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Original Research Article

Dysphonia: Associated with Inhalation Corticosteroids

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Abstract

Inhaled corticosteroid (ICS) therapy has emerged as a cornerstone in the pharmacological management of asthma, exerting potent anti-inflammatory effects within the respiratory tract. Despite its efficacy, the occurrence of dysphonia, characterized by alterations in voice quality, represents a prevalent local adverse event associated with ICS administration, affecting a substantial proportion of patients, with reported incidence rates ranging from 5% to 58%.The precise pathophysiological mechanisms underlying dysphonia secondary to ICS therapy remain incompletely elucidated. However, it is hypothesized that dysphonia may be attributed to the deposition of active corticosteroid particles within the oropharyngeal region during inhalation. Subsequent local effects, such as myopathy or mucosal irritation in the laryngopharynx, are postulated to contribute to the development of dysphonia. In the clinical evaluation of dysphonia, a comprehensive assessment must incorporate considerations of concurrent ICS use, given its potential role as a contributing factor. In order to mitigate this adverse effect, several pragmatic strategies have been proposed. These include the judicious utilization of the lowest effective dosage of ICS, the implementation of spacer devices during medication administration to optimize drug delivery to the lower airways while minimizing oropharyngeal deposition, and adherence to post-inhalation hygiene practices, such as gargling, mouth rinsing, and facial washing, aimed at mitigating local corticosteroid accumulation. Regular maintenance of spacer devices through meticulous cleaning procedures is also advocated to prevent the accumulation of medication residues.

Keywords: Inhaled corticosteroid therapy, dysphonia, oropharynx deposition, spacer device, asthma control.

Introduction

Voice represents a multifaceted aspect of human communication, embodying not only the conveyance of thoughts and ideas but also the essence of personal identity. [1] A normal voice is not merely pleasing to the ear but also resonates with a balance of sound emanating from the mouth and nose, aligning harmoniously with the individual's age, gender, and occupation.

The process of voice production involves a symphony of physiological mechanisms, [2] orchestrated by the coordinated interaction of various anatomical structures, including the lungs, pharynx, larynx, mouth, and an array of muscles. Essential prerequisites for the production of voice include phonation, resonance, and articulation, each playing a crucial role in the formation of spoken words and communication. [3,4] Voice disorders encompass a spectrum of conditions that disrupt the normal function and quality of the voice. These disorders may arise from a myriad of factors, ranging from vocal abuse and environmental exposures to systemic diseases and neurological abnormalities. [5,6] Classified into categories such as organic, non-organic, movement disorders, and systemic disorders, each subtype presents with distinct pathological characteristics and clinical manifestations. [5] From benign conditions like vocal nodules and polyps to more serious ailments such as laryngeal carcinoma and neurological movement disorders, voice disorders can significantly impair an individual's ability to communicate effectively and impact their overall quality of life. [7-9]

Inhaled corticosteroids (ICSs) are a cornerstone in the management of reactive airway diseases such as asthma and chronic obstructive pulmonary disease (COPD). While ICSs offer substantial benefits in improving lung function and reducing exacerbations, their use is not without potential adverse effects on voice production. [10-12] Oropharyngeal and laryngeal adverse effects, often overlooked, can manifest as hoarseness, throat irritation, and dysphonia. [7] Laryngeal examination may reveal mucosal edema, vocal cord

lesions, and other structural abnormalities indicative of steroid inhaler laryngitis. The impact of ICSs on voice production remains a topic of on-going research, with conflicting evidence regarding their effects on voice quality and function. [13-15]

Factors influencing the adverse effects of ICSs on voice production include the type of steroid, delivery method, dose, and patient-specific factors such as underlying comorbidities and individual susceptibility. Strategies to mitigate these adverse effects include optimizing ICS formulations with lower oropharyngeal deposition, adjusting dosing frequency, and considering alternative medications with a more favorable side effect profile. [16] Ciclesonide, a non-halogenated ICS with reduced oropharyngeal deposition and high lung deposition, presents a promising alternative for individuals experiencing voice-related side effects with traditional ICS formulations. [17,18]

Evaluation and diagnosis of voice disorders encompass a comprehensive approach involving various assessment techniques. Perceptual analysis, acoustic and aerodynamic measures, quality of life assessments, and laryngeal imaging serve as invaluable tools in characterizing the severity of voice disorders, assessing treatment outcomes, and guiding therapeutic interventions. Through a holistic understanding of voice production and disorders, healthcare providers can optimize management strategies to alleviate symptoms, restore vocal function, and improve the overall quality of life for individuals affected by voice-related conditions. [19]

In conclusion, voice serves as a cornerstone of human interaction and expression, reflecting not only the nuances of language but also the intricacies of individual identity. Voice disorders, while diverse in etiology and presentation, pose significant challenges to communication and well-being. By recognizing the complexities of voice production and the potential impact of pharmacological interventions such as ICSs, healthcare providers can tailor management strategies to mitigate adverse effects and optimize outcomes for individuals with voice-related conditions. Through a multidisciplinary approach encompassing assessment, intervention, and on-going support, individuals can regain their voice and reclaim their ability to connect, communicate, and thrive in their personal and professional lives.

Methodology:

Ethical Clearance: Prior to commencement, ethical clearance was obtained from the Institutional Ethical Committee of the Department of Otorhinolaryngology, Head and Neck Surgery, SMHS Srinagar, in collaboration with the Department of Medicine, Government Medical College, and Srinagar.

Study Design: This cross-sectional study was conducted over a period of two years, from September 2019 to September 2021.

Participant Enrollment: A total of 400 patients were enrolled in the study after obtaining written informed consent in the local language.

Inclusion Criteria: Patients attending the medical outpatient department (OPD) who had been using inhaled corticosteroids (ICS) for more than six months.

Exclusion Criteria: Patients with organic causes for voice changes were excluded from the study.

Data Collection: Detailed medical history was obtained from each participant, focusing on chronic obstructive airway disease (COAD) and bronchial asthma. Information regarding the type, duration, and frequency of ICS use was recorded. Participants were questioned about any history of voice changes. Evaluation of voice quality was performed using the Grade, Roughness, Breathiness, Asthenia, and Strain (GRBAS) score. The Voice Handicap Index (VHI) was also utilized to assess the impact of voice disorder on the participants' quality of life. Laryngeal examination was conducted using indirect laryngoscopy (I/L), fiber optic laryngoscopy (FOL), and detailed videoscopic examination of the larynx.

Stroboscopy was performed in selected cases to assess vocal cord vibratory patterns. Various parameters and abnormal findings of the vocal cords were noted, including vocal cord mobility, status of the laryngeal mucosa, and approximation of the vocal cords.

Assessment Tools:

GRBAS Score: Each participant's voice quality was assessed based on the severity of grade, roughness, breathiness, asthenia, and strain, with scores ranging from 0 to 3 for each parameter. The total score ranged from 0 to 15.

Voice Handicap Index (VHI): Participants completed the VHI questionnaire, which evaluates the impact of voice disorder on physical, functional, and emotional aspects of their quality of life.

Data Analysis: Collected data were analyzed using appropriate statistical methods to determine correlations between ICS use, voice quality, and laryngeal abnormalities.

Table 1: Voice handicap index [20]

My Voice makes it difficult for people to hear me	0	1	2	3	4
People have difficulty understanding me in noisy	0	1	2	3	4
room	0	1	2	3	4
My voice difficulties restrict personal and social life	0	1	2	3	4
I feel left out of conversations because of my voice	0	1	2	3	4
My voice problem ,causes me to lose income	0	1	2	3	4
I feel as though I have to strain to produce voice	0	1	2	3	4
The clarity of my voice is unpredictable	0	1	2	3	4
My voice problem upsets me	0	1	2	3	4
People ask what's wrong with your voice	0	1	2	3	4

0= Never 1= Almost never 2= Sometimes 3= Almost always 4= Always. Total score will range from 0-40

Laryngeal Examination: The larynx was examined using indirect laryngoscopy (I/L), fiber optic laryngoscopy (FOL), and detailed videoscopic examination. These methods allowed for a comprehensive assessment of the laryngeal structures.

Stroboscopy: Stroboscopy was performed in symptomatic cases to further evaluate vocal cord vibratory patterns. This technique provided valuable insights into the dynamic behaviour of the vocal cords during phonation.

Assessment of Vocal Cord Parameters: During examination, various parameters and abnormal findings of the vocal cords were meticulously noted. This included assessing the mobility of vocal cords, evaluating the status of the laryngeal mucosa, and examining the approximation of vocal cords. These observations were crucial for identifying any potential abnormalities or pathologies.

Statistical Analysis: Data collected during the study were entered into a Microsoft Excel spreadsheet for analysis. Continuous variables were summarized using mean and standard deviation, while categorical variables were presented as percentages. Statistical comparison was performed using the Paired t-test. Two-sided p-values were reported, with a significance level set at $p < 0.05$ indicating statistical significance. This rigorous statistical analysis helped to elucidate any significant associations or differences between variables of interest.

Result & Discussion

In the current study, a total of 111 subjects were included. The average age of the enrolled participants was 59.5 years, with a standard deviation of 11.8 years. The youngest participant was 24 years old, while the oldest was 91 years old.

Table 2: Mean age of the enrolled subjects

Parameters	No. of patients	Min.	Max.	Mean	SD
Age (years)	111	24	91	59.47	11.80

Min = Minimum; Max = Maximum; SD = Standard deviation

Table 3: Age Distribution of enrolled subjects (n=111)

Age group (years)	No. of patients	percent
0-30	3	2.7
31-60	44	39.6
61-90	63	56.8
>90	1	0.9
total	111	100.0

Majority of the enrolled subjects (56.8%) were of 61-90 years age group. Only one subject enrolled was aged above 90 years.

Table 4: Gender distribution of the enrolled subjects

Gender	No. of patients	percent
Male	49	44.14
Female	62	55.86
total	111	100.0

Among the total enrolled subjects, majority (55.86%) were females.

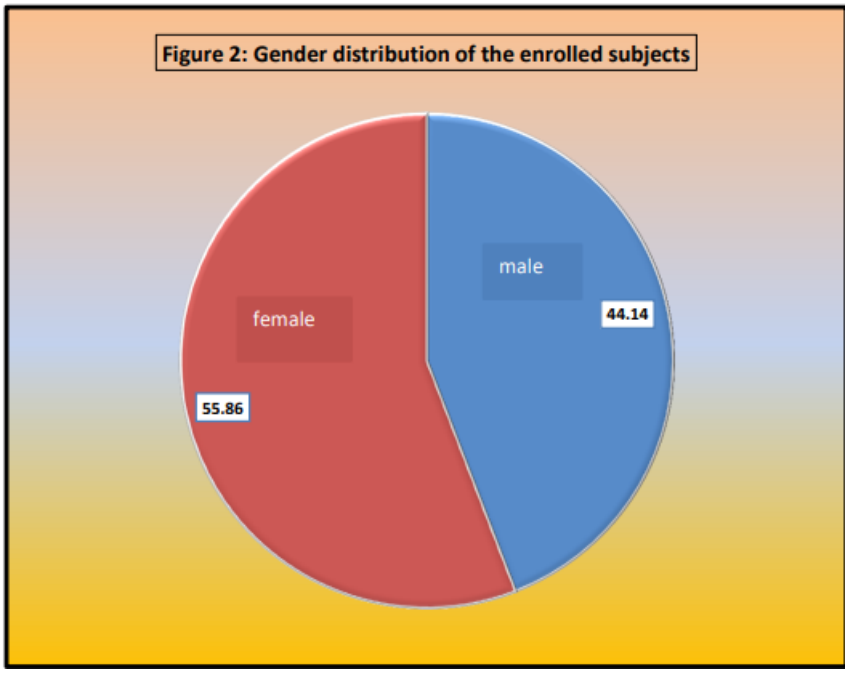

Figure 1: Gender distribution of the enrolled subjects

Table 5: Representing patient distribution as per laryngeal symptoms.

	Number	percent
Asymptomatic	25	22.52
symptomatic	86	77.48
Total	111	100

Out of 111 patients, 86 (77.48%) were symptomatic for Laryngeal effects of ICS and 25 (22.52%) were asymptomatic.

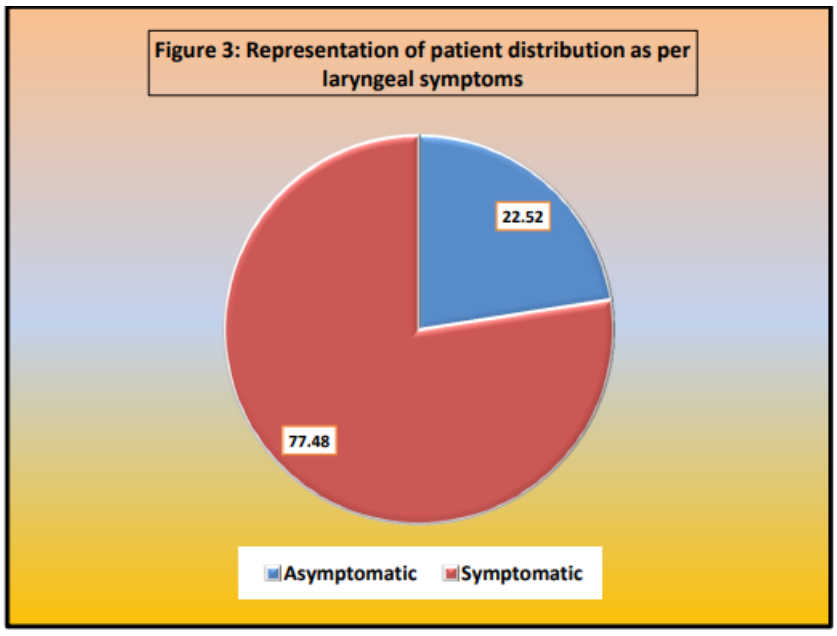

Figure 3: Representing patient distribution as per laryngeal symptoms

Table 5: Representing symptoms of laryngeal effects of inhalational corticosteroids (n=86)

Symptoms	No. of patients (N =86)	Percent
Dysphonia	47	55
Dry Cough	5	6
Reduced Power	8	9
Cough During Inhalation	5	6
Dryness Of Throat	5	6
Throat Irritation	4	5
Fissured Tongue	1	1
Vocal Strain and Fatigue	9	10
Throat Clearing	1	1
Dysphagia	1	1

Table Representing symptoms of Laryngeal effects of inhalational Corticosteroids (ICS) in symptomatic patients (86). Among the symptomatic patients, most common presenting symptom is dysphonia (55%), vocal strain and fatigue (10%), reduced power (9%)

Table 7: Presenting the laryngeal findings on video-stroboscopy in patients on Inhalational corticosteroids. (n=111)

findings	Frequency	percent
Normal findings	49	44
abnormal findings	62	66

Among 111 patients on ICS 66% had abnormal laryngeal findings (66%) on video-stroboscopy, while as 44% had normal stroboscopy.

Table 8: Presenting abnormal laryngeal findings on Videostroboscopy in patients on ICS. (n=62)

Findings	No. of patients	Percent
Hyperaemia /Mucosal Oedema	20	32.25
Leukoplakia /Granulations /Hyperkeratosis	5	8.06
Irregular Vocal Cords /Vocal Cord Atrophy/Vocal Fold Bowing on Phonation	24	38.70
Candidiasis	7	11.29
Posterior Commissure Hypertrophy	3	4.83
Vocal Cord Nodule	3	4.83
Total	62	100.0

Majority of the subjects have, irregular vocal cords/vocal cord atrophy/vocal fold bowing on phonation (38.70%) followed by hyperaemia/mucosal oedema (32.25%).

Table 9: Presenting relation between type of inhaler and their respective duration of use

Inhaler Used	No. of patients	Percent	Mean duration of Use (Years)
Beclomethasone	1	.9	21.0
Budesonide	87	78.4	5.39
Ciclesonide	3	2.7	2.9
Fluticasone Propionate	20	19.0	2.7
Total	111	100.0	4.74

Majority of the enrolled subjects (78.4%) were using Budesonide, the mean duration of use was 5.39 years, Fluticasone Propionate in 19% subjects, the mean duration of use of 2.7 years

Table 10: Showing relation between use of different types of ICS (mcg/day) in symptomatic patients (n=86)

Drugs	Symptomatic (%)
Beclomethasone400	1(1.16)
Budesinide400	50(58.13)
Budesinide800	20(23.25)
Ciclesonide160	2(2.32)
Ciclesonide320	1(1.16)
Fluticasone Propionate1000	5(5.81)
Fluticasone Propionate500	7(8.13)
Total	86(100)

Among the symptomatic patients (n=86), majority of patients (58.13%) were using Budesonide 400mcg/day followed by Budesonide. 800mcg/day in 23.25% patients and Fluticasone propionate 500mcg/day in 8.13% patients.

Table 11: Representing duration of inhalational corticosteroid use in 111 subjects

Duration of Steroid Use (Years)	No of Asymptomatic Patents	No of Symptomatic Patents (%)	Total
<2	9	13 (15.11)	22
2-4	8	32 (37.20)	40
>4	8	41 (47.67)	49
Total	25	86 (100)	111

Among the 86 symptomatic patients, maximum number of patients (47.67%) was using ICS > 4 years, 32 (37.20%) patients between 2-4 years.

Table 12: presenting the relation between daily doses (mcg/d) of different types of ICS with laryngeal symptoms.

Drugs	Dose	DYS	DC	RP	CDI	DT	TI	FT	VSF	TC	DYSP
	400								1		
BDP	Total								1		
	400	28	3	3	3	5	4	1	2		
BUD	800	14	1	3	0	0	0	0	2		
	500	0		1	2				3	1	1
FP	1000	3		1	0				1	0	0
CIC	160	1	1								
	320	1	0								
Total		47	5	8	5	5	4	1	9	1	1

Abbreviations: BDP-Beclomethasone dipropionate, BUD-Budesonide; FP-Fluticasone propionate; CIC: Ciclesonide; Dys: Dysphonia; DC- Dry Cough; RP: Reduced Power; CDI: Cough during Inhalation; DT: Dryness of Throat; TI: Throat Irritation, FTD: Fissured Tongue and Dry Throat; VSF: Vocal Strain and Fatigue; TC: Throat Clearing; Dysp: Dysphagia,

Among the symptomatic patients (86), a total of 47 subjects suffered. dysphonia, majority of them (n=28) were on Budesonide (400mcg/day) followed by Budesonide 800mcg/day (n=14).

A total of 9 subjects suffered vocal strain and fatigue, of which 3 subjects were on Fluticasone. Propionate 500 mcg/d and 1 patient on Fluticasone propionate 1000 mcg/day.

4 patients were on Budesonide (2 patients on 200 and 2 patients on 400mcg/d). The data is represented in table 11.

Table 13: Representing relation between laryngeal findings on video stroboscopy and daily dose (mcg/day) in asymptomatic patients (n=25) on ICS use

Drug	Dose	VCN	HYP/ME	IVC/VCA/VFB	CAND	Normal
Budesonide	400	1	1	2		10
	800		1	1	1	
Fluticasone Propionate-	500		1			3
	1000		2	1	1	
Total		1	5	4	2	13

Majority (13) of asymptomatic patients have normal findings followed by hyperaemia/mucosal oedema

Table 14: representing relation between Laryngeal findings in symptomatic patients (n=86) on video-stroboscopy and daily dose (mcg/day) in patients on ICS

Drug	Dose	LEU/GRA/HYPK	HYP/ME	IVC/VCA/VFB	CAND	Normal	VCN
BDP	400					1	
BUD	400		6	9	3	27	5
	800	1	6	8	1	4	0
CIC	160		1			1	
	320		1			0	
FP	500		1	1	1	4	
	1000	1	1	3	0	0	
Total		2	16	21	5	37	5

Majority of the subjects show normal laryngeal findings (37) followed by IVC/VCA/VFB (21). ABBREVIATIONS: LEU- Leukoplakia; GRA- Granulations; HYPK Hyperkeratosis; HYP-Hyperaemia; ME-Mucosal Oedema; IVC-Irregular vocal cord; VCA-Vocal cord atrophy; VFB-Vocal fold bowing; CAND Candidiasis; VCN-Vocal cord nodule.

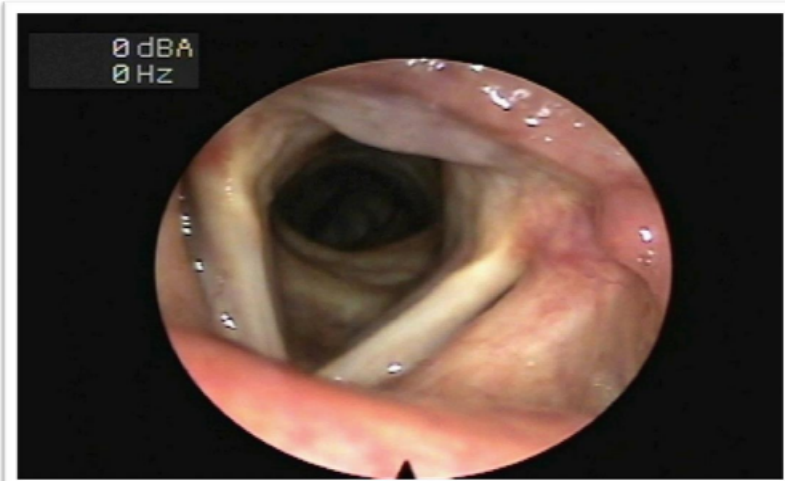

Image 1: Image showing normal bilateral vocal cords and surroundings structures

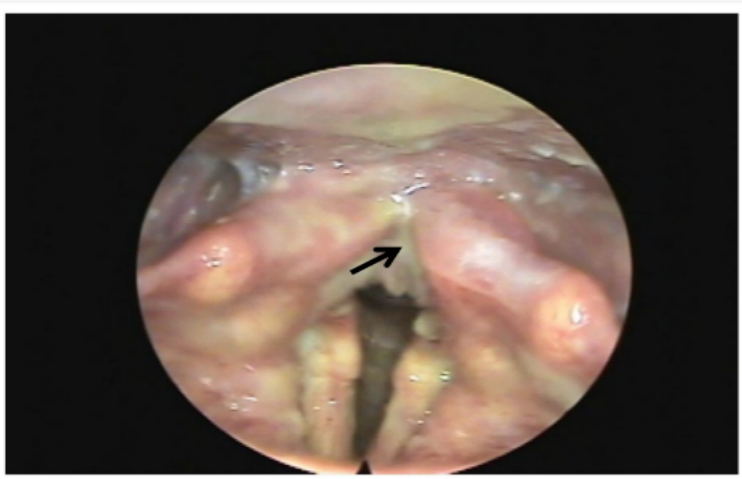

Image 2: Image showing normal bilateral vocal cords and surroundings structures

Image 3: Image showing bilateral leukoplakia and atrophic vocal cords

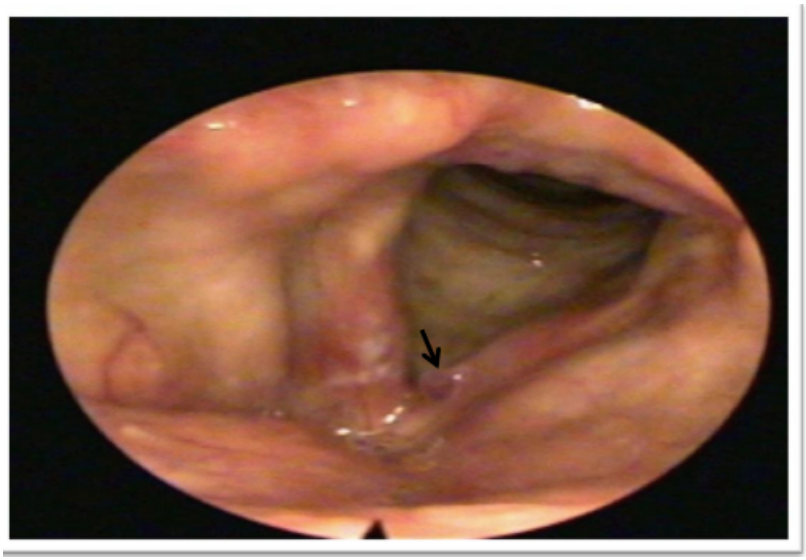

Image 4: Image showing bilateral vocal cord oedema and hyperemia (R > L) and left vocal cord polyp

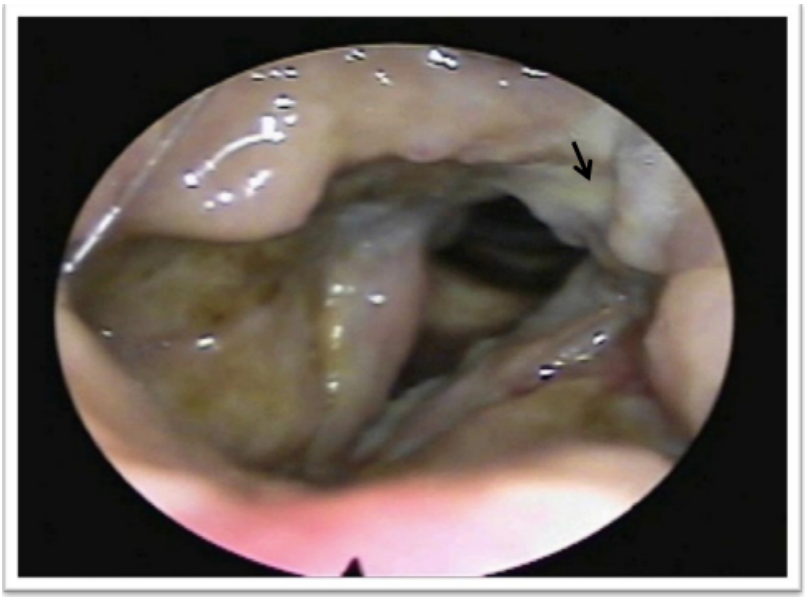

Image 5: Image showing right vocal cord oedema, left irregular vocal cord and posterior pachyderma

Discussion

The study titled "Laryngeal effects of inhalational corticosteroids (ICS) in patients with bronchial asthma and chronic obstructive airway disease (COAD): a hospital-based cross-sectional study" was conducted at the Department of Otorhinolaryngology and Head and Neck Surgery, SMHS Hospital Srinagar. It included 111 patients using ICS for more than 6 months, encompassing both genders and various age groups attending the medical OPD. Patients with organic causes for voice changes were excluded.

The primary objectives were to determine the frequency of voice disorders in patients using ICS, evaluate the effects of ICS on the larynx, and assess other local pathologies associated with steroid inhaler laryngitis. The majority of participants were in the 6th-9th decade of life, with a mean age of 59.47 years. Most patients (77.48%) experienced symptomatic voice changes related to ICS use. Dysphonia was the most common symptom reported (55%), followed by vocal strain and fatigue (10%).

Video-stroboscopy revealed abnormal laryngeal findings in 66% of patients, including irregular vocal cords, vocal fold atrophy, vocal fold bowing, hyperaemia, mucosal edema, candidiasis, vocal cord nodules, and leukoplakia/ granulations/ hyperkeratosis. Budesonide was the most used ICS (78.4%), followed by fluticasone propionate (19%). Among symptomatic patients, those using budesonide at varying doses reported the highest incidence of dysphonia. Similar studies have reported dysphonia rates ranging from 5% to 58%.

Overall, our findings highlight the significant impact of ICS on laryngeal health, emphasizing the

need for careful monitoring and management of potential adverse effects associated with their long-term use.

Conclusion

In conclusion, our cross-sectional study conducted at the Department of Otorhinolaryngology and Head and Neck Surgery, SMHS Hospital Srinagar, sheds light on the laryngeal effects of inhalational corticosteroids (ICS) in patients with bronchial asthma and chronic obstructive airway disease (COAD). With a sample size of 111 patients, encompassing both genders and various age groups, we aimed to determine the frequency of voice disorders in individuals using ICS for more than 6 months. Our findings reveal that a significant majority of patients (77.48%) using ICS experienced symptomatic voice changes, with dysphonia being the most reported symptom. Video-stroboscopy further unveiled abnormal laryngeal findings in 66% of patients, ranging from irregular vocal cords to mucosal abnormalities such as hyperaemia and edema. Budesonide emerged as the most used ICS, with a higher incidence of dysphonia reported among its users compared to those using other corticosteroids.

These results underscore the substantial impact of long-term ICS use on laryngeal health, emphasizing the importance of vigilant monitoring and management of potential adverse effects. Given the high prevalence of voice disorders and laryngeal abnormalities associated with ICS use, healthcare providers should exercise caution and consider alternative treatment options or adjunct therapies to mitigate these effects.

Overall, our study contributes to the growing body of evidence highlighting the need for comprehensive assessment and management strategies tailored to the laryngeal effects of ICS in patients with bronchial asthma and COAD. By raising awareness of these potential complications, we hope to enhance patient care and improve outcomes for individuals relying on long-term corticosteroid therapy for respiratory conditions.

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