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# Some properties of inhaled and intranasal corticosteroids: Further detailing in comparison with oral forms

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The article presented compares inhaled and intranasal corticosteroids with oral forms in the treatment of respiratory disorders, especially bronchial asthma and allergic rhinitis.

Earlier we have reviewed the properties of oral and inhaled corticosteroids (CS) used for the treatment of respiratory and other disorders [1]. The present work served for discussion of such properties in more detailed manner, including also intranasal forms. First of all, CS with predominantly glucocorticoid activity are highly suitable for treating several respiratory disorders, especially bronchial asthma and rhinitis with allergic component, since these drugs inhibit rather specifically the functions of eosinophils, causing their apoptosis and elimination by macrophages [2]. In addition, CS decrease contractile activity and proliferation of smooth muscle cells in airways, as well as the production by these cells of pro-inflammatory cytokines [3]. Finally, CS increase the expression of beta2-adrenergic receptors in airways, preventing also their down-regulation, what justifies combined use of CS and long-acting beta2-adrenergic agonists [4].

The main problem with CS, especially in oral forms is their adverse effects, particularly somatic growth inhibition and suppression of hypothalamo-pituitary-adrenal (HPA) axis [5-7]. The introduction of inhaled and intranasal CS to clinical practice has allowed for great diminution of these adverse effects, but unfortunately, not their complete elimination.

What practitioners should consider when using CS for treatment of respiratory disorders? First of all, it is almost impossible not to use oral CS for several reasons. One of them, of course, is a price that is much higher for inhaled and intranasal forms. Another one is convenience in application of oral CS, especially for outpatients [8]. Therefore, typically oral CS are used either temporally, for the treatment of seasonal exacerbations or in combination with inhaled forms. Both of these regimens help in diminishing adverse effects but obviously, are less safe as compared with regimens without oral CS applications.

The best mode to use inhaled and intranasal CS is titration, i.e. choosing the lowest dose that at the same time is clinically effective. What for the number of daily applications, here a contradiction exists, since on the one hand, exclusion of application in the evening allows for largely preventing adverse effects, such as suppression of HPA axis and inhibition of somatic growth [9], but on the other hand, evening application has the highest efficiency in controlling the disease symptoms [10]. That's why the choice of practitioner in this case will probably depend on clinical situation, including primarily the severity of disease.

The employment of only pharmacologic criteria for clinical judgment is not always entirely suitable. For example, swallowed fluticasone propionate is almost completely eliminated during the first-pass metabolism in the liver [11,12]. However, due to extremely high potency [13,14], the amount of this drug absorbed in airways is sufficient to cause HPA axis suppression that may result in acute crisis of adrenal insufficiency, when the patient and / or practitioner tries to stop rather abruptly the treatment with this inhaled steroid [15,16].

When considering adverse effects, some authors suggest differentiating minimally detectable effects and clinically significant adverse actions. As a matter of fact, although inhaled and intranasal CS inhibit short-term growth of lower leg segment, as measured by knemometry [17-20], generally such influence does not result in significant diminution of final height, probably due to catch-up growth [21,22]. Nevertheless, on our opinion it is not acceptable to use even inhaled and intranasal CS without considering their adverse effects. Really, both of these forms do cause somatic growth inhibition (see above) and HPA axis suppression [23,24], but fortunately, without detectable immunosuppression on systemic level [25] or higher risk of bone fractures [26]. Therefore, our previous appeal to consider pharmacotoxicologic embedding [27] is valid much more to the cases of high dose treatment with inhaled and intranasal CS for a long time and especially, when applied several times daily.

Finally, we should mention that the treatment with CS of some other respiratory disorders has not received the same extent of approval as treatment of asthma and rhinitis, mainly because of the doubts in clinical efficiency, together with elevated risk of pneumonia, as for chronic obstructive pulmonary disease [28,29] or due to unacceptable degree of adverse influence, e.g. myopathy that prolongs too much the period of time with mechanical ventilation in the cases of acute respiratory failure [30]. But even for asthma and rhinitis it appears that practitioners should balance between the treatment limited by patient's steroid phobia and therefore, with significant risk of mortality [31] and complete neglect of adverse effects with probable undesirable consequences, mainly on the long-term scale.

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