

## Inhaled Steroids in Asthma: Aren't without Side Effects

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Inhaled corticosteroids are commonly used as the first-line therapy for chronic respiratory illnesses including asthma. With the advent of more potent drugs, more concentrated formulations and more efficient delivery systems use of inhaled corticosteroids has largely expanded across the globe over last few decades. In the setting of more frequent and longer durations of use, the possible side effect profile of inhaled corticosteroids has become a topic of concern for the physicians as well as patients. Even though the long-term use of inhaled corticosteroids has more favorable safety profile than the oral corticosteroids, uncertainty persists about the systemic complications. Systemic side effects of long term oral steroid use including compromised linear growth, poor bone mineralization, glucose intolerance, cushing syndrome, obesity and suppression of the hypothalamic-pituitary-adrenal (HPA) axis have also been reported with the chronic use of inhaled steroids however with less frequency and severity. In this review, the clinicians will be able to understand the local as well systemic side effects of inhaled corticosteroids that they need to be vigilant about.

### Local side effects

Local side effects of the inhaled corticosteroids are generally minor however may affect the medication adherence directly and may in turn complicate the clinical picture of an asthmatic individual. At least one local side effect has been reported among sixty percent of the asthmatic children using inhaled corticosteroid [1]. A variety of local symptoms including hoarseness, candidiasis, pharyngeal inflammation and dysphonia have been described. Meter dose inhaler (MDI) use has been more commonly associated with cough. Candidiasis, a common complaint, can be prevented by the instructions to rinse the mouth after steroid inhaler use. Perioral dermatitis, a papulopustular eruption involving the nasolabial folds, chin and perioral region, sparing the vermillion border, is due to a local effect of steroids on the skin likely secondary to interaction with collagen synthesis. Washing the perioral area with mild soap and water may serve to minimize perioral dermatitis while severe cases may require treatment with topical antibiotics [1,2].

### Systemic complications

#### Effects on hypothalamic pituitary adrenal (HPA) axis

The HPA axis suppression, even though rare, is the most serious potential adverse effect of inhaled corticosteroid use and has been even reported in patients taking standard dosages. Some of the presenting signs and symptoms of possible adrenal insufficiency include development of cushingoid features, anorexia, weight loss, fatigue, growth failure, or hypoglycemia. In most cases however the typical symptoms of chronic adrenal insufficiency may not occur. Growth failure is a late finding and is not highly sensitive for detecting HPA axis suppression [3]. Concomitant nasal corticosteroid use, low BMI and cumulative dose of inhaled corticosteroids are contributing factors to the development of HPA axis suppression [4,5]. Cortisol levels between 7 and 9 am should be obtained in all symptomatic patients. If the morning cortisol level is less than 3 µg/dL, a diagnosis of adrenal insufficiency is made. However, if the morning cortisol level is 3 µg/dL or greater, an ACTH stimulation test is required [6]. Symptoms of adrenal crisis, such as hypotension, lethargy and hypoglycemia, warrant

immediate testing, including a cortisol level in all cases and stimulation testing when possible. If the patient is unstable or ill appearing, treatment with stress doses of corticosteroids should be done promptly while awaiting results [6]. Inhaled corticosteroid dose reduction, if safe, should be considered possibly by adding a corticosteroid-sparing agent such as leukotriene receptor antagonists.

### Effects on linear growth

In most patients, inhaled corticosteroids have minor and short-term effects on growth and the minor growth risks outweigh the beneficial effects on the respiratory illness. Most long term studies have found not found significant difference in the final adult heights of children treated with inhaled corticosteroids and untreated asthmatic controls [7,8]. However, few studies have found a minor effect on final height of 1 cm [9,10].

### Effects on bone mineral density

Inhaled corticosteroids have mild effects on bone mineral density (BMD) that are not usually clinically significant [6]. BMD may be substantially affected in patients receiving high-dose inhaled corticosteroids if they also have concomitant risk factors such as frequent oral corticosteroid use, malnutrition, or any chronic systemic illnesses. Evidence suggests that optimizing serum Vitamin D concentrations in these patients may have protective role on bone health [11].

### Effects on glucose metabolism

The effects of inhaled corticosteroids on glucose metabolism are primality of concerns in patients who have a previous diagnosis of diabetes mellitus (DM) or are at high risk of developing DM. The corticosteroids decrease insulin sensitivity in several tissues [12], decrease insulin stimulated glucose uptake in skeletal muscle [13] and increase hepatic glucose production [14]. Patients with DM in whom inhaled corticosteroids are initiated or increased may require changes in their DM medication regimen. Patients at high risk of developing type 2 DM from obesity along with other risk factors such as ethnicity and/or a positive family history, should be screened for diabetes during inhaled corticosteroid treatment [6].

### Immunologic effects

Unlike oral corticosteroids, exceptionally high doses of budesonide administered by means of a high-efficiency spacer do not cause humoral immunosuppression [15,16] however similar data are not available for other corticosteroids. A few cases of complicating pulmonary tuberculosis have been reported with inhaled corticosteroid use [17]. Inhaled corticosteroids should be avoided or used with great caution in asthmatic patients who are immunosuppressed, who have coexisting drug-resistant or atypical tuberculosis, or who have structural lung lesions.

### Conclusion

In conclusion, inhaled corticosteroids are generally safe and effective medications for asthma however local and systemic side effects may occur. Health providers need to be aware about these side effects while prescribing these medications and should take preventive and therapeutic measures at indicated.

### Conflict of Interest

Authors declare no conflict of interest.

### Financial Declaration

Author have no financial declaration.

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