ORIGINAL RESEARCH PAPER

ENT

KEY WORDS:

LARYNGEAL EFFECTS OF INHALATIONAL CORTICOSTEROIDS IN PATIENTS OF BRONCHIAL ASTHMA AND CHRONIC OBSTRUCTIVE AIRWAY DISEASE

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ABSTRACT

Dysphonia, a common voice disorder, significantly impacts the quality of life for individuals affected by bronchial asthma and chronic obstructive airway disease (COAD). This cross-sectional study aimed to assess the prevalence of voice disorders in patients using inhaled corticosteroids (ICS) and investigate their impact on laryngeal function. A total of 111 patients were enrolled, with 77.48% presenting symptomatic laryngeal effects of ICS. Dysphonia was the most prevalent symptom (55%), followed by vocal strain and fatigue (10%). Video-stroboscopy revealed abnormal laryngeal findings in 66% of patients, with irregular vocal cords/vocal cord atrophy/vocal fold bowing being most common (38.70%). Budesonide was the most commonly used ICS (78.4%), followed by Fluticasone Propionate (19%). Among symptomatic patients, Budesonide 400mcg/day was most frequently prescribed (58.13%). Duration of ICS use varied, with 47.67% using it for more than 4 years. Dysphonia was predominant among symptomatic patients, with Budesonide (400mcg/day) being most associated. Among asymptomatic patients, normal laryngeal findings were most common (13). The study provides insights into demographics, symptoms, and laryngeal findings associated with long-term ICS use in bronchial asthma and COAD. Dysphonia was common, and video-stroboscopy revealed various laryngeal abnormalities. Monitoring laryngeal function in patients on long-term ICS therapy is crucial. Limitations include the study's single-center design and cross-sectional nature. Further research is warranted to elucidate mechanisms underlying steroid inhaler laryngitis.

INTRODUCTION:

Dysphonia, characterized by altered vocal quality, pitch, loudness, or vocal effort, significantly impacts communication and quality of life related to voice (1). It has a lifetime prevalence of 29.9% and a point prevalence of 6.6% among adults aged ≤64 years, with women being more frequently affected than men (2,3). It can be categorized into organic and functional types. Organic dysphonia results from factors unrelated to voice use and encompasses various etiologies(4). On the other hand, functional dysphonia (FD) occurs without structural or neurological laryngeal pathologies and may represent 10%-40% of cases in multidisciplinary voice clinics (5).

The gold standard examination for visualizing LDP is the video-laryngo stroboscopic exam (6). The effectiveness of inhaled corticosteroids (ICS) in managing stable chronic obstructive pulmonary disease (COPD) remains uncertain, unlike their established role in asthma treatment. While inflammation is present in COPD airways, it differs from asthma's immunopathology (7,8). Short-term use of corticosteroids, both inhaled and systemic, may benefit certain COPD patients with partially reversible airway obstruction (9). Long-term uncontrolled studies suggest systemic corticosteroids could slow lung function decline, but pose serious side effects (10). Prospective trials on ICS in COPD demonstrate varying degrees of efficacy, with some suggesting better outcomes in patients exhibiting "asthma features," such as high bronchodilator response and bronchial responsiveness. (11) The study aims to assess the prevalence of voice disorders in patients using inhaled corticosteroids (ICS) in medical outpatient departments (OPDs) and to investigate the impact of ICS on laryngeal function, including evaluating local pathologies like steroid inhaler laryngitis (SIL).

MATERIALS AND METHODS:

This cross-sectional study, conducted with Institutional Ethical Committee clearance, spanned from September 2019 to September 2021 at the Department of Otorhino laryngology, Head and Neck Surgery, SMHS Srinagar, in collaboration with the Department of Medicine, Government Medical College, Srinagar. A total of 400 patients, providing written informed consent in the local language, were enrolled from the medical outpatient department (OPD). Inclusion criteria comprised patients on inhaled corticosteroids (ICS) for over 6 months, while those with organic causes for voice changes were excluded. Detailed medical histories, including information on Chronic Obstructive Airway Disease (COAD) and Bronchial Asthma, were obtained, along with details regarding ICS type, duration, and frequency of use, and any history of voice changes. Voice assessment utilized the Grade, Roughness, Breathiness, Asthenia, and Severity (GARBS) score and the Voice Handicap Index (VHI). Laryngeal examination, encompassing indirect laryngoscopy (I/L), fiber optic laryngoscopy (FOL), and detailed videoscopic assessment, was conducted, with stroboscopy performed in symptomatic cases. Various parameters and abnormal findings of the vocal cords were noted, including vocal cord mobility, laryngeal mucosa status, and vocal cord approximation. Data was entered in Microsoft Excel spreadsheet. Continuous variables were summarized as mean and standard deviation. Categorical variables were summarized as percentages. Comparison was done using Paired ,,t test.Two-sided P values was reported and a p value of <0.05 was considered as statically significant.

RESULTS:

In the current study, a total of 111 subjects participated, with a mean age of 59.5 years (Standard deviation = 11.8). The age range spanned from 24 to 91 years, with the majority (56.8%) falling within the 61-90 years age group. Females constituted 55.86% of the enrolled subjects.

Among the enrolled patients, 77.48% presented with symptomatic laryngeal effects of inhalational corticosteroids (ICS), while 22.52% were asymptomatic. Dysphonia emerged as the most common presenting symptom among symptomatic patients (55%), followed by vocal strain and fatigue (10%) and reduced power (9%).

Video-stroboscopy revealed abnormal laryngeal findings in 66% of patients, with irregular vocal cords/vocal cord atrophy/vocal fold bowing on phonation being the most prevalent (38.70%), followed by hyperaemia/mucosal edema (32.25%).

Budesonide emerged as the most commonly used ICS (78.4%), with a mean duration of use of 5.39 years, followed by Fluticasone Propionate (19%) with a mean duration of 2.7 years. Among symptomatic patients, Budesonide 400mcg/day was the most frequently prescribed dosage (58.13%), followed by Budesonide 800mcg/day (23.25%) and Fluticasone propionate 500mcg/day (8.13%).

The duration of ICS use varied, with 47.67% of symptomatic patients using ICS for more than 4 years and 37.20% using it between 2-4 years. Among symptomatic patients, dysphonia was the predominant symptom, with the majority of affected individuals using Budesonide (400mcg/day) or Budesonide 800mcg/day.

Among asymptomatic patients, normal laryngeal findings were most common (13), followed by hyperaemia/mucosal edema (5). Overall, the study provides detailed insights into the demographics, symptoms, and laryngeal findings associated with long-term ICS use in patients with bronchial asthma and chronic obstructive airway disease.

DISCUSSION:

The study conducted at SMHS Hospital Srinagar aimed to investigate the laryngeal effects of long-term inhalational corticosteroid (ICS) therapy in patients with bronchial asthma and chronic obstructive airway disease (COAD). A total of 111 patients, comprising both males and females across all age groups, who had been using ICS for more than 6 months were included in the study. The primary objectives were to estimate the frequency of voice disorders in these patients, evaluate the impact of ICS on the larynx, and identify any other local pathologies associated with steroid inhaler laryngitis.

The majority of the patients (56.8%) were in their 6th to 9th decade of life, with a mean age of 59.47 years. This demographic distribution was consistent with previous studies, indicating a similar age profile among patients with asthma and COAD. Similar findings were reported by **Krecicki et al.(12) and Soriano et al.(13),** suggesting that the prevalence of asthma and COPD overlap syndrome increases with advancing age.

In terms of symptomatic presentation, 77.48% of the patients reported voice changes associated with ICS use, while 22.52% were asymptomatic. Dysphonia was the most commonly reported symptom, affecting 55% of the symptomatic patients. Other laryngeal symptoms included vocal strain and fatigue, reduced power, cough during inhalation, dryness of throat, dry cough, throat irritation, and throat clearing. These findings were consistent with previous studies by **Monika et al.(14) and Williams et al.(15),** which reported dysphonia as a common side effect of ICS use, with incidences ranging from 5% to 58%.

Video-stroboscopy was utilized to assess the laryngeal effects of ICS in all 111 patients. The findings revealed abnormal laryngeal findings in 66% of the patients, with 44% showing normal results. Among the abnormal findings, irregular vocal cords, vocal cord atrophy, vocal fold bowing, hyperemia, mucosal edema, candidiasis, leukoplakia, granulations, hyperkeratosis, posterior commissure hypertrophy, and vocal cord nodules were observed. These findings were consistent with previous studies by Acar et al., **Krecicki et al.(12),** and **Hassan et al.(16),** which reported similar laryngeal abnormalities associated with ICS use.

Budesonide was the most commonly used ICS in 78.4% of the patients, followed by fluticasone propionate, ciclesonide, and beclomethasone dipropionate. Higher doses of ICS were associated with a higher prevalence of adverse effects, particularly dysphonia. Studies by **Galvan et al(17) and Rachelefsky et al(18)** demonstrated that budesonide was associated with a higher risk of dysphonia compared to other ICS medications.

In summary, the study highlights the significant impact of long-term ICS therapy on laryngeal health in patients with bronchial asthma and COAD. Dysphonia was the most common symptom reported, and video-stroboscopy revealed various laryngeal abnormalities associated with ICS use. These findings underscore the importance of monitoring laryngeal function in patients receiving long-term ICS therapy and warrant further investigation into the mechanisms underlying steroid inhaler laryngitis. The study's small sample size from a single hospital and its cross-sectional design limit the generalizability and ability to establish causal relationships, respectively.

CONCLUSION:

In conclusion, our study underscores the significant adverse impact of inhalational corticosteroids (ICS) on the laryngeal mucosa, manifesting primarily as dysphonia, vocal strain and fatigue, and reduced vocal power. Through video-stroboscopy, we identified common laryngeal findings in patients experiencing adverse effects of ICS, including irregular vocal cords, vocal cord atrophy, vocal fold bowing on phonation, hyperaemia, mucosal oedema, and candidiasis. Notably, Budesonide in 400mcg and 800mcg doses, along with Fluticasone propionate in 500mcg, emerged as the most frequently prescribed ICS. Our findings emphasize the importance of considering both the type of ICS and the duration of its use in understanding the pathogenesis of laryngeal adverse effects, offering valuable insights for clinical management and patient care.

TABLE 1: Mean age of the enrolled subjects

PARAMETER	NO.OF PATIENTS	MIN	MAX	MEAN	SD
Age	111	24	91	59.47	11.8

TABLE2: Presenting abnormal laryngeal findings on video stroboscopy in patients on ICS. (n=62)

Findings	No.of patients	Percentage
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

Table 3: Presenting relation between type of inhaler and their respective duration of use.

Inhaler Used	No. of patients	percent	Mean Duration of Use (Years)
Beclomethasone P	1	0.9	21.0
Budesonide 2.9	87	78.4	5.39
Ciclesonide	3	2.7	2.9
Fluticasone Propionate	20	19.0	2.7
Total	111	100.0	4.74

Table 4: 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)

Table 5: 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
BDP	400								1		
	TOTAL								1		
BUD	400	28	3	3	3	5	4	1	2		
	800	14	1	3	0	0	0	0	2		
FP	500	0							3	1	1
	1000	3							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

Table 6: 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
Bude sonide	400	1	1	2		10
	800		1	1	1	
Fluticaso ne pro pionate	500		2			
	1000		2	1	1	
		1	5	4	2	13

Table 7: 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	NOR MAL	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	
PP	500		1	1	1	4	
	1000	1	1	3	0	0	
		2	16	21	5	37	5

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.

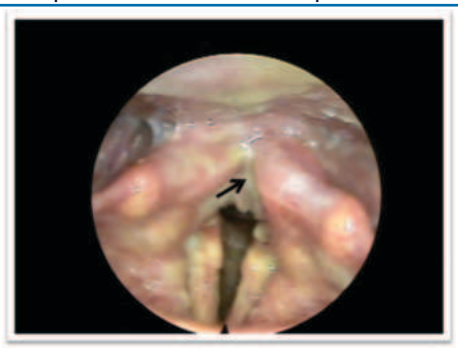

Fig 1:Image showing irregular vocal cords and posterior pachyderma (→) and mucosal hyperemia.

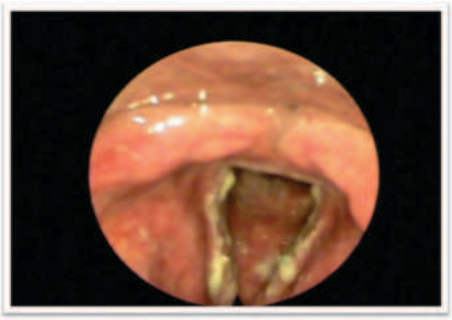

Figure2: Image showing bilateral leukoplakia and atrophic vocal cords.

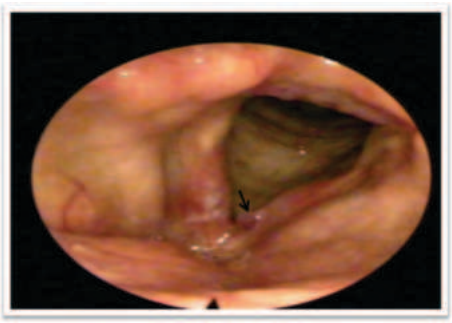

Figure 3: Image showing bilateral vocal cord oedema and hyperemia (R > L) and left vocal cord polyp (→)

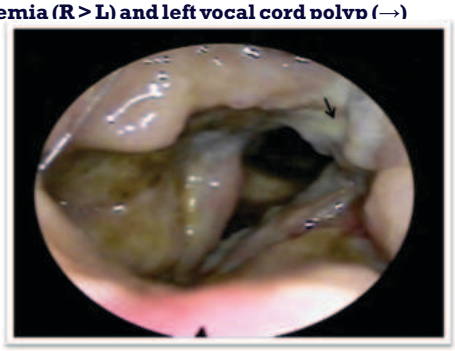

figure 4: Image showing right vocal cord oedema, left irregular vocal cord and posterior pachyderma (→)

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