Original article

Glycaemic Status of COPD Patients on Long-term Steroid Therapy

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Abstract

Background:
Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Among the pharmacological therapy, inhaled beta-2 agonist and anticholinergics are the mainstay therapy of COPD along with corticosteroid. Steroid therapy is associated with various potential adverse effects like steroid induced deranged glycemic status.

Objective:
This study was aimed to assess the glycaemic status of COPD patients on long term steroid therapy.

Methods:
This cross-sectional observational study was conducted in the department of Medicine, Rangpur Medical College and Hospital, Rangpur, Bangladesh from January 2022 to June 2022. A total of 55 COPD patients were included in the study based on inclusion and exclusion criteria. Detailed information was obtained in each case according to protocol. Complete history was taken either from patient or accompanying attendants. A thorough clinical examination was done. Relevant investigation reports were collected. All the information was recorded according to fixed protocol. Collected data were classified, edited, coded and entered the computer for statistical analysis by using SPSS version 23.

Results:
Out of 55 COPD patients, the majority (41.8%) patients belonged to age 51-60 years with mean age 55.5±8.3 years. Male patients were predominant 47(85.5%) and male to female ratio was 5.88:1. Most (72.7%) of the patients received inhaled and 15(27.3%) received systemic with or without inhaled corticosteroid. Only 1 (2.5%) patient was found FBS ≥7.0 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled corticosteroid group. One (2.5%) patient was found plasma glucose 2 hours after a 75-gm glucose ≥11.1 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled corticosteroid group. One (2.5%) patient was found HbA_1C > 6.5% in inhaled group and 2(13.3%) in systemic with or without inhaled group. The differences were not statistically significant (p>0.05) between two groups.

Conclusion:
Majority of the patients had normal HbA1c who were taking inhaled corticosteroid than systemic with or without inhaled corticosteroids.

Keywords: COPD, Glycaemic status, Steroid therapy, Long-term

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Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a progressive and partially reversible lung inflammatory disorder caused by long-term exposure to noxious particles and gases.[1] It is defined as chronic cough and sputum from airways for at least three months in two consecutive years without other causes, and is associated with irreversible airflow limitation, making it a part of chronic bronchitis and

emphysema.[2] COPD is a major cause of mortality worldwide, accounting for 5% of all deaths in 2005.[3] It is predicted to become the third leading cause of death by 2030.[4] In Bangladesh, COPD prevalence is estimated at 12.5%,[5] while in India, it is 3.7%, with an estimated 15 million cases. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria predict a prevalence of 13.5% in Bangladesh [6] and 13.5% in India and the estimated burden of COPD in India is about 15 million cases.[7,8] Inhaled corticosteroid therapy, commonly prescribed for COPD, has been linked to an increased incidence of Type 2 Diabetes Mellitus.[9] COPD patients are at risk of developing diabetes due to factors such as sedentary lifestyle, smoking, obesity, oxidative stress, and increased inflammation. Inhaled beta-2 agonists and anticholinergics are the mainstay therapy for COPD,[10] with only 5-10% being truly oral steroid dependent.[11] Inhaled corticosteroid is preferred over oral steroids for improving symptoms and reducing exacerbations (approx. in 65% the of the COPD population in some studies).[12,13] However, steroid therapy can have potential adverse effects on the adrenal axis, peptic ulcer disease, infections, skin, bone mineral density, and fractures.[14-17] However, glucose control is more difficult with steroid-based therapy in COPD.[18,19] One study shows 15% of COPD patient requires additional treatment for hyperglycemia as compared to 4% of a control group.[20,21] In addition to this some case reports describe the loss of glucose control in patients receiving ICS-based therapy.[22,23] On the other hand, lung health studies did not demonstrate an increased risk for a new diagnosis of diabetes mellitus in individuals receiving ICS-based therapy.[24,25] But it was associated with the individual on prolonged oral steroids.[26,27] Recent studies suggest high-dose inhaled corticosteroid (ICS) therapy may contribute to diabetes mellitus in COPD patients, but this concept remains controversial. Overuse of ICS is a critical issue, and adequate patient selection and monitoring are necessary to improve safety and efficacy. This study aims to explore the association between steroid therapy and glycemic state in the COPD population.

Methods:

This cross-sectional observational study was conducted in the inpatient department of Medicine, Rangpur Medical College and Hospital, Rangpur, Bangladesh from January 2022 to June 2022 on 55 diagnosed patients with COPD on steroid based therapy (continuous inhaled/ Interrupted systemic or both) for at least 6 months, both sexes and who give written informed consent to participate in the study were enrolled in the study. Patients with known conditions like type 2 diabetes, bronchial asthma, interstitial lung disease, coronary artery disease, cardiomyopathies, connective tissue disorders, organ transplant recipients, immunosuppressive therapy recipients, co-morbidities like renal, liver, and heart failure, and those on hyperglycemia-causing drugs were excluded from the study. The data collected from COPD patients using a semi-structured interview questionnaire, including socio-demographic factors, medical examinations, diagnosis, and drug history. Physical examinations were documented, and patients were divided into two groups based on steroid therapy: one group took only inhaled corticosteroid, and another group took systemic steroids with or without inhaled corticosteroid. Patients were required to remain fasting for at least 10 hours and not more than 16 hours, and tests were conducted in the morning due to hormonal diurnal effects on glucose. Patients were also prohibited from exercising, eating, drinking, and smoking before the test. A venous blood sample about 5ml was collected by venipuncture during fasting and 2 hours after 75 gm glucose intake by trained laboratory technician. Blood samples were collected in tubes with or without EDTA. Samples were centrifuged for 5 min of 3000 rpm to collect the plasma. Collected plasma was used to determine for Fasting blood sugar and 2 hours after 75gm glucose by spectrophotometric methods using an autoanalyzer. HbA1C by HPLC (high performance liquid chromatography) method using an another autoanalyzer. The data set was analyzed using SPSS and MS Excel, with a Chi square test used to compare populations. Statistical significance was determined at p values <0.05.

Results:

Out of 55 COPD patients, mean age was found 55.5±8.3 years with a range from 42 to 73 years. Majority (41.8%) patients belonged to age 51-60 years, 47(85.5%) were male, 17(30.9%) were service holder and 12(21.8%) were overweight. The mean BMI was found 23.0±3.5 kg/m^2 with range from 17.9 to 30.9 kg/m^2 (Table-I).

Table-I: Socio-demographic characteristics of the study participants (N=55)

Characteristics	no. (%)
Age (years)	
41-50	16(29.1)
51-60	23(41.8)
61-70	15(27.3)
71-80	1(1.8)
Mean±SD	55.5±8.3
Range (min-max)	42.0-73.0
Sex	
Male	47(85.5)
Female	8(14.5)
Occupational status	
Service holder	17(30.9)
Farmer	15(27.3)
Businessman	9(16.4)
Housewife	7(12.7)
Rickshaw puller	5(9.1)
Unemployed	2(3.6)
BMI (kg/m2)	
<18.5	4(7.3)
18.5-24.9	37(67.3)
25.0-29.9	12(21.8)
≥30.0	2(3.6)
Mean±SD	23.0±3.5
Range (min-max)	17.9-30.9

40 (72.7%) patients received inhaled and 15(27.3%) received systemic with or without inhaled corticosteroid. Regarding the glycaemic status, 3(5.5%) patients were found HbA_1C >6.5 percent. The mean HbA_1C was found 5.2±0.5 percent with range from 4.4 to 6.7 percent (Table-II).

Table-II: Mode of steroid therapy and Glycaemic status based on HbA1C of the study participants (N=55)

Variables	no. (%)
Mode of steroid therapy	
Inhaled	40(72.7)
Systemic with or without inhaled	15(27.3)
Glycaemic status based on HbA1C	
4.0-5.6 (Normal)	48(87.3)
5.7-6.4 (Pre-diabetes)	4(7.3)
>6.5 (Diabetes)	3(5.4)
Mean HbA1C	5.2±0.5%
Range	4.4-6.7 %

One (2.5%) patient was found FBS ≥7.0 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.072). One (2.5%) patient was found plasma glucose 2 hours after a 75 gm glucose ≥11.1 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.072). One (2.5%) patient was found HbA_1C >6.5 percent in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.146). These differences were not statistically significant between the two groups (Table-III).

Table-III: Association between mode of steroid therapy with FBS, Plasma glucose 2 hours after a 75-gm glucose and HbA1C (%) (N=55)

Glycaemic status	Mode of steroid therapy (n=55)		p-value
	Inhaled (n=40, 72.7%)	Systemic with or without inhaled (n=15, 27.3%)	
FBS (mmol/L)- no. (%)			
<6.0 (Normal)	38(95)	11(73.3)	
6.1-6.9 (Impaired fasting glucose)	1(2.5)	2(13.3)	0.072ns
≥7.0 (Diabetes)	1(2.5)	2(13.3)	
Plasma glucose 2 hours after a 75-gm glucose (mmol/L) - no. (%)			
<7.8 (Normal)	38(95)	11(73.3)	
7.8-11.0 (Impaired fasting glucose)	1(2.5)	2(13.3)	0.072ns
≥11.1 (Diabetes)	1(2.5)	2(13.3)	
HbA1C (%) - no. (%)			
4.0-5.6 (Normal)	37(92.5)	11(73.3)	
5.7-6.4 (Pre-diabetes)	2(5)	2(13.3)	0.146ns
>6.5 (Diabetes)	1(2.5)	2(13.3)	

ns=not significant; p-value reached from chi square test

Discussion:

This cross-sectional study was carried out with the aim of assessing the glycaemic status of 55 COPD patients on long term steroid therapy from January to June 2022. The present study findings were discussed and compared with previously published relevant studies. Out of 55, 40(72.7%) of the patients received inhaled and 15(27.3%) received systemic with or without inhaled. In a study done by Verma et al[27] reported that 26 patients (56.52%) were taking both inhaled and systemic corticosteroids, 12 patients (26.09%) were taking only inhaled corticosteroids, and 8 patients (17.39%) were taking systemic corticosteroid therapy. Which is quite lower than studies conducted in developed countries by Donohue et al,[12] Spencer et al,[13] and Calverley et al.[14] In the study 15.22% patients had diabetes mellitus which is comparable to studies conducted by Slatore et al,[19] Faul et al,[20] McEvoy et al,[22] Suissa et al[21] and Gartlehner et al.[28] Razzaque et al[29] also found clinically diagnosed 80 consecutive COPD patients (50%) receiving only bronchodilator without inhaled corticosteroid/systemic steroid were recruited as control. Present study observed that 1(2.5%) patient was found FBS ≥7.0 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.072). In this study observed that 1(2.5%) patient was found plasma glucose 2 hours after a 75 gm glucose ≥11.1 mmol/L in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.072). In a study conducted by Verma et al[27] observed that among 12 patients (100%) on inhaled corticosteroid therapy only, 8 patients (66.67%) were euglycemic, 3 patients (25%) had impaired glucose tolerance and 1 patient (8.33%) had diabetes mellitus. Among 8 patients (100%) taking systemic corticosteroid therapy only, 3 patients (37.5%) were euglycemic, 3 patients (37.5%) had impaired glucose tolerance and 2 patients (25%) had diabetes mellitus. Among 26 patients (100%) on inhaled and systemic corticosteroid therapy, 14 patients (53.85%) were euglycemic, 8 patients (30.77%) had impaired glucose tolerance and 4 patients (15.38%) had diabetes mellitus.[27] Present study observed that 1(2.5%) patient was found HbA_1C >6.5 percent in inhaled group and 2(13.3%) in systemic with or without inhaled group (p=0.146). Verma et al[27] revealed that out of 7 patients (100%) having diabetes mellitus, 1 patient (14.29%) were taking inhaled corticosteroids, 2 patients (28.57%) were taking systemic corticosteroid therapy and 4 patients (57.14%) were taking both inhaled and systemic corticosteroid therapy. Smyllie et al[30] and Slatore et al[9] concluded that glucose control is more difficult with steroid based therapy in COPD. Impaired glucose tolerance and diabetes mellitus is less common in patients taking inhaled corticosteroid therapy which is comparable to previous studies conducted by Spencer et al[13] and Calverley et al.[14] In our country a study conducted by Razzaque et al documented that the relationship between glycemic control and various complications, such that for a reduction in 1% of HbA1c, there was a 35% reduction in the risk of complications, a 25% reduction in diabetes-related deaths, a 7% decrease in all-cause mortality and an 18% reduction in combined fatal and non-fatal myocardial infarction.[29] Using a population-based study on COPD patients, they found that the use of inhaled corticosteroids is associated with a significant increase in the risk of incidence of diabetes. The observed treatment-related changes in HbA1c in their study are consistent with another report of hyperglycemia and glucosuria in an asthmatic patient who took very high doses of inhaled Fluticasone propionate (FP) at a dose of 2 mg/day; however, the mean increase resulting from Fluticasone propionate (FP) therapy, relative to the individual's baseline, is substantially smaller than in that individual case.[31]

Conclusion:

In this study it was observed that glycemic control was better in most of the patients of COPD on inhaled corticosteroid than systemic with or without inhaled corticosteroids. Patients instituting therapy with high doses of inhaled corticosteroids should be assessed for possible hyperglycemia, warrant further studies to clarify this issue in larger numbers of patients with COPD.

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