REPORT

24(103), May - June, 2020

ISSN
2321–7359
EISSN
2321–7367

Medical Science

Pattern of change in blood glucose level in hospitalized patient treated with inhaled corticosteroid

Moumita Das[1]✉, **Tushar Sontakke**[2], **Sourya Acharya**[3], **Samarth Shukla**[4]

[1]MBBS student, Datta Meghe Institute of Medical Sciences (deemed to be university), J.N. Medical College, ABVR Hospital, Sawangi Meghe, Wardha 442001, Maharashtra, India; Email: aisharay07@gmail.com
[2]Asst. Professor, Dept. of Medicine, Datta Meghe Institute of Medical Sciences (deemed to be university), J.N. Medical College, ABVR Hospital, Sawangi Meghe, Wardha 442001, Maharashtra, India; Email: tushar.ihmp@gmail.com.
[3]Professor, Dept of Medicine, Datta Meghe Institute of Medical Sciences (deemed to be university), J.N. Medical College, ABVR Hospital, Sawangi Meghe, Wardha 442001, Maharashtra, India; Email: souryaacharya74@gmail.com.
[4]Professor, Dept of Pathology, Datta Meghe Institute of Medical Sciences (deemed to be university), J.N. Medical College, ABVR Hospital, Sawangi Meghe, Wardha 442001, Maharashtra, India; Email: samarth21174@gmail.com.

✉**Corresponding author**
MBBS student, Datta Meghe Institute of Medical Sciences (deemed to be university), J.N. Medical College, ABVR Hospital, Sawangi Meghe, Wardha 442001, Maharashtra, India.
Email: aisharay07@gmail.com

Article History
Received: 22 December 2019
Reviewed: 23/December/2019 *to* 12/February/2020
Accepted: 13 February 2020
E-publication: 18 February 2020
P-Publication: May - June 2020

Citation
Moumita Das, Tushar Sontakke, Sourya Acharya, Samarth Shukla. Pattern of change in blood glucose level in hospitalized patient treated with inhaled corticosteroid. *Medical Science*, 2020, 24(103), 1122-1127

ABSTRACT

Background: Systemic corticosteroids are used to treat bronchial asthma and COPD. It is known that corticosteroid alters blood sugar level. In addition inhaled corticosteroids promote gluconeogenesis by direct hepatic stimulation and also by increasing resistance to insulin. However the effect of inhaled corticosteroids on carbohydrate metabolism is comparatively lesser and systemic adverse effects are not as significant as compared to oral or parenteral routes. This study was conducted to assess the effect of inhaled corticosteroids on blood sugar level in COPD and asthma patients taking inhaled corticosteroids (ICSs). *Aim:* To study the pattern of change in blood glucose level in hospitalized patient while on treatment with inhaled corticosteroid. *Method:* This cross sectional study was conducted in Jawaharlal Nehru Medical College, AVBRH hospital, Wardha. After taking clearance from the Institutional ethical committee, 45 cases of bronchial asthma and COPD were selected. Frequency and dosing of corticosteroid was evaluated, along with evaluation of fasting and post prandial glucose. *Result:* In this study we found that as the dose of inhaled corticosteroid increased , fasting blood sugar and post meal blood sugar were altered in higher doses of corticosteroids ($p=0.00$). Significant difference in the blood sugar value were found in fasting and postprandial state with dose less than 600 ug/day and in dose between 600 to 1200 ug/day .Mean value in fasting state was 98 mg/dl (SD 4.47) with a dose less than 600 ug /day and mean value of blood sugar was 110.2 mg/dl (SD 4.43) with dose of 600 to 1200 ug /day. As the frequency of dose increased, fasting and post meal blood sugar values were also increased in a linear correlation ($p<0.05$) which is significant. *Conclusion:* This study hence shows that there is a positive correlation between inhaled corticosteroid and blood sugar levels, with increasing dose the fasting and post meal blood sugar level increases in non diabetic individuals. Therefore it is necessary to keep a check on a regular basis of blood sugar in hospitaised patients taking inhaled corticosteroids.

Keywords: Bronchial asthma, COPD, Inhaled corticosteroids, Hyperglycemia

1. INTRODUCTION

Systemic glucocorticoid therapy can lead to various metabolic complications in glucose homeostasis including insulin resistance, hyperglycaemia and increased risk of diabetes (Schacke H et al., 2002). In comparison to the oral or parenteral routes of administration, inhaled corticosteroids (ICS) are known to produce relatively less systemic adverse effects and their effect on carbohydrate metabolism is less well recognized. Inhaled corticosteroids (ICSs) are used to prevent and treat asthma and recurrent wheezing attacks. Fluticasone propionate (FP), and budesonide either alone or in association with other bronchodilators are commonly prescribed inhaled corticosteroids (ICSs) because it is considered effective and well tolerated (Lelii M et al., 2016). Long-term treatment with inhaled corticosteroid significantly higher than recommended dosages has been associated with clinical complications, including growth retardation, bone osteoporosis, and acute adrenal crisis with hypoglycaemia (Todd GR et al., 2002, Mortimer KJ et al., 2006). Additionally gluconeogenesis is promoted by inhaled corticosteroids, the mechanism behind gluconeogenesis promotion is that inhaled corticosteroid acts by direct hepatic stimulation and also increases insulin resistance as insulin is the primary suppressor of hepatic glucose production. A study reported that adults receiving inhaled corticosteroid can develop diabetes or experience the progression of already diagnosed diabetes (Suissa S et al., 2010). Moreover, this risk for diabetes onset and progression was because of higher inhaled-corticosteroid doses and are similar to those currently prescribed for COPD treatment, as was observed in multiple studies across literature (Suissa S et al., 2010; Egbuonu F et al., 2014; Glaser S et al., 2015). This study was done to assess the effect of inhaled corticosteroids on blood sugar level in COPD and asthma patients taking inhaled corticosteroids (ICSs).

Aim

To study the pattern of change in blood glucose level in hospitalized patient while on treatment with inhaled corticosteroid.

Objectives

1. To correlate fasting blood sugar and post meal blood sugar levels with doses of inhaled corticosteroids (ICSs).
2. To correlate fasting blood sugar and post meal blood sugar levels with frequency of inhaled corticosteroids (ICSs) prescribe.

2. MATERIAL AND METHOD

This cross sectional study was carried out in the department of medicine of Datta Meghe Institute of Medical Sciences University, ABVR Hospital which is a tertiary care rural medical hospital over 6 months period (july 2019 to December 2019). The study was

started after ethical committee clearance. Reference number is DMIMS (DU)/IEC/2019/7999. Diagnosed cases of COPD and asthma who were admitted for treatment were included as study subjects.

Sample size

Study population was estimated using n = Z 1-α/2×P× (1-P)/d2

Where;

Z 1-α/2 is the level of significance at 5% i.e. 95% confidence interval=1.96

P=global prevalence of asthma = 3% = 0.03[6]

d = desired error of margin = 5% = 0.05

n = 1.962×0.03× (1-0.03)/0.052

=44.71

˜ 45

Thus, 45 patients were selected as study population.

Inclusion and exclusion criteria

Inclusion criteria: Age>18 years receiving inhaled corticosteroid and euglycemic on admission. Diabetic patient and patient on oral corticosteroid were excluded. Those who were found to have raised blood sugar level on admission were excluded.

Data collection

All the study subjects were explained the study procedure. We enrolled consecutive patients treated with inhaled corticosteroid drugs. Blood sugar was monitored on admission, after 5 days of inhaled corticosteroid therapy along with assessment of fasting and post prandial blood sugar level was done. With the use of predesigned study proforma, recorded relevant history and physical examination was recorded.

Statistical analysis

We entered the data in Microsoft excel sheet and used SPSS version 22 software for analysis. Categorical data are presented as percentages and compared using chi-square test.

3. OBSERVATIONS AND RESULT

Assessment of parameters including blood sugar including fasting blood glucose level, postprandial and random blood glucose revealed data, which was formulated in the tables as depicted below.

FBS: Fasting Blood Sugar.

PMBS: Post Meal Blood Sugar.

SD: Standard Deviation.

Table 1 Dose of inhaled corticosteroid per day and mean blood sugar value of fasting, random and post meal state with p value.

	Daily Dose of ICS(n=45)		P_Value
	<600 Mean(sd)	600 to 1200 Mean(sd)	
FBS	98(4.47)	110.2(4.43)	0.000
PMBS	129.6(2.95)	146.17(7.48)	0.000

Table 1 shows significant difference in the blood sugar value in fasting and postprandial state with dose less than 600 ug/day and in dose between 600 to 1200 ug/day. Mean value in fasting state was 98 mg/dl (4.47) with a dose less than 600 ug /day and mean value of blood sugar is 110.2 mg/dl (4.43) with dose of 600 to 1200 ug /day. Comparison of blood sugar value in post meal state between patient taking a dose of <600 ug/day and 600 to 1200 ug/day ,show a significant rise of blood sugar with dose of 600 to 1200 ug/day. Mean value of blood sugar is 129.6 mg/dl (2.95) with dose less than 600 ug/day and it is 146.17 mg/dl (7.48) with dose of 600 to 1200 ug/day.

Table 2 Frequency of inhaled corticosteroid per day and mean blood sugar value of fasting and post meal state

Frequency of dose	Observation	FBS	PMBS
		Mean(SD)	Man(SD)
4 hourly	16	111.18(6.89)	146.62(10.17)
6 hourly	15	108.4(3.81)	144.3(7.17)
8 hourly	10	103.3(6.46)	138.1(8.58)
12 hourly	4	99.75(4.78)	130(3.74)

Table 2 shows significant difference in the blood sugar value in fasting and postprandial state with frequency of dose at 4 hourly, 6 hourly, 8 hourly and 12 hourly. With increase in frequency of dose of inhaled corticosteroid the mean value of blood sugar at fasting state and post meal state increases. Mean value of fasting blood sugar is 111.18mg/dl(6.89) which was at the highest frequency that is 4 hourly and it decreased at 6 hourly frequency with mean value 108.4mg (3.81) then further decreased at 8 hourly frequency with the mean value of 103.3mg/dl (6.46) and minimum at 12 hourly frequency with mean value of 99.75mg/dl (4.78). Similarly comparison between blood sugar value in post meal state showed rise in blood sugar with highest mean value of 146.62mg/dl (10.17) at 4 hrly frequency of dose and minimum at lowest frequency that is 12 hourly with mean value of blood sugar 130mg/dl(3.74). Hence we got a linear correlation between blood sugar level and frequency of inhaled corticosteroid.

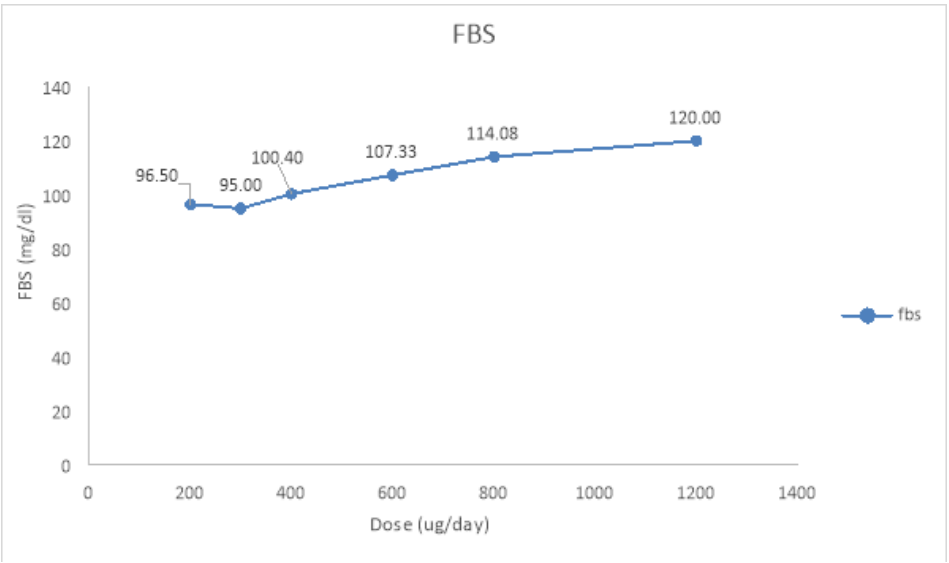

Figure 1 Linear correlation between fasting blood sugar value and dose of inhaled corticosteroid

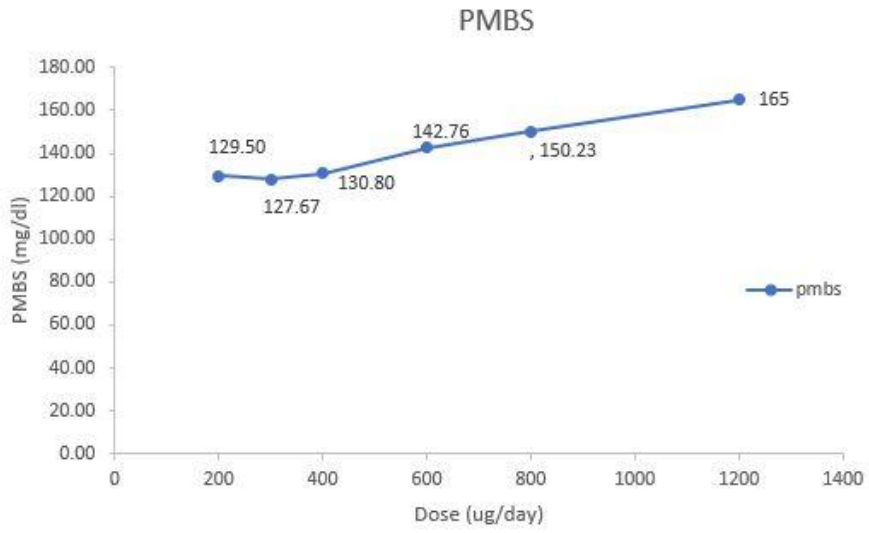

Figure 2 linear correlations between post meal blood sugar value and dose of inhaled corticosteroid.

In figure 1 Y axis denotes Fasting Blood Sugar level in mg/dl and X axis denotes Dose of inhaled corticosteroid in ug/day. Linear correlation between the doses of inhaled corticosteroid and fasting blood sugar in figure 1 show that the blood sugar value in the fasting state rise with the higher dose of inhaled corticosteroid. Mean blood sugar value is 96.5 mg/dl at dose of 200 ug/day and 120 mg /dl at dose of 1200 ug/day.

In figure 2 Y axis denotes Post meal blood sugar level in mg/dl and X axis denotes dose in ug/day. Linear correlation between the dose of inhaled corticosteroid and post meal blood sugar in figure 2 shows that the blood sugar value in the post meal state rise with the higher dose of inhaled corticosteroid. Mean blood sugar was 129.5 mg/dl at dose of 200ug/day and 165 mg /dl at dose of 1200 ug/day.

4. DISCUSSION

Corticosteroid therapy is the most common cause of drug-induced diabetes (Lasang MC et al., 2011). Sometimes symptoms of frank diabetes are not seen but only hyperglycemic state exists in patients taking inhaled corticosteroids (ICSs) in low to moderate doses. However, frank T2 DM develops in a significant proportion of patients who are on large doses of steroids especially while on long-term treatment (Lasang MC et al., 2011).

In our study, we tried to assess the variability of blood sugar levels in patient treated with inhaled corticosteroid. Both FBS and PMBS blood glucose levels were raised in ICS group taking higher doses. Linear correlation between the dose of inhaled corticosteroid and fasting blood sugar were detected. Linear correlation between the dose of inhaled corticosteroid and post meal blood sugar was also detected. Also when correlation was done between blood sugar level and the frequency of inhaled corticosteroid it was found statistically significant. Linear correlation between the frequency of inhaled corticosteroid and fasting blood sugar as well as post meal blood sugar shows that the blood sugar value rises with the higher frequency of inhaled corticosteroid.

In another study among uncontrolled asthmatics, high dose ICS therapy was noted to improve glucose tolerance and decrease the insulin resistance during the early phase of the follow up for asthma treatment (Kiviranta K et al., 1993). It was due to increased endogenous catecholamine production because of the physical stress. The favorable glycemic effect noted during the early phase of treatment might be the effect of reduction of endogenous catecholamines as a result of resolution of unstable asthma rather than the ICS therapy (Kiviranta K et al., 1993). Therefore treatment with inhaled corticosteroids was found to be beneficial in patients with uncontrolled asthma. In our study we did not get this result as none of the patients had uncontrolled asthmatic condition so there was no improvement in glucose tolerance with high dose of inhaled corticosteroid in the initial phase of treatment, instead there was impaired glucose tolerance seen as both frequency and dose of inhaled corticosteroids (ICSs) was increased. Systemic glucocorticoid therapy can lead to various metabolic complications in glucose homeostasis including insulin resistance, hyperglycaemia and increased risk of diabetes (Schacke H et al., 2002). In comparison to the oral or parenteral routes of administration, inhaled corticosteroids (ICS) are known to produce relatively less systemic adverse effects and their effect on carbohydrate metabolism is less well recognized (Lelii M et al., 2016).

Similar findings were obtained in the the study conducted by Donihi AC et al., that hyperglycemia occurred in hospitalised patients receiving high dose of corticosteroid therapy for a longer duration and long hospital stay. The study was conducted for a period of one month. Out of 617 patients 66 received high doses of corticosteroids, among this 66 patients 50 patients blood glucose was measured. Hyperglycemia was documented in 32 of these 50 patients (64%), and multiple hyperglycemic episodes occurred in 26 (52%) (Donihi AC et al., 2006). Therefore the result of this study has a resemblance with the outcome of our study that is blood glucose level rises with dose of corticosteroids. O'Byrne P.M et al. in their study concluded that inhaled corticosteroid is not found to be associated with new onset of diabetes mellitus. The result of the study was that, in the primary asthma dataset, the occurrence of diabetes mellitus/hyperglycaemia adverse events (AEs) was 0.13% for budesonide and 0.13% for placebo (HR 0.98 [95% CI: 0.38–2.50], p = 0.96) and serious adverse events (SAEs) was 0% for budesonide and 0.05% for placebo (O'Byrne P.M et al., 2012). In the COPD dataset, the occurrence of diabetes mellitus/hyperglycaemia AEs was 1.3% for budesonide and 1.2% for non-ICS (HR 0.99 [95% CI: 0.67–1.46], p = 0.96) and SAEs was 0.1% for budesonide and 0.03% for non-ICS (O'Byrne P.M et al., 2012). In contrast to the result of our study which showed that in non diabetic hospitalised patient taking inhaled corticosteroid there is an association between ICS therapy and risk of onset of diabetes with high dose and frequency .

A paper was published by Suissa S et al. which showed that the risk of onset of diabetes and progression increases moderately with the use of inhaled corticosteroid. In the study it was calculated that current use of inhaled corticosteroids was associated with a 34% increase in the rate of diabetes (rate ratio [RR] 1.34; 95% confidence interval [CI], 1.29-1.39) and in the rate of diabetes progression (RR 1.34; 95% CI, 1.17-1.53) (Suissa S et al., 2010). The risk of hyperglycemia increases with the dose of inhaled

corticosteroid therapy, as we have seen in our study the linear positive correlation between dose of inhaled corticosteroids and fasting blood sugar and post prandial blood sugar level. In order to prevent the development of drug induced hyperglycemia in patient taking inhaled corticosteroids (ICSs), a careful monitoring of blood sugar with increase in dose and frequency of corticosteroid plays a key role and also helps to assign a better therapeutic regimen to the patient considering this complication.

5. CONCLUSION

Our study revealed a positive linear correlation between inhaled corticosteroid and blood sugar level with increasing dose of inhaled corticosteroids in non diabetic individuals, emphasising the importance of regular monitoring of blood sugar in hospitalised patients on inhaled corticosteroids. There is a potential risk of hyperglycemia induced by inhaled corticosteroid therapy. In order to reduce the risk associated with Inhaled corticosteroids, the efficacy and pharmacokinetics of these drugs at low dose (i.e. <400ug/day) and moderate dose (i.e. 400-600ug/day) need to be more thoroughly evaluated. Also, the overuse of inhaled corticosteroid predisposes a patient to critical complications such as steroid induced dysglycemia which often presents as post prandial and fasting hyperglycemia. These issues must be addressed in order to prevent the side effects of inhaled corticosteroids like diabetes.

Increased evidences in recent literature regarding the adverse effects associated with inhaled corticosteroid therapy indicate that there is necessity of adequate patient selection and monitoring in order to improve the safety and efficacy of these treatments. An important implication of the research is essentially to prevent the complications of hyperglycemia by inhaled corticosteroids, and also to improve the therapeutic regimens to reduce side effects. These measures can lead to improvement in management of patients on inhaled corticosteroids.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

REFERENCE

1. Donihi AC, Raval D, Saul M, Korytkowski M.T., and DeVita M.A. Prevalence and predictors of corticosteroid-related hyperglycemia in hospitalized patients. Endocrine Practice. 2006;12(4):358-362.
2. Egbuonu F, Antonio FA, Edavalath M. Effect of inhaled corticosteroids on glycemic status. The Open Respiratory Medicine Journal. 2014; 8:101-105.
3. Gläser S, Krüger S, Merkel M, Bramlage P, Herth F.J.F. Chronic Obstructive Pulmonary Disease and Diabetes Mellitus: A systematic review of literature. Respiration. 2015;89:253-264.
4. Kiviranta K, Turpeinen M. Effect of eight months of inhaled beclomethasone dipropionate and budesonide on carbohydrate metabolism in adults with asthma. Thorax. 1993;48:974–8.
5. Lansang MC, Hustak LK. Glucocorticoid-induced diabetes and adrenal suppression how to detect and manage them. Cleveland Clinical Journal of Medicine. 2011;78:748–56.
6. Lelii M, Principi N, Esposito S. Transient symptomatic hyperglycaemia secondary to inhaled fluticasone propionate in a young child. BMC pulmonary medicine. 2016; 16:9.
7. Mortimer KJ, Tata LJ, Smith CJ, West J, Harrison TW, Tatters field AE, et al. Oral and inhaled corticosteroids and adrenal insufficiency: a case-control study. Thorax. 2006;61(5):405-8.
8. O'Byrne P.M., Rennard S, Gerstein H, Radner F, Peterson S, et al. Risk of new onset diabetes mellitus in patients with asthma or COPD taking inhaled corticosteroids. Respiratory medicine. 2012;106(11):1487-1493.
9. Schacke H, Docke WD, Asadullah K. Mechanisms involved in the side effects of glucocorticoids. Pharmacology & therapeutics. 2002;96(1):23-43.
10. Suissa S, Kezouh A, Ernst P. Inhaled corticosteroids and the risks of diabetes onset and progression. The American journal of medicine. 2010; 123(11):1001-6.
11. Todd GR, Acerini CL, Buck JJ, Murphy NP, Ross-Russell R, Warner JT, et al. Acute adrenal crisis in asthmatics treated with high-dose fluticasone propionate. The European respiratory journal. 2002;19(6):1207-9.