ORIGINAL ARTICLE

Effect of Moderate Dose of Inhaled Budesonide on HbA1c in Asthmatic Children

Wasim A Wani[1], Sheeraz A Dar[1], Mudasir N. Mir[1], Javeed I. Bhat[2], Bashir A Charoo[3]

Author's Affiliations: [1]Senior Resident; [2]Asst. Prof; [3]Prof & Head, Department of Pediatrics and Neonatology, Sher-I-Kashmir Institute of Medical Sciences Hospital, Srinagar, Jammu & Kashmir, India.
Correspondence: Dr. Sheeraz A Dar, Email**:** sheerazdar123@gmail.com

ABSTRACT

Objective: The objective of the study was to find out effect of inhaled corticosteroids on HbA1c.

Methods: Asthma patients in the age group 5-15 years who were started on moderate doses of inhaled budesonide (400-800 microgram/day) for the first time were selected for the study. HbA1c level was measured before initiating inhaled corticosteroids (ICS) and after 6 months using venous blood samples.

Results: The mean (SD) HbA1c levels before and after 6 months of starting inhaled corticosteroids was 4.75(0.16) and 5.25(0.29) respectively. The difference was statistically significant (p value <0.0001). After 6 months of inhaler use, HbA1c level of 5 patients (8.33%) reached at high risk level (5.7-6.4%).

Conclusion: inhaled corticosteroids have a significant effect onHbA1c level after prolonged usage. We recommend monitoring HbA1c levels in children on long term inhaled corticosteroids.

Key words: Budesonide, HbA1c, Asthma, Children

INTRODUCTION

Inhaled corticosteroids (ICS) remain the cornerstone for management of asthma in children of all ages [1,2]. They are the most effective anti-inflammatory medication currently available. Corticosteroids block late-phase reaction to allergens, decrease airway hyperesponsiveness, and inhibit migration and activation of inflammatory cells[3]. ICS decrease asthma symptoms, improve quality of live, reduce frequency and severity of exacerbations, and reduce asthma mortality[4].The risk of systemic adverse effects depends upon its dose and potency. The efficacy and tolerability of the ICS, budesonide, is proven in the treatment of pediatric asthma[5]. The safety profile of inhaled corticosteroids (ICSs) is better than the systemic steroids[6]. However, children can develop significant adverse effects on high doses of inhaled corticosteroids if used for prolonged periods. The level of glycosylated hemoglobin (HbA1c) reflects average blood glucose level over a longer period of time[7]. While systemic steroids are documented to affect glucose metabolism, there is growing concern about effect of ICS on glucose metabolism. This study was carried out to find out effect of ICS on level of HbA1c.

METHODS

This study was carried out in the asthma clinic of a tertiary care hospital in north India over a period of one year from January 2017 to December 2017. Asthma patients in the age group 5-15 years who were started on moderate doses of inhaled budesonide (400-800 microgram/day) for the first time were selected for the study. Glycosylated hemoglobin (HbA1c) level was measured before initiating inhaled corticosteroids (ICS) and after 6 months using venous blood samples. Venous blood samples were collected in tubes containing EDTA. HbA1c was measured in the department of biochemistry using immunoassay. Informed consent was taken from the parents of the subjects. The study was given clearance by the ethical clearance committee of the hospital.

Exclusion criteria: Children having co-existing diabetes, children who received oral steroids during the study period, Children who were overweight or obese, children with not well controlled and poorly controlled asthma on moderate doses of ICS or who used short acting beta agonists frequently, children whose parents refused participation in the study, and children with acute severe asthma during the study period were excluded from the study.

Statistical analysis: All the continuous variables of the study have been shown in terms of descriptive statistics. In order to analyse the data, we have applied unpaired t-test. The results obtained have been discussed on 5% level of significance i.e $p < 0.05$ considered significant. Moreover, the appropriate statistical charts have been used to represent the da-

ta. The statistical software SPSS V-20 has been used for the statistics.

RESULTS

After applying exclusion criteria, sixty patients were selected for the study. Of these, 60 percent were females and 40 percent were males table 1. Mean ±SD age of the study population in years was 9.23±2.98 table 2. The age ranged from 5-15 years. The mean±SD weight of the study population was 26.7±9.2 kgs table 2. The mean dose of inhaled budesonide as shown in table 4 was 726µg/day (range 400-800).

Table 1: Gender distribution of study population

Gender	Cases (%)
Male	40
Female	60

Table 2: Measurement of age, weight and dose of steroid in study population

Variables	Mean	Sd	Range
Age (yers)	9.23	2.98	5-15
Weight (kgs)	26.7	9.2	15-49
Mean Dose of inhaled steroids (budesonide) in micrograms/day	726	156	400-800

Table 3: Mean HbA1c at start and 6 months of study.

	Mean	SD
HbA1c (initial)	4.75	0.16
HbA1c (6 months)	5.25	0.28

P value <0.0001

Table 4: Percentage of patients with HbA1c level in high risk range

HbA1C	Number (%)
Normal < 5.7%	55 (91.66)
High risk 5.7-6.4%	5 (8.33)

In our study, the mean (SD) HbA1c levels before and after 6 months of starting inhaled corticosteroids (budesonide) was 4.75(0.16) and 5.25(0.29) respectively. The difference was statistically significant (p value <0.0001) table 3.

After 6 months of inhaler corticosteroid use, HbA1c level of 5 patients (8.33%) reached high risk level (5.7-6.4%) (**table 4).**

DISCUSSION

Inhaled corticosteroids are first line treatment for allergic disorders like asthma and allergic rhinitis[8]. Inhaled corticosteroids have a more favourable safety profile than oral steroids, still there is uncertainty about systemic absorption and complications. Advances in design of inhalers have reduced the incidence of local side effects. However, improved delivery of ICSs to lungs also increased systemic absorption, and an adverse effect profile similar to, although milder than oral corticosteroids have emerged[9]. The metabolic effects of corticosteroids include decreased insulin sensitivity in several tissues[10]. Peripheral insulin resistance is considered to be the predominant mechanism causing corticosteroid-induced hyperglycemia. It has also been suggested that toxic effects on islet cell causing apoptosis occur in patients exposed to corticosteroids[11]. Additionally, corticosteroids are known to cause inhibition of insulin secretion by pancreatic β-cells[12]. Glycosylated haemoglobin is a simple, objective measure of average blood glucose concentrations over several weeks and is not affected by short term fluctuation. This study was carried out to find out the effect of long term usage of inhaled corticosteroids on HbA1c levels.

In the present study, 8.33% children had HbA1c level in high risk range (5.7-6.4%). However, no child had HbA1c level high enough to be labelled as steroid induced diabetes. These findings were in accordance with the study by Kaarthikeyani Sankaravadivelu et al.[13] who showed 9.3% of children on long term ICS having elevated Hba1c. Daniel S et al. reported high risk HbA1c in only 3.5% subjects. However, 48.2% of subjects in his study group were on low dose ICS[14].

The mean HbA1c level at the start of study was 4.75±0.16% . After 6 months of inhaled steroid use, the mean HbA1C in our study was found to be 5.25±0.28%. The difference was statistically significant (p<0.0001). Our results were in agreement with the study by YÜCEL et al[15]. They compared HbA1c level in asthmatic children on low dose inhaled steroids with normal children without asthma. They found out a mean HbA1c value of 5.44±0.75% among the children with asthma and 5.14±0.41% in the control group. HbA1c levels in children with asthma was significantly higher than the control group (*P*=0.006). Similar results were reported by Daniel S et al. They found out that there was a significant increase in mean HbA1c of total study population before (mean HbA1c=4.98%) and after (mean HbA1c=5.13%) treatment with inhaled corticosteroids. They also concluded that higher the dose of ICS, more the risk for abnormal HbA1c.

Beta agonists are supposed to have an effect on glucose metabolism. A study by Dawson KP et al. showed that high dose nebulized salbutamol signifi-

cantly increased mean blood glucose levels[16]. We advice the patients to use beta agonists as needed. As the main aim of our study was to find out effect of inhaled corticosteroids on glucose metabolism we excluded the patients who needed frequent usage of beta agonists. So the effect of beta agonists was not significant on the HbA1c level of our study group.

Our study had certain limitations. The number of patients in our study was small due to strict exclusion criteria. Effect of only moderate dose of inhaled corticosteroids on HbA1C was obtained. The reason being the policy of starting moderate dose of inhaled corticosteroids in most patients so as to balance the control of disease on one side and minimise the adverse effects of high dose inhaled corticosteroids. The correlation between cumulative doses of inhaled corticosteroids and HbA1c couldn't be determined due to small sample of asthmatic patients on 400μg of inhaled budesonide.

CONCLUSION

HbA1c levels were significantly higher in asthmatic patients on moderate dose of inhaled corticosteroids (budesonide) after 6 months of usage.8.33% of patients had HbA1c level in high risk range. However no patient had HbA1c level high enough to be labelled as steroid induced diabetes. We recommend monitoring HbA1c levels in children on long term inhaled corticosteroids.

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