SHORT REPORT

INTRANASAL FLUNITRASOL TREATMENT IN CHILDREN WITH ADENOIDAL HYPERTROPHY

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Adenoidal hypertrophy (AH) represents one of the most frequent indications for surgery in children and it has been proposed that treatment with intranasal corticosteroids can decrease the size of AH. Therefore, the aim of the study is to evaluate the effect of the use of intranasal flunisolide among children affected by AH. 178 children with AH were evaluated in this randomised and controlled study. Inclusion criteria for the study required that each patient had to have a III or IV degree of AH on the initial endoscopic examination. Children were treated with intranasal flunisolide or isotonic saline solution for 8 weeks. After treatment, endoscopy was performed to re-evaluate AH degree. Flunisolide treatment was associated with significant (p<0.04) reduction of AH degree. There was moreover a consistent reduction of children (46 out of 58) proposed to adenoidectomy. No clinically important adverse events were reported. In conclusion, this preliminary study demonstrates that an 8-week treatment with intranasal flunisolide is significantly associated with reduction of AH, thus preventing the recurrence to adenoidectomy, and is safe.

Adenoidal hypertrophy (AH) represents one of the most frequent indications for surgery in children (1). In addition, AH is associated with significant morbidity ranging from nasal airway obstruction, recurrent otitis media, chronic rhinosinusitis to obstructive sleep apnoea (2-4). The obstructive sleep apnoea syndrome affects approximately 2% of pre-school children and can result in serious complications, including neuro-cognitive disabilities, failure to thrive, and cor pulmonale (5). However, the treatment for the majority of children with uncomplicated AH is relatively easy: adenoidectomy that is curative. Nevertheless, significant risks and problems are associated with this operation (5). General complications consist of adverse anaesthetic events, dehydration, and haemorrhages. Respiratory complications include upper airway oedema, increased secretions, respiratory depression, and pulmonary oedema. The incidence of these complications has been reported to be 16% to 27% (5). Even surgery-dependent deaths do very rarely occur.

Key words: adenoidectomy, adenoidal hypertrophy, children, intranasal corticosteroids, intranasal flunisolide, fiberoptic endoscopy, placebo-controlled, therapeutical trial, upper airway obstruction

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Non-surgical alternatives for AH are limited to treatment of co-existing upper airway infections. However, it has been recently reported that treatment with intranasal corticosteroids can decrease the size of AH, using beclomethasone (6), fluticasone (7), and mometasone (8). Moreover, it has been demonstrated that nasal beclomethasone may decrease the frequency of adenotonsillectomy (9).

The present study is therefore aimed at evaluating the effect of the use of intranasal flunisolide among children affected by AH.

MATERIALS AND METHODS

Study Population

One hundred seventy-eight children, aged 3 to 6 years (mean age 4.5), 97 males and 81 females, were recruited from 4 Hospitals in Naples with the complaint of chronic nasal obstruction and were on the waiting list for adenoidectomy. Most children had been treated and followed-up previously for both chronic nasal obstruction and symptoms of chronic otitis media, serum otitis media, or chronic rhinosinusitis.

Inclusion criteria for the study required that each patient had to have a III or IV degree of AH on the initial endoscopic examination according to validated criteria (10). It is to note that IV degree represents mandatory indication for surgery. Subjects were excluded if they had used intranasal, topical, or systemic corticosteroids within the last year; had used any intranasal medication within 2 weeks of entering the study; had an active upper respiratory infection within 2 weeks of entering the study; or had a history of chronic epistaxis, immunodeficiency, or hypersensitivity to flunisolide.

Study Design

The study was single blind, randomised, and controlled in design. All children enrolled in the study were individually randomised to receive either 8 weeks of intranasal flunisolide nasal spray or isotonic saline solution with a ratio 3:1. This ratio was chosen to obtain a large number of actively treated patients. Both the active drug and the saline solution were dispensed by the Rinowash aerosolizer.

As modern therapeutic strategies involve the use of a device able to administer a correct aerosol therapy, Rinowash is a device specifically designed to administer a correct endonasal therapy, and proves particularly effective in the treatment of the upper respiratory ways (URW). Rinowash selectively treats the osteomeatal complex and the rhino-pharynx thanks to the dimension of the nebulized particles (11). The mass median aerodynamic diameter (MMAD) of the particles is greater than 10 micron, in accordance with the European Respiratory Society Guidelines.

Informed consent for participation in the study was obtained from the parents of children. The study was approved by the Review Committees.

At the first visit, flunisolide or saline solution was randomly prescribed to children. The physicians performing visits were blinded to know whether children assumed active drugs or not. During the 8-week study, patients took flunisolide (drop number=0.5xKg/bw) or saline solution twice daily.

Evaluation and Patient Management

Initial assessment of each patient upon entering the study included the following: history and physical examination, skin prick test and fiberoptic endoscopy to evaluate adenoid tissue as well as to assess nasal and sinus disease. Sequent assessment was made at 8 weeks, including history and fiberoptic endoscopy.

Skin prick test was performed according to validated criteria and using a common panel for inhalant allergens (12-13). Adenoid size was assessed during rhinolaryngoscopic examination with an Olympus flexible P-2 Rhinolaryngoscope.

AH degree has been extensively described previously (10). Briefly, during and at second evaluation, color 35-mm transparencies were taken with the child in quiet nasal respiration. Photographs were taken of both left and right posterior choanae and adenoid using an Olympus OM-2 camera adapted to the rhinoscope.

It is to note that IV AH degree suggests adenoidectomy.

Any adverse event was recorded.

Statistical Analysis

Statistical analysis was performed using the appropriate non-parametric test for nominal or ordinal data: the Wilcoxon signed-rank.

RESULTS

Among the children enrolled in the study, 178 completed the 8-week trial (139 and 39 in two groups). The use of intranasal flunisolide was associated with a significant (p<0.02) reduction of AH in 72.6% of the children (Fig. 1). On the contrary, isotonic saline solution was associated with a not significant improvement of AH as reported in 30.7% of children.

The analysis of AH degrees showed that 46
children reduced their degree from IV to III, thus avoiding adenoidectomy. In particular, the percentage of IV degree diminished from 41.7 to only 8.6. Moreover, after flunisolide treatment 48 children (34.5%) had II degree and 15 (10.8%) had I degree.

On the other hand, in the isotonic group, 6 children had IV AH degree at baseline and only 5 after treatment. Only 30.7% of children had globally a reduction of AH.

Intergroup analysis showed that flunisolide-treated children achieved a significant reduction of AH in comparison with the saline solution group (p<0.04).

There was no significant difference between atopic and non-atopic children who were actively treated.

No clinically relevant adverse events were reported in either group.

**DISCUSSION**

Adenoidal hypertrophy which obstructs the nasal airway in children is associated with numerous symptoms, including: snorting, snoring, nasal obstruction, oral breathing, rhinolalia, restless sleep, hypersomnolence, and enuresis (2-3, 14-15).

AH is also the most common cause of obstructive sleep apnea and the cardiorespiratory syndrome, with severe complications (3, 16). Moreover, AH plays a major role in the pediatric syndromes of chronic rhinosinusitis and chronic otitis media.

Adenoidecotomy has been the definitive treatment for relief of upper airway obstruction and diseases complicated by or attributable to AH (2, 17). The most common complication of adenoidecotomy is postoperative bleeding (2), but other complications, also life-threatening, may be associated. In addition, re-growth of the adenoid tissue may occur after surgical removal (16). In non-life-threatening AH, medical alternatives to adenoidecotomy are usually directed toward treatment of symptoms and concurrent infections.

Systemic corticosteroids produce a prompt, but temporary, decrease in adenoid size (18). However, significant side effects preclude their prolonged use to suppress AH. Recent trials demonstrated that intranasal corticosteroids, such as beclomethasone, fluticasone, and mometasone, reduced AH (6-8). The rationale for using topical corticosteroids is that they have limited or absent side effects and exert their anti-inflammatory activity locally on the upper airways. Moreover, a recent study provided evidence that treatment with nasal corticosteroids could represent for some children an effective means of avoiding adenoidecotomy (9).

This study is aimed at evaluating the possible effect of intranasal flunisolide in the treatment of children with III or IV degree of AH. The results confirming previous trials demonstrate that also intranasal flunisolide reduced the size of adenoid

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<tr>
<th>Flunisolide</th>
<th>At baseline</th>
<th>After treatment</th>
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<tbody>
<tr>
<td>IV degree</td>
<td>58 (41.7%)</td>
<td>12 (8.6%)</td>
</tr>
<tr>
<td>III degree</td>
<td>81 (58.3%)</td>
<td>64 (46%)</td>
</tr>
<tr>
<td>II degree</td>
<td>48 (34.5%)</td>
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<tr>
<td>I degree</td>
<td>15 (10.8%)</td>
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<table>
<thead>
<tr>
<th>Saline Solution</th>
<th>At baseline</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV degree</td>
<td>6 (15.4%)</td>
<td>5 (12.8%)</td>
</tr>
<tr>
<td>III degree</td>
<td>33 (84.6%)</td>
<td>24 (61.5%)</td>
</tr>
<tr>
<td>II degree</td>
<td>10 (25.6%)</td>
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<td>I degree</td>
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Table I. Number and percentage of children belonging to different AH degrees before and treatment with Flunisolide or saline solution.
tissue. This effect may be due to a direct lympholytic activity and to a general anti-inflammatory action in respiratory upper airway.

Moreover, this study provides evidence that flunisolide may also avoid adenoidectomy in a large cohort of children. This issue deserves an important evaluation as it has important social and pharmacoeconomic aspects.

In conclusion, this preliminary study demonstrates that an 8-week treatment with intranasal flunisolide is significantly associated with the reduction of AH, thus preventing the recurrence to adenoidectomy in a large number of children, and is safe.

REFERENCES


