EDITORIAL

Do Inhaled Corticosteroids Adversely Influence Glucose Metabolism?

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Glucocorticoids have been the mainstay of therapy of asthma because of their anti-inflammatory action. They have potential for many adverse effects, especially with continued use. However, the inhaled corticosteroids (ICS) have a better safety profile than the oral steroids. In view of the long term requirement for ICS in childhood asthma, there have been lots of investigations on the adverse effects in the growing children. The major areas of concern have been the local side-effects due to the deposition of the ICS aerosol in the oropharynx and the upper airway, effects due to the absorption of the ICS which may lead to systemic effects on growth, hypothalamus-pituitary-adrenal axis and on various metabolic pathways. The documented effects on the growth are minimal. Similarly, the suppression of the hypothalamus-pituitary-adrenal axis with low doses of ICS is minimal.

The effects on the metabolism are an interesting area of study. Steroid hormones have multiple effects on the body metabolism, particularly the carbohydrate and lipid metabolism. Systemic steroid therapy leads to hyperglycemia and the adverse effects of hyperglycemia have been well documented. The concern about the changes in the blood glucose levels with the use of ICS has been investigated. For information about the summary of glucose levels over a longer period of time, measurement of glycosylated hemoglobin (HbA1c) is useful. Glycosylated hemoglobin concentrations reflect average blood glucose values over the preceding weeks, the mean value in the red cell population being that contained by those cells of an age equal to half their average life span - namely, 50-60 days(1).

In addition to steroids, the use of β_2 agonists for acute asthma and the severity of illness can also influence the glucose metabolism. However, studies in adult asthmatics have documented beneficial effects of ICS on carbohydrate metabolism. Kiviranta and Turpeinen(2) demonstrated that the antiasthmatic effect of high dose beclomethasone dipropionate and budesonide was accompanied by a significant initial decrease in insulin resistance with a parallel improvement in glucose tolerance. During the prolonged treatment, a small increase in insulin sensitivity was found(2).

Pediatric studies on the effects of ICS on carbohydrate metabolism are scant. Turpeinen, *et al*.(3) observed the antiasthmatic and metabolic effects of budesonide inhalations in initially high (800 $\mu g/m^2$/day for 1 month) and subsequently lower (400 $\mu g/m^2$/day for 4 months) dosage in nine children with asthma, aged 5 to 10 years. They observed that the high dosage increased significantly the ratio of serum insulin to blood glucose (a marker of insulin sensitivity); after lower dosage, the ratio declined significantly to 13.5 mU/mmol. The dose of 400 $\mu g/m^2$ for 4 months did not have any significant systemic effects.

In a previous study on 15 asthmatic children treated with inhaled beclomethasone dipropionate (mean 490 μg/day) and 11 asthmatic control subjects receiving no corticosteroid therapy, measurements of 24-h urinary free cortisol and 17 hydroxy corticosteroids, serum cortisol, response to

ACTH, and the oral metyrapone test showed no significant difference between the two groups(4). All the results were within normal limits, and carbohydrate metabolism, as shown by blood glucose and HbA1c, was not affected by beclomethasone(4).

In this issue of *Indian Pediatrics*, Yücel, *et al.*(5) have reported in their cross sectional study that HbA1c was marginally higher in children with asthma getting ICS as compared to the controls (5.44±0.75% *vs* 5.14±0.41%). There was no relationship between doses and duration of ICS with levels of HbA1c. It is unlikely that this marginal increase in HbA1c levels is of any clinical significance as the levels are well within the normal range (5- 8%). In addition, absence of any relation between the dose of inhaled steroid and the HbA1c levels may suggest that the increased HbA1c may not be due to the effects of inhaled steroids. It will be interesting and more appropriate to evaluate these effects in children who receive high doses of ICS.

While there is concern over the systemic effects of ICS on glucose metabolism, current evidence does not suggest any adverse influence on the same.

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REFERENCES

1. Peacock I. Glycosylated haemoglobin: measurement and clinical use. J Clin Pathol 1984; 37: 841-851.
2. Kiviranta K, Turpeinen M. Effect of eight months of inhaled beclomethasone dipropionate and budesonide on carbohydrate metabolism in adults with asthma. Thorax 1993; 48: 974-978.
3. Turpeinen M, Sorva R, Juntunen-Backman K. Changes in carbohydrate and lipid metabolism in children with asthma inhaling budesonide. J Allergy Clin Immunol 1991; 88: 384-389.
4. Goldstein DE, König P. Effect of inhaled beclomethasone dipropionate on hypothalamic-pituitary-adrenal axis function in children with asthma. Pediatrics 1983; 72: 60-64
5. Yücel O, Eker Y, Nuhoglu C, Ceran O. Hemoglobin A1c levels in children with asthma using low dose inhaled corticosteroids. Indian Pediatr 2009; 46: 300-303.