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Effectiveness of Steroid Stewardship on Glycemic Control among Asthma and COPD Patients at a Tertiary Care Hospital

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ABSTRACT

To estimate the glycemic control among Asthma and Chronic Obstructive Disease (COPD) Patients prescribed with corticosteroids and to identify their adverse effects. A prospective cross-sectional study was conducted in pulmonology department at multi-speciality hospital after obtaining ethical approval. Totally, 74 patients were enrolled based on inclusion criteria. Glycemic levels were monitored using random blood sugar (RBS) levels before and after steroid administration. Out of 74 patients, 28 patients received budesonide alone, 27 patients received budesonide and oral methyl prednisolone combination and 13 patients received fluticasone propionate as inhalation therapy. RBS values were monitored before and after administration of steroid, which showed hyperglycemia in three diabetic patients (17.65%) with asthma and COPD. There were no significant changes (p value >0.05) in RBS levels before and after steroid intake among non-diabetic and diabetic patients in both asthma and COPD. Steroid stewardship program conducted showed that glycemic monitoring is essential in diabetic patients with asthma and COPD to prevent hyperglycemic episodes. Thereby, we conclude that accurate insulin dosage can be administered with periodic RBS level monitoring, which can be implemented by a steroid stewardship program.

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Introduction

The synthetic analogues of the natural steroid hormones produced by the adrenal cortex are called corticosteroids, and these include glucocorticoids and mineralocorticoids. Glucocorticoids are primarily engaged in metabolism and have anti-inflammatory, vasoconstrictive, and immunosuppressive properties.[1] The methodical process of rationally prescribing and monitoring glucocorticoids while weighing the advantages and potential risks for individuals is known as "steroid stewardship".[2] It encompasses the critical components of pre-prescription screening, judicious prescription, and medical management during corticosteroid administration and monitoring after corticosteroid use has been discontinued.[3]

Corticosteroids emphasize hyperglycemia by disrupting glucose metabolism, impairing insulin signalling and promoting insulin resistance in skeletal muscle, liver, and adipose tissue. It also reduce insulin-stimulated glucose uptake and glycogen synthesis while increasing glucose production, leading to hyperglycemia in susceptible individuals.[4,5] In addition to raising episodes of hyperglycemia in people with diabetes, glucocorticoids also have the ability to raise blood glucose levels in non-diabetic individuals. This could result in the development of diabetes in healthy individuals.[6] The Endocrine Society and the American Diabetes Association (ADA) jointly published a consensus report that defined clinically significant hyperglycemia as a Random Blood Sugar level (RBS) higher than 180 mg/dL.[7]

The adverse effects of corticosteroid are dose-dependent, and guidance is to use the lower effective dose in most disease conditions. Low doses of oral steroids are advised for acute exacerbation of COPD (AECOPD) in consensus with GOLD guidelines. Regardless this advice, reports of higher steroid dosage were used in real-world situations are frequent.[8]

Inhaled corticosteroids (ICS) exhibit fewer systemic adverse effects than oral or parenteral, though their impact on glucose metabolism remains less certain.[9] While their effectiveness in treating moderate Chronic obstructive pulmonary disease (COPD) is debated, ICS are considered vital for managing asthma as a key component of anti-inflammatory therapy, particularly recommended for severe COPD and frequent exacerbations.[10]

The development and implementation of steroid stewardship programs (SSP) is critically needed, as their widespread usage is comparable to the over prescription of antibiotics. Better therapeutic outcomes of steroids can be attained with adopting strategies from Thoracic Society of Australia and New Zealand by rational use of steroids in asthma and COPD for adults and paediatrics.[11]

As a result, the pharmacist's active pharmacovigilance reporting is essential to identify the potential adverse events and safety profile associated with various corticosteroids.[3]

Subjects and Methods

Study design and study population:

This prospective cross-sectional study was conducted for six months at Pulmonology Department in a multi-speciality hospital. With25% prevalence of hyperglycemia after steroid administration from previous studies was used to determine sample size with confidence interval of 95%.[12]

The minimum sample required was 72 including the 10% error. About 74 patients were enrolled during our study period. About 74 patients who were willing to participate above 18 years of age and were prescribed corticosteroids as orally and inhalers for the treatment of COPD and asthma with RBS tests results were included in the study. Individuals who were previously on corticosteroids or who were on medications that can cause hyperglycemia are excluded.

Ethical Consideration:

The study protocol was approved by Institutional Human Ethics Committee **(Ref No. EC/AP/1123/02/2024)**.A written informed consent was provided from all individuals prior to their enrollment.

Study Procedure:

Based on inclusion criteria patients who were prescribed corticosteroids for the treatment of Asthma and COPD were enrolled. A data collection form was designed to collect the necessary information for the study. This data collection form included patient demographics, diagnosis, the type of steroid, dosage, mode of administration, duration of therapy and laboratory test results (HbA1c, RBS, and FBS) primarily RBS before and after steroid intake. Monitoring of potential adverse effects from using corticosteroids using the WHO-UMC Causality Assessment Scale. Corticosteroid tapering was done wherever necessary.

Statistical Analysis:

Data were analyzed using Statistical Package for the Social Sciences (SPSS) software (version 25.0). Categorical variables were indicated as frequency (n) and percentage (%). Frequency analysis was performed for all sociodemographic variables and chi-square goodness fit and chi -square test of association were performed to determine the relation between steroids and hyperglycemia. P value <0.05 was considered statistically significant.

Results

The study comprised of 74 patients, with males 54 (73%) and females 20 (27%). Overall, 33 individuals were between the age group of 41-60 years followed by 28 individuals in the age group of 61-80 years. Based on BMI values, 5 patients were obese and 13 patients were considered overweight in this study. Among the total study population, 17 (23%) patients were known to be diabetic. Diagnosis included asthma in 45 patients (60.8%) and COPD in 29 patients (39.2%). The demographics of the study population are shown in Table 1.

This study evaluated the prescription pattern for steroidsin asthma and COPD which reveals budesonide and methylprednisolone combination is prescribed for 27 patients (36.48%), budesonide alone 20 patients (20.7%) and fluticasone propionate for 13 patients (17.57%) was mentioned in table 2. Oral methylprednisolone and budesonide is prescribed for more number of patients in this study.

Table 1. Demographic variables of the study population (n=74)

Demographic Variables	Categories	Frequency (n =74)	Percentage of
Gender	Male	54	73.0%
	Female	20	27.0%
Age (in years)	20-40	11	14.9%
	41-60	33	44.6%
	61-80	28	37.8%
	81-100	2	2.7%
BMI (in kg/m²)	<18	3	4.1%
	18.5-24.9	53	71.6%
	25-29.9	13	17.6%
	>30	5	6.8%
Diabetes	Male	13	17.6%
	Female	4	5.4%
Diagnosis	Asthma	45	60.8%
	COPD	29	39.2%

For all patients enrolled in this study, RBS levels were assessed before administration of steroids and after administration of steroids during afternoon or 2 hours after meals which is demonstrated in table 3. This show that in 18 non-diabetic patients, RBS levels were elevated after initiation of steroids in asthma and COPD whereas, in diabetic patients 3 (17.65%) patients developed hyperglycemia (>200mg/dl) after steroid initiation in asthma and COPD patients. Statistical interference showed that there was no significant difference ($p > 0.05$) between before and after initiation of steroids in both diabetic and non-diabetic patients for the treatment of asthma and COPD but episodes of hyperglycemia (>200mg/dl) was observed in diabetic patients after steroid administration.

Table 2.Prescribing pattern of Steroids in Asthma and COPD (n=74)

Steroids	Route & Dose		Frequency	Percentage
Budesonide	MDI	200 mcg	11	14.86%
		100 mcg	7	9.46%
		160/4.5 mcg	2	2.70%
	Respules	0.5 mg	8	10.81%
Fluticasone propionate	MDI	100 mcg	1	1.35%
		250 mcg	6	8.10%
	Nasal spray	27.5 mcg	6	8.10%
Budesonide + Methyl prednisolone	MDI + Oral MP	250 mcg / 16mg	3	4.05%
		200 mcg/ 16 mg	9	12.16%
	Respules + Oral MP	0.5 mg/ 16 mg	15	20.27%
Fluticasone + Methyl Prednisolone	MDI + Oral MP	250 mcg/ 16 mg	3	4.05%
Budesonide + Hydro-cortisone	Respules + Oral HC	0.5 mg/ 10 mg	2	2.70%
Fluticasone + Hydro-cortisone	MDI + Oral HC	250/ 10 mg	1	1.35%

MDI: Metered Dose Inhaler; MP: Methyl Prednisolone; HC: Hydrocortisone

Table 3. RBS values of Asthma and COPD patients before and after initiation of Cortico-steroids (n=74)

	Non-diabetic patients(n=57)			Diabetic patients(n=17)		
	Sugar levels	Before ster-oid intake	After ster-oid intake	Sugar levels	Before steroid intake	After steroid intake
Asth-ma (n=45)	<120	35	27	<140	3	3
	121-140	3	9	141-160	0	0
	141-160	2	3	161-180	0	0
	161-180	0	1	181-200	2	0
	>180	0	0	>200	0	2
COPD (n=29)	<120	10	10	<140	4	7
	121-140	4	3	141-160	4	2
	141-160	2	4	161-180	1	0
	161-180	1	0	181-200	2	1
	>180	0	0	>200	1	2
P value		0.076	0.363	P value	0.116	0.558

Discussion

Corticosteroids are the primary treatment for asthma and COPD.It is essential to periodically review and prescribe corticosteroids sensibly in order to maximise therapeutic efficacy and minimise adverse events. So, this study mainly aimed to focus on steroid stewardship program on glycemic control in asthma and COPD patients prescribed with inhalation and oral corticosteroids at tertiary care hospital.

Totally, 74 patients with COPD and asthma were included in this prospective cross-sectional study. Among them 73% were male and 27% were female.This finding was similar to studies by Ranaet.al.,[13] and Aryal et.al.,[14] which found that 61.3% and 52.4% of the patients were males respectively. This shows that males are having higher frequencies of asthma and COPD in Indian population.

Based on analysis of the prescription pattern, all 74 patients (100%) were prescribed inhalational steroids, while only 33 patients (44.6%) were prescribed with both oral and inhaled corticosteroids. These results coincide with previous research by D Cruz et.al.,[15] which found that inhaled corticosteroids wasthe most frequently prescribed medication for 74.46% of the population.

In this study budesonide and fluticasone were the two inhaled corticosteroids prescribed for asthma and COPD. Among various corticosteroids budesonide was most frequently prescribed (77%) for asthma and COPD patients in this study which coincides with the earlier studies by Aryal et.al., [14] where budesonide was prescribed in 43.45% of total population. The doses of budesonide were 100 mcg, 160 mcg 200 mcgand 250 mcg as MDI and 0.5 mg as Respuleswhile fluticasone propionate prescribed in 100mcg, 250mcg as MDI and 27.5mcg as nasal spray which correlates with the studies by Haikarainen et.al.,[16] and Hoekx et.al.,[17] where budesonide and fluticasone were prescribed in dose ranges between 100-400mcg.

In oral corticosteroids, methylprednisolone was prescribed in the majority of the patients in this current study for duration of three to five days. This is in evidence with guidelines of Australian Asthma Handbook [18] and GINA [19] (Global Initiative for Asthma) guidelines, which suggest short bursts of OCS, can be prescribed for five to ten days to alleviate the symptoms and severity.

Oral corticosteroids such as hydrocortisone or methyl prednisolone were prescribed for 33 (44.6%) patients in this study. Among them 27 (36.5%) patients received methyl prednisolone, sixpatients undergone suitable steroid tapering from 16 mg to 8 mg, in line with the Williams textbook of endocrinology's 14th edition and the study by Suehs et al.,[20] which suggests tapering off OCS is essential to lessen side effects and adrenal insufficiency.

The glycemic levels were assessed with periodic monitoring of RBS which shows that 2(4.44%) asthma and 1 COPD (3.44%) patients developed steroid induced hyperglycemia (>200mg/dl) which is similar to the study by Price et.al.,[21] where 5% of the study population experienced an increase in blood glucose level.

Patients who received methyl prednisolone combination had shown elevated RBS levels (>200mg/dl) than patients who received other corticosteroids, which is in comparable to the findings of Sweeney et.al.,[22]

In this study we identify that corticosteroids plays a vital role in treating respiratory disease conditions. Combinations of inhaled corticosteroid available globally in different doses. In spite of its adverse events steroids were more commonly prescribed without precautions and safety monitoring. Even though, they were prescribed in minimal doses they may affect the normal homeostasis and impact on disease progression. Here we implemented a steroid stewardship program on glycemic control in asthma and COPD patients and found that there was no significant difference in glycemic levels of patients before and after steroid initiation, but in diabetic patient who received methylprednisolone had developed episodes of hyperglycemia after steroid administration.

So, we recommend that glycemic monitoring of RBS levels in diabetic patients need to be done periodically on daily basis and less frequently for non-diabetic patients, while long acting corticosteroids (Methylprednisolone) should not be recommended in diabetic patients to reduce the

risk hyperglycemia.

The present study had some limitations to be considered. The study had a relatively small sample of 74 patients, which may limit the generalizability of the findings to a broader population. A large sample size would provide more robust results and increase the reliability of the study. The duration of follow-up for assessing outcomes related to steroid intake and glycemic control was short. A longer follow-up period would provide more insights into the long-term effects of treatment and the stability of glycemic control.

Based on glycemic levels of the study population there is a slight raise in glycemic levels but was not able to achieve statistical significance in post administration of corticosteroids in both non-diabetic and diabetic population. The common adverse effect exhibited was only hyperglycemia whichwas controlled successfully by insulin administration. Thus we conclude that, steroid stewardship program is essentiality in ameliorating the adverse effects such as glycemic control and helps in assessing the prescribing pattern of corticosteroids for asthma and COPD in a tertiary care hospital.

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