients had various grades of dysphonia and strained and leaky voice was seen in 12%; this can be attributed to the choice of stable nondysphonic patients in this study. This is in agreement with Muzeyyen *et al.* [22], who reported that allergic asthma might cause a faulty use of voice and vocal fold injury. They detected impaired voice quality in 17.5% of cases.

Laryngoscopic examination showed that 20% of patients had structural changes in the vocal folds. These findings are consistent with the study by Viveka *et al.* [23], who detected laryngeal findings, including edema and ventricular hypertrophy in 30% of bronchial asthma patients, but it was lower than that detected by Darweesh *et al.* [12].

Muzeyyen *et al.* [22] attributed these changes mainly to tissue reaction and fluid accumulation due to irritation by inhaled steroids. Chronic cough, throat clearing, allergens, and release of inflammatory mediators such as histamine may also cause congestion and fluid accumulation.

In the asthma group, stroboscopy showed glottic gap in 6.7%. It was much less than that reported by Darweesh *et al.* [12], who found that 64% of patients had an incomplete glottic closure (glottic gap). Muzeyyen *et al.* [22] showed that an incomplete glottal closure was the most prominent symptom in these asthmatic patients and constituted about 60% of the examined cases, and this could reflect detection of an early vocal fold pathology in our patients before significant complaints, in contrast to the patients in the previous studies who were already dysphonic.

The dysphonia that was detected in 20% of the bronchial asthma patients was due to organic causes as detected using videolaryngostroboscopy and acoustic analysis. These findings are consistent with the study by Eva *et al.* [24], who found dysphonia in 25% of bronchial asthma patients.

The present study showed a highly significant correlation between spirometric severity and both grade of dysphonia and character of voice in bronchial asthma patients.

Voice affection was detected (by means of laryngo-stroboscopy and auditory perceptual assessment) in only 30% of the 83% of COPD patients using inhaled steroid inhaler and in 20% of the 80% of asthma patients on ICS. The same was stated in the study by Lavy *et al.* [17], in which the physical findings were minimal in patients with dysphonia caused by the use of steroid inhalers, with only mild edema of the vocal cords. The changes appear to be the result of a mucosal inflammatory reaction to the steroid. This matched the study conducted in 1983 by Williams *et al.* [25]. The use of ICS predisposes to the development of an inflammatory infiltrate; however, this does not necessarily have a clinical correlate [26].

Patients on pMDIs showed higher voice abnormalities (43.7%) than those on DPIs (11.1%), although there was no significant correlation between these parameters and type of inhaler device. This is consistent with the study by Selroos *et al.* [27], who noted that the frequency of dysphonia decreased from 21 to 6% when patients switched from an MDI to a DPI. This change may be attributable to differences in vocal cord positioning when using a DPI compared with an MDI.

The present study also showed that FP users in the asthma group had a significantly lower H/N ratio compared with beclomethasone dipropionate and budesonide, as well as least pitch and highest shimmer and jitter. Lavy *et al.* [17] and Roland *et al.* [28] stated that the prominent mucosal changes seen was attributable to fluticasone's greater potency and tissue affinity compared with other inhaled steroid preparations.

The present study showed a significant statistical correlation between ipratropium inhalation usage and increased shimmer in the COPD group.

The problem is probably multifactorial, depending on the following factors: the steroid (e.g. preparation, carrier substance, dose of steroid, and regimen); the manner in which it is propelled into the airways (i.e. the inhaler device); intrinsic inflammation of the upper airway in asthmatic patients; mechanical irritation because of cough; intercurrent inflammatory disease (e.g. rhinitis and postnasal catarrh); and intercurrent inflammatory stimuli (e.g. smoking and noxious agents in the workplace).

However, we are aware that our study has several limitations; it included a limited number of patients. Future research may decide to reduce intragroup variability among key demographic factors, duration of the disease, and doses of medications used. Moreover, aerodynamic characteristics were not studied; it would have been of value to correlate them with the pulmonary function testing in our patients, for better assessment of the breath support provided for each glottic cycle. Finally, our patients were stable and did not have any voice complaints, indicating that our results represent early voice affection in those asymptomatic patients.

In conclusion, all COPD and bronchial asthma patients had dysphonia, either due to organic or functional causes. Voice changes were directly correlated with degree of severity and FP inhalation use in bronchial asthma patients and with ipratropium bromide inhalation in the COPD group.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1 Cassiani RA, Aguiar-Ricz L, Santos C, Martinez J. Glottal competence in COPD. *Audiol Commun Res* 2013; **18**:149–154.

2 Shastry A, Balasubramanium RK. Acoustic and perceptual analysis of voice in individuals with chronic obstructive pulmonary disease. *Proceedings of 43rd Annual Convention of Indian Speech and Hearing Association (ISHCON 46); February 7–9* 2014, Kochi, Kerala, India. [Last accessed 2014 Feb 7].

3 Buffels J, Degryse J, Decramer M, Heyrman J. Spirometry and smoking cessation advice in general practice: a randomized clinical trial, *Respir Med* 2006; **100**:2012–2017.

4 Kim S, Mon J, Chung S, Lee H. A short-term investigation of dysphonia in asthmatic patients using inhaled budesonide. *J Voice* 2011; **25**:88–93.

5 Dworkin J. Laryngitis: types, causes, and treatments. *Otolaryngol Clin North Am* 2008; **41**:419–436.

6 Menvielle G, Luce D, Goldberg P, Bugel I, Leclerc A. Smoking, alcohol drinking and cancer risk for various sites of the larynx and hypopharynx: a case-control study in France. *Eur J Cancer Prev* 2004; **13**:165–172.

7 Global Initiative for Asthma. Global strategy for asthma management and prevention; 2016. Available at: http://www.ginasthma.org. [Accesed May 2016].

8 Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2016. Available at: Http//Www.Goldcopd.Org/ [Accesed May 2016].

9 American Thoracic Society/European Respiratory Society Task Force. *Standardization of spirometry: Eur Resp J* 2005; **26**:319–338.

10 Kotby NM. *Clinical vocology*. Egyptian Society Of Phoniatrics and Logopedics; 2016. 15–30

11 Behlau MS, Gama AC. Study of constancy of acoustic measurements of prolonged vowels and Consecutive trials in women without voice complaints and in women with dysphonia Ana Cristina Côrtes Gama 1, Mara Suzana Behlau. *Revsocbrasfonoaudiol* 2009; **14**:8–14.

12 Darweesh E, Saleh M, Elkholy A, Elassal N *The effect of chronic obstructuve pulmonary diseases and bronchial asthma on the larynx*. Cairo: Ain Shams University; 2006.

13 Jeffery PK. Structural and inflammatory changes in COPD: acomparison with asthma. *Thorax* 1998; **53**:129–136.

14 Fabbri L, Coggo Al, Cosmo P. Asthma diagnosis Chapter 6 In: Byme PO, Thomson NC editors. *Adults in manual of asthma management*. UK: 1997. 83–102.

15 Paerson MG, Claverley PM. Clinical and laboratory assessment. In: Claverley P, Pride N. *Chronic obstructive pulmonary disease*. London: Chapman and Hall l; 1996. 310–322

16 Kotby NM. Voice disorders, recent diagnostic advances. *Egypt J Otolaryngol* 1986; **3**:89.

17 Lavy J, Wood G, Rubin J. Dysphonia associated with inhaled steroids. *J Voice* 2000; **14**:581–588.

18 Acharya R, Anuradha S, Balasubramanium R. Voice related quality of life in individuals with chronic obstructive pulmonary disease. *Int J Med Res Health Sci* 2014; **4**:110–117.

19 Santos KW, Echeveste SS, Vidor DC Association between lung function and vocal affections arising from tobacco consumption. *Int Arch Otorhinolaryngol* 2014; **18**:11–15.

20 Damborenea TaJada J, Fernandez Liesa R, Llorente A, Naya G, Marín G, Rueda G, *et al.* The effect of tobacco consumption on acoustic voice analysis (Spanish). *Acta Otorrinolaringol Esp* 1999; **50**: 448–452.

21 El-Maghraby A, Mohamed E. Voice changes in patients with COPD. *Egypt J Chest Dis Tuberc* 2014; **63**:561–567.

22 Muzeyyen D, Emel E, Ismail K. Subjective and objective evaluation of the voice quality in patients with asthma. *J Voice* 2005; **10**:1016.

23 Viveka LA, Lucyna S, Marika H, Lena S. Vocal function in relation to inhalatory steroid therapy in patients with asthma. *J Voice* 2002; **XX**:60–72.

24 Eva ZO, Ihre EI, Hammarberg B. Voice problems as side effects of inhaled corticosteroids in asthma patients – a prevalence study. *J Voice* 2004; **18**:403–414.

25 Williams AJ, Baghat MS, Stableforth DE. Dysphonia caused by inhaled steroids: recognition of a characteristic laryngeal abnormality. *Thorax* 1983; **38**:813–821.

26 Bhalla RK, Taylor W, Jones AS. The inflammation produced by corticosteroid inhalers in the pharynx in asthmatics. *Clin Otolaryngol* 2008; **33**:581–586.

27 Selroos O, Backman R, Forsen KO. Local side effects during 4-year treatment with inhaled corticosteroids: a comparison between pressurized metered-dose inhalers and turbohaler. *Allergy* 1994; **49**:888–890.

28 Roland NJ, Bhalla RK, Earis J. The local side effects of inhaled corticosteroids: current understanding and review of the literature. *Chest* 2004; **126**:213–219.