INCS.....

Doubts about safety

Dr. Labebe Sailan   F1   24.4.2017
The Pituitary-Adrenal-Axis

- Hypothalamus
  - CRF (corticotrophin releasing factor)
    - Anterior pituitary
      - ACTH (adrenocorticotropic hormone)
        - Adrenal cortex
          - Cortisol
            - Cortisol exerts a negative feedback effect on the hypothalamus that inhibits further release of CRF
            - Cortisol increases: blood glucose, blood pressure, amino acids
Adverse effects

- Occur with prolonged use of high doses
- Cushing’s disease

**Psychiatric**
- Sleep disturbance/activation
- Mood disturbance
- Psychosis

**Skin/soft tissue**
- Cushingoid appearance
- Abdominal striae
- Acne
- Hirsutism
- Oedema

**Neurologic**
- Neuropathy
- Pseudomotor cerebri

**Cardiovascular**
- Hypertension

**MSK**
- Osteoporosis
- Asceptic necrosis of bone
- Myopathy

**Endocrine**
- Diabetes mellitus
- Adrenal cortex suppression

**Immunologic**
- Lymphocytopenia
- Immunosuppression
- False-negative skin test

**Ophthalmic**
- Cataract
- Narrow-angle glaucoma

**Developmental**
- Growth retardation
- **First generation**: beclomethasone (unknown bioavailability);
- **Second generation**: budesonide (10-34% bioavailability);
- **Third generation**: fluticasone propionate (<2%), mometasone furoate (undetectable), and fluticasone furoate (<1%).
Bioavailability

- the fraction absorbed into the systemic circulation is the drug’s bioavailability

\[
BA = \frac{AUC_{po}}{AUC_{iv}} \times 100
\]

- e.g. Propranolol
  \[BA = 26 \pm 10\%
  \]
  (↑BA with Cirrhosis)
Intranasal corticosteroid 200 μg

Swallowing

Gut 70%

(Nasociliary clearance)

Nose 30%

Deposition

140 μg

77% hepatic first-pass

32.2 μg
e.g., TAA

99% hepatic first-pass

1.4 μg
e.g., FP/MF

Systemic circulation

60 μg

No first-pass

60 μg
<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Systemic Bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone (oral)</td>
<td>76%</td>
</tr>
<tr>
<td>Flunisolide</td>
<td>49%</td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>46%</td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>44%</td>
</tr>
<tr>
<td>Budesonide</td>
<td>34%</td>
</tr>
<tr>
<td>Fluticasone propionate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Fluticasone furoate</td>
<td>0.5%</td>
</tr>
<tr>
<td>Mometasone furoate&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.1%</td>
</tr>
<tr>
<td>Ciclesonide aqueous</td>
<td>Below lower limits of</td>
</tr>
<tr>
<td></td>
<td>assay quantification</td>
</tr>
</tbody>
</table>
Mechanisms and clinical implications of glucocorticosteroids in the treatment of allergic rhinitis
Mechanisms of glucocorticosteroid

Molecular level
GC exerts its anti-inflammatory effects through at least two pathways, transactivation and transrepression [42]. Transactivation occurs when the receptor complex binds to the glucocorticosteroid-response elements (GRE) in the
Transactivation occurs when the receptor complex binds to the glucocorticosteroid-response elements (GRE) in the promoter regions of glucocorticosteroid-responsive genes, which encode anti-inflammatory genes such as annexin 1, IκB and CD163 [43]. Alternatively, the GR complex represses
the transcription of proinflammatory genes by protein–protein interactions such as GR–nuclear factor kappa B (NFκB) and GR–activator protein 1 (AP-1) [44]. Evidence for a co-activator competition model of transrepression involving CBP/p300 was first provided for GR transrepression of AP-1 target genes [45].
Cellular level (Fig. 2)

GC inhibits the functions of infiltrating inflammatory cells and their recruitment into the nasal mucosa. GC inhibits the maturation, cytokine production, FcεRI expression and mediator release of mast cells [46,47]. GC inhibits histamine release from basophils [48,49], induces apoptosis of eosinophils [50] and reduces the recruitment of antigen-presenting cells such as Langerhans cells [51]. GC decreases the numbers of GATA-3⁺ Th2 cells and the production of Th2
the transcription of proinflammatory genes by protein–protein interactions such as GR–nuclear factor kappa B (NFκB) and GR–activator protein 1 (AP-1) [44]. Evidence for a co-activator competition model of transrepression involving CBP/p300 was first provided for GR transrepression of AP-1 target genes [45].
Inflammatory cells

- Number ↓ (apoptosis)
- Cytokine ↓
- Number ↓ Mediator ↓ Cytokine ↓ FcεRI ↓
- IgE ↓
- Number ↓
- Mediator ↓

Constitutive cells

- Cytokine ↓ Adhesion molecule ↓
- Epithelial cells
- Adhesion molecule ↓ Permiability ↓
- Endothelial cells
- Proliferation ↓ Adhesion molecule ↓ Chemokine ↓
- Fibroblasts
- Mucin secretion ↓

Glucocorticosteroid

- Eosinophils
- Th2 cells
- Mast cells
- B cells
- Dendritic cells
- Regulatory T cells (Treg)
- Basophils
- Number ↑ Regulatory cytokines ↑ (IL-10, TGF-β)
- Glands
- Goblet cells
Local and Systemic Safety of Intranasal Corticosteroids

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Abstract

The safety and efficacy of intranasal corticosteroids (INCIs) are well established for the management of allergic rhinitis, rhinosinusitis, and nasal polyps. As seen in numerous studies, INCIs demonstrate markedly reduced systemic bioavailability compared with oral and even inhaled corticosteroids and have shown an excellent safety profile over 3 decades of use. Nonetheless, concerns remain among some prescribers and patients that these agents may reach the systemic circulation in sufficient concentration to produce adverse effects (AEs). Available evidence does not support these concerns. A review of the published literature indicates that the side effect profiles of INCIs consist primarily of a low incidence of mostly mild and often transient local AEs, such as nasal irritation and epistaxis. The second-generation INC agents currently in use (mometasone furoate nasal spray, fluticasone propionate, ciclesonide, and fluticasone furoate) have favorable pharmacokinetic characteristics that further minimize systemic bioavailability (<1%) compared with older INCIs and compared with oral agents, thereby limiting the risk for systemic adverse events.

Key words: Glucocorticoids, Seasonal allergic rhinitis. Drug safety. Mometasone furoate. Fluticasone. Ciclesonide.
Objective:

investigate the safety profile of INCS and provides an overview of relevant pharmacokinetic differences between older and newer INCs.
Table 1. General characteristics of the formulations of intranasal steroids, age from which they can be used in allergic rhinitis, and corresponding dosages for children and adults.

<table>
<thead>
<tr>
<th>Name</th>
<th>Formulation</th>
<th>Minimum age</th>
<th>Dose per spray mcg*/nostril</th>
<th>Maximum dose/children mcg/day</th>
<th>Dose/adults mcg/day</th>
<th>Maximum dosage for rhinitis and nasal polyps** mcg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triamcinolone acetonide</td>
<td>Isotonic</td>
<td>4 years</td>
<td>55</td>
<td>110</td>
<td>220</td>
<td>220</td>
</tr>
<tr>
<td>Budesonide</td>
<td>Isotonic</td>
<td>6 years</td>
<td>32, 50, 64, 100</td>
<td>100</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Ciclesonide</td>
<td>Hypotonic</td>
<td>6 years</td>
<td>50</td>
<td>100</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Beclomethasone dipropionate</td>
<td>Isotonic</td>
<td>6 years</td>
<td>50</td>
<td>100</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Isotonic</td>
<td>2 years</td>
<td>50</td>
<td>100</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Isotonic</td>
<td>2 years</td>
<td>50</td>
<td>100</td>
<td>200</td>
<td>400</td>
</tr>
<tr>
<td>Fluticasone furoate</td>
<td>Isotonic</td>
<td>4 years</td>
<td>27.5</td>
<td>52.5</td>
<td>105</td>
<td>210</td>
</tr>
</tbody>
</table>

* mcg micrograms. Source: Medication inserts, ** Standard dosages are not available for nose polyps at present; clinical trials usually use the medication’s maximum dosage³.
Local Adverse Effects

The most common AEs associated with INCs are:
Epistaxis
throat irritation
and nasal dryness
burning, and stinging

The incidence in most cases (except epistaxis) is similar to that of placebo, and most are mild, self-limiting, and resolve without discontinuing therapy

the incidence of epistaxis reported with placebo in some clinical trials is similar to that of active INC treatment, suggesting that direct physical trauma from the nasal applicator tip pressing against the septum or the anterior end of the inferior turbinate may contribute to occurrence.

Severe local AEs, such as nasal mucosal atrophy or ulceration and septal perforation, have rarely been associated with INCs and can be prevented with an appropriate administration technique that helps avoid dryness, crusting, and bleeding from the septum.
<table>
<thead>
<tr>
<th>Step</th>
<th>Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Hold head in a neutral, upright position</td>
</tr>
<tr>
<td>2.</td>
<td>Clear nose of any thick or excessive mucus, if present, by gently blowing the nose</td>
</tr>
<tr>
<td>3.</td>
<td>Insert spray nozzle into the nostril</td>
</tr>
<tr>
<td>4.</td>
<td>Direct the spray laterally or to the side, away from the middle of the nose (septum) and toward the outer portion of the eye or the top of the ear on that side. (If possible, use the right hand to spray the left nostril and left hand to spray the right nostril, to direct the spray away from the septum)</td>
</tr>
<tr>
<td>5.</td>
<td>Activate the device as recommended by the manufacturer, and use the number of sprays recommended by the doctor</td>
</tr>
<tr>
<td>6.</td>
<td>Gently breathe in or sniff during the spraying</td>
</tr>
<tr>
<td>7.</td>
<td>Breathe out through the nose</td>
</tr>
</tbody>
</table>
Histologic data generated from long-term studies of several INCs in patients with perennial allergic rhinitis demonstrate no evidence of atrophy or deleterious pathologic changes in the nasal mucosa after 6 months to 5 years of use.

<table>
<thead>
<tr>
<th>Table 2. Summary of Commonly Reported Local Adverse Effects in Clinical Trials of Intranasal Corticosteroids, by Condition Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active Treatment Group</strong></td>
</tr>
<tr>
<td><strong>Acute RS Trials</strong></td>
</tr>
<tr>
<td>Epistaxis</td>
</tr>
<tr>
<td>Nasal burning/irritation</td>
</tr>
<tr>
<td>Pharyngitis</td>
</tr>
<tr>
<td><strong>Chronic RS/Nasal Polyposis</strong></td>
</tr>
<tr>
<td>Sneezing</td>
</tr>
<tr>
<td><strong>Allergic Rhinitis Trials</strong></td>
</tr>
<tr>
<td>Epistaxis</td>
</tr>
<tr>
<td>Sneezing</td>
</tr>
<tr>
<td>Coughing</td>
</tr>
<tr>
<td>Pharyngitis</td>
</tr>
</tbody>
</table>
Systemic Adverse Effects
Effects on the HPA Axis

A large number of short- and long-term studies in adults and children have found no significant impact on HPA axis function with the newer INC agents.
MFNS

6 RCT parallel-group or crossover trials in adults and children at doses ranging from 100 μg once daily to 400 μg twice daily for periods ranging from 21 days to 52 weeks.

No evidence of HPA axis suppression by MFNS in adults or children.
FP

7 RCT in adults and children at dosages of 88 μg to 800 μg daily

The results of these studies indicated no significant effect of FP on the HPA axis
In 2 studies investigating the concurrent use of intranasal FP with orally inhaled FP for the treatment of comorbid rhinitis and asthma, the combination did not increase the risk of HPA axis abnormalities compared with orally inhaled FP alone.
Effects on Statural Growth in Children

Overall, studies have shown that most INCs administered at recommended doses are not associated with impairment of growth or final adult height.

Growth suppression reported with long-term use of some INCs when recommended doses were exceeded.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Study</th>
<th>N</th>
<th>Patient</th>
<th>INC</th>
<th>Treatment</th>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Howland 1996 [81]</td>
<td>81</td>
<td>Adults (male, 18-40 y)</td>
<td>FP 200 μg QD</td>
<td>1 y</td>
<td>Mean and peak morning plasma cortisol and AUC similar to PL at screening, 24 wk and 52 wk. No evidence of altered HPA-axis response to cosyntropin compared with PL. No changes in bone density or markers of bone turnover within or between FP and PL groups at 52 wk. No occurrence of posterior subcapsular cataract or glaucoma in either group at 52 wk.</td>
</tr>
<tr>
<td></td>
<td>Ngamphaiboon et al., 1997 [82]</td>
<td>106</td>
<td>Children (5-11 y)</td>
<td>FP 100 μg QD</td>
<td>4 wk</td>
<td>No evidence of effects on adrenal function based on similar mean morning plasma cortisol concentrations between FP and PL before and after treatment.</td>
</tr>
<tr>
<td></td>
<td>Teper and Ratner, 2008 [83]</td>
<td>251</td>
<td>Children (6-11 y)</td>
<td>MFNS 100 μg QD</td>
<td>52 wk</td>
<td>No clinically relevant HPA-axis suppression (cosyntropin stimulation). No significant changes in IOP. No posterior subcapsular cataracts.</td>
</tr>
<tr>
<td></td>
<td>Murphy et al., 2005 [84]</td>
<td>229</td>
<td>Children (4-8 y)</td>
<td>BUD 64 μg QD</td>
<td>52 wk</td>
<td>No significant difference in growth rate vs PL.</td>
</tr>
<tr>
<td>Unclassified rhinitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bross-Soriano et al., 2004 [85]</td>
<td>360</td>
<td>Adult (18-60 y)</td>
<td>BDP 200 μg BID</td>
<td>1 y</td>
<td>Observed variations in IOP in all treatment groups remained within normal limits.</td>
</tr>
<tr>
<td>Condition</td>
<td>Study</td>
<td>N</td>
<td>Patient</td>
<td>INC</td>
<td>Treatment</td>
<td>Safety</td>
</tr>
<tr>
<td>-----------</td>
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<td>-----------</td>
<td>--------</td>
</tr>
<tr>
<td></td>
<td>Chervinsky et al, 2007 [31]</td>
<td>663</td>
<td>Adolescent and adult (12-75 y)</td>
<td>CIC 200 µg QD</td>
<td>Up to 1 y</td>
<td>No effect on morning plasma cortisol or 24-h urinary cortisol. No difference vs PL in IOP, visual acuity or lens opacification.</td>
</tr>
<tr>
<td></td>
<td>Rosenblut et al, 2007 [34]</td>
<td>806</td>
<td>Adolescent and adult (12-77 y)</td>
<td>FF 110 µg QD</td>
<td>12 mo</td>
<td>No clinically meaningful differences vs PL in 24-h urinary cortisol excretion or ophthalmic parameters.</td>
</tr>
<tr>
<td></td>
<td>Maspero et al, 2008 [70]</td>
<td>558</td>
<td>Children (2-11 y)</td>
<td>FF 110 µg or 55 µg QD</td>
<td>12 wk</td>
<td>No clinically meaningful differences vs PL in 24-h urinary cortisol excretion or ophthalmic parameters (IOP, cararact).</td>
</tr>
<tr>
<td></td>
<td>Tripathy et al, 2009 [71]</td>
<td>112</td>
<td>Children (2-11 y)</td>
<td>FF 110 µg QD</td>
<td>6 wk</td>
<td>No significant difference between PL and FF in change from baseline in 24-h plasma or urinary cortisol level following 6 wk of treatment.</td>
</tr>
<tr>
<td></td>
<td>Martinati et al, 1993 [72]</td>
<td>39</td>
<td>Children</td>
<td>BDP 200 or 400 µg QD</td>
<td>2 mo</td>
<td>No significant changes from baseline in markers of bone metabolism.</td>
</tr>
<tr>
<td></td>
<td>Agertoft and Pedersen, 1999 [73]</td>
<td>22</td>
<td>Children (7-12 y)</td>
<td>MFNS 100 or 200 µg QD or BUD 400 µg QD</td>
<td>2 wk</td>
<td>No short-term effects on growth rate (kemometry).</td>
</tr>
<tr>
<td></td>
<td>Skoner et al, 2000 [36]</td>
<td>100</td>
<td>Children (6-9 y)</td>
<td>BDP 168 µg BID</td>
<td>1 y</td>
<td>No effect on morning cortisol levels or response to cosyntropin; a growth-suppressive response was observed with BDP.</td>
</tr>
<tr>
<td></td>
<td>Schenkel et al, 2000 [26]</td>
<td>98</td>
<td>Children (3-9 y)</td>
<td>MFNS 100 µg QD</td>
<td>1 y</td>
<td>No effect on cortisol (cosyntropin stimulation) or growth rate (kemometry).</td>
</tr>
<tr>
<td></td>
<td>Allen et al, 2002 [79]</td>
<td>150</td>
<td>Children (3-5.9 y)</td>
<td>FP 200 µg QD</td>
<td>1 y</td>
<td>No growth changes.</td>
</tr>
<tr>
<td></td>
<td>Gradman et al, 2007 [74]</td>
<td>58</td>
<td>Children</td>
<td>FF 110 µg QD</td>
<td>2 wk</td>
<td>No short-term effects on growth rate (kemometry).</td>
</tr>
<tr>
<td></td>
<td>Ozturk et al, 1998 [75]</td>
<td>26</td>
<td>Adults (18-66 y)</td>
<td>BUD 200 µg BID</td>
<td>3-19 mo</td>
<td>No increase in IOP, no cataracts, no changes in visual acuity.</td>
</tr>
<tr>
<td></td>
<td>Simons et al, 1993 [76]</td>
<td>95</td>
<td>Children and adult (6-25 y)</td>
<td>BDP or BUD (median dose: 750 µg/d)</td>
<td>Median: 5 y (range 1-15 y)</td>
<td>No posterior subcapsular cataracts.</td>
</tr>
<tr>
<td></td>
<td>Cutler et al, 2006 [77]</td>
<td>56</td>
<td>Children (2-6 y)</td>
<td>MFNS 100 µg QD</td>
<td>42 d</td>
<td>No significant changes vs PL in serum cortisol or 24-h urinary-free cortisol.</td>
</tr>
<tr>
<td></td>
<td>Fluticasone Propionate Collab Ped Working Group 1994 [78]</td>
<td>249</td>
<td>Children (4-11 y)</td>
<td>FP 100 or 200 µg QD</td>
<td>4 wk</td>
<td>No significant changes vs PL in serum cortisol or baseline in 24-h urinary cortisol.</td>
</tr>
</tbody>
</table>
|           | Galant et al, 2003 [79] | 65 | Children (2-3 y) | FP 200 µg QD | 6 wk | FP equivalent to PL in mean change from baseline in 12-h creatinine-
In a double-blind study, 100 prepubertal children with perennial allergic rhinitis were treated with BDP 168 μg or placebo twice daily for 1 year. Overall growth rate was significantly slower in the BDP group: mean changes in standing height after 1 year were 5 cm in the BDP group vs 5.9 cm in the placebo group.

Effects on Bone Density

Based on the lack of significant changes in biochemical markers in a 1-year study of FP 200 μg daily, these INCS agents do not appear to be associated with reductions in bone mineral density or osteoporosis.

Ocular Effects

several recent long-term studies have demonstrated no evidence of ocular changes with INCs.

In a 12-month active control trial in 251 children aged 6 to 11 years, no significant changes in IOP were observed with MFNS 100 μg daily (n=166); 1 patient receiving BDP 168 μg (n=85) had increased IOP at 52 wks.

Pregnancy

all second-generation INCs are generally considered relatively safe to use in pregnancy

and no data indicate an association between INCs and congenital malformations

A meta-analysis of the use of ICS during pregnancy, as well as a systematic review showed no increase in risk of:

- major malformations
- preterm delivery
- low birth weight
- pregnancy-induced hypertension
- with inhaled corticosteroids
The FDA Pregnancy Category B rating given to BUD (all other INCs are Category C)

This was based on a review of 3 Swedish registries covering over 2000 births from 1995 to 2001 that indicated no increased risk for overall congenital malformation from the use of intranasal BUD during early pregnancy
Approximately two-thirds of approved drugs are rated Category C because data in pregnant women are lacking and animal studies have either not been performed or revealed AEs.
Conclusion

Robust clinical evidence demonstrates the safety and efficacy of the newer INCs for management of AR, CRS & polyposis.
Intranasal corticosteroids do not affect intraocular pressure or lens opacity: a systematic review of controlled trials
INCS use.

**Methodology:** A systematic review of literature from Medline and Embase databases (January 1974 to 21st of November 2013) was performed. Using the PRISMA guidelines, all controlled clinical trials of patients using INCS, that reported original measures of IOP, LO, glaucoma or cataract incidences were included. Studies with adjuvant administration of oral, inhaled and intravenous steroids were excluded.
Conclusion: Data from studies with low levels of bias do not demonstrate a clinically relevant impact of INCS on neither ocular pressure, glaucoma, lens opacity nor cataract formation.

Key words: Intranasal steroids, Intraocular pressure, Glaucoma, Cataract, Chronic upper airway disease
Safety of intranasal corticosteroids

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Objective

To discuss INCS safety data for the use of INCSs in patients with asthma and allergic rhinitis.
Results

Data on concurrent use of INCSs and ICSs are limited, but these limited data reveal no evidence of systemic effects on the hypothalamic-pituitary-adrenal axis.
Results

clinically significant. Early growth studies indicated that beclomethasone dipropionate but not other INCSs have systemic effects on growth; however, newer, larger, and better designed studies are needed to confirm these results.
Pharmacy Benefits Management Services

Clinical Guidance - Drug Class Reviews
**Drug Class Review: Intranasal Corticosteroids**

**Table 7. Dosage and Administration of the Intranasal Corticosteroids in Adult Patients**

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Dose per Actuation (# doses per unit)</th>
<th>Usual daily dose (possible number of sprays/month)</th>
<th>Usual daily dose in micrograms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beclomethasone Dipropionate (BDP)</td>
<td>Beconase</td>
<td>42 mcg (80 or 200)</td>
<td>1-2 sprays in each nostril bid-qid (120-240)</td>
<td>168-336</td>
</tr>
<tr>
<td></td>
<td>Beconase AQ</td>
<td>42 mcg (200 or &gt;)</td>
<td>1-2 sprays in each nostril bid-qid (120-240)</td>
<td>168-336</td>
</tr>
<tr>
<td></td>
<td>Vancenase</td>
<td>42 mcg (80 or 200)</td>
<td>1-2 sprays in each nostril bid-qid (120-240)</td>
<td>168-336</td>
</tr>
<tr>
<td></td>
<td>Vancenase Pocket</td>
<td>42 mcg (200 or &gt;)</td>
<td>1-2 sprays in each nostril bid-qid (120-240)</td>
<td>168-336</td>
</tr>
<tr>
<td></td>
<td>Vancenase AQ</td>
<td>84 mcg (120 or &gt;)</td>
<td>1-2 sprays in each nostril qd (60-120)</td>
<td>168-336</td>
</tr>
<tr>
<td>Budesonide (BUD)</td>
<td>Rhinocort</td>
<td>32 mcg (200 or &gt;)</td>
<td>2 sprays in each nostril bid or 4 sprays in each nostril qd (240)</td>
<td>256</td>
</tr>
<tr>
<td></td>
<td>Rhinocort Aqua</td>
<td>32 mcg 200 or &gt;</td>
<td>2 sprays in each nostril bid or 4 sprays in each nostril qd (240)</td>
<td>256</td>
</tr>
<tr>
<td>Flunisolide (FLU)</td>
<td>Nasalide</td>
<td>25 mcg (200 or &gt;)</td>
<td>2 sprays in each nostril bid-tid (240-360)</td>
<td>200-300 Max=400</td>
</tr>
<tr>
<td></td>
<td>Nasarel</td>
<td>25 mcg (200 or &gt;)</td>
<td>2 sprays in each nostril bid-tid (240-360)</td>
<td>200-300 Max=400</td>
</tr>
<tr>
<td>Fluticasone Propionate (FP)</td>
<td>Flonase</td>
<td>50 mcg (120)</td>
<td>2 sprays in each nostril qd (120)</td>
<td>200</td>
</tr>
<tr>
<td>Mometasone Furoate (MF)</td>
<td>Nasonex</td>
<td>50 mcg (120)</td>
<td>2 sprays in each nostril qd (120)</td>
<td>200</td>
</tr>
<tr>
<td>Triamcinolone Acetonide (TAA)</td>
<td>Nasacort</td>
<td>55 mcg (100 or &gt;)</td>
<td>2 sprays in each nostril qd (120)</td>
<td>220 Max=440</td>
</tr>
<tr>
<td></td>
<td>Nasacort AQ</td>
<td>55 mcg (30 or 120)</td>
<td>2 sprays in each nostril qd (120)</td>
<td>220 Max=440</td>
</tr>
<tr>
<td></td>
<td>Tri-Nasal Spray</td>
<td>50 mcg (120)</td>
<td>2 sprays in each nostril qd (120)</td>
<td>220 Max=440</td>
</tr>
</tbody>
</table>
Safety analysis of long-term budesonide nasal irrigations in patients with chronic rhinosinusitis post endoscopic sinus surgery
Methods

This was retrospective case series. Adrenal function was assessed by using the high-dose cosyntropin stimulation test.
Results

A total of 48 patients were assessed, with a mean duration of budesonide irrigations of 22 months. Stimulated cortisol levels were abnormally low in 11 patients (23%). None reported to have symptoms of adrenal suppression. Three of 4 patients who
levels. Logistic regression analysis revealed that concomitant use of both nasal steroid sprays and pulmonary steroid inhalers was significantly associated with HPAA suppression ($p = 0.024$). Patients with low
Conclusion

Long-term use of budesonide nasal irrigations is generally safe, but asymptomatic HPAA suppression may occur in selected patients. Concomitant use of both nasal steroid sprays and pulmonary steroid inhalers while using daily budesonide nasal irrigations is associated with an increased risk. Rhinologists should be alerted to the
Management of rhinosinusitis during pregnancy: systematic review and expert panel recommendations.
(PMID:26800862)

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Affiliations

Rhinology [2016, 54(2):99-104]
rhinorrhea. Eighty-eight manuscripts underwent full review after screening 3052 abstracts. No relevant level 1, 2, or 3 studies
were found. Expert panel recommendations for rhinosinusitis management during pregnancy included continuing nasal corticosteroid sprays for CRS maintenance, using pregnancy-safe
References

Thanks