Purpose of the Study. To evaluate the effects of triamcinolone acetonide (TAA) and fluticasone propionate (FP) aqueous nasal sprays on short-term, lower-leg growth velocity and hypothalamic-pituitary-adrenal (HPA) axis function among pediatric subjects.

Study Population. The subjects were 59 children (4–10.5 years of age) who were within normal limits for height and had a ≥1-year history of allergic rhinitis that required treatment and positive prick skin test responses to an inhalant allergen. Patients who had used corticosteroids in the previous 60 days were excluded from the study.

Methods. The study was a randomized, 4-way, crossover trial comparing 2 doses of TAA nasal spray, 1 dose of FP nasal spray, and placebo among pediatric patients with perennial allergic rhinitis. The study was conducted from October 1998 through September 1999, at Children’s Hospital of Pittsburgh (Pittsburgh, PA). After a 2-week baseline period, subjects entered 4 treatment periods, each lasting 2 weeks, with a 2-week washout period between treatments. Lower-leg growth velocity was measured knemometrically. HPA axis function was assessed by measuring 12-hour (overnight) urine samples for cortisol/creatinine ratios. Three clinic visits occurred during each treatment period.

Results. Of the 59 subjects, 49 completed the study in all 4 treatment periods. Four subjects discontinued participation because of adverse events (110-µg TAA group: broken foot, nasal burning sensation, asthma exacerbation; placebo group: asthma exacerbation), 3 were lost to follow-up monitoring, 1 withdrew consent, and 2 were noncompliant. In terms of lower-leg growth velocity, no differences were found between either dose of TAA and FP or between the treatment group and the placebo group. In terms of HPA axis function, the urinary cortisol/creatinine ratios from the beginning to the end of the 2-week treatment period did not differ significantly between the TAA doses and placebo; however, the mean value for the FP group was lower than those seen for other treatment groups (statistically significant). Because the coefficient of variation for the cortisol measurements was quite high, the clinical relevance of this finding is unclear.

Conclusions. This study showed that daily use of nasal sprays with TAA at 110 µg, TAA at 220 µg, or FP at 200 µg did not produce any clinically meaningful effects on lower-leg growth velocity during the 2 weeks of treatment. FP was shown to produce a statistically significant level of HPA axis suppression, compared with placebo; however, the clinical relevance of this finding is unclear.

Reviewer’s Comments. Many pediatricians and parents have concerns regarding the effects of corticosteroid use, whether for treatment of allergic rhinitis (as a nasal spray) or for treatment of asthma, on the growth and HPA axis function of children. This study provides additional reassurance that short-term use of nasal corticosteroid sprays at standard doses does not affect growth or the HPA axis.

SALLY JOO BAILEY, MD
New York, NY

INTRACAPSULAR TONSILLAR REDUCTION
(PARTIAL TONSILLETOY): REVIVING A
HISTORICAL PROCEDURE FOR OBSTRUCTIVE
SLEEP-DISORDERED BREATHING IN CHILDREN


Purpose of the Study. To compare the safety and efficacy of intracapsular tonsillar reduction (partial tonsillectomy) with those of conventional tonsillectomy for treating obstructive sleep-disordered breathing among children.

Study Population. The authors reviewed the medical records for a total of 350 children who underwent either partial (243 children) or standard (107 children) tonsillectomy for treatment of obstructive sleep-disordered breathing. The diagnosis of sleep-related obstruction was made on the basis of history findings.

Methods. This was a retrospective chart review of patient records for all children with obstructive sleep-disordered breathing who underwent either partial or standard tonsillectomy, performed by 1 of 3 primary surgeons. The choice of surgical technique was made by the parents, who were told that the new partial tonsillectomy might be associated with less postoperative discomfort but might have a greater chance of recurrence, compared with standard tonsillectomy. Subjective assessments of outcomes and quality of life, recorded in a telephone survey of parents, included postoperative pain assessment, measurement of the days to return to a normal diet, measurement of analgesic use, and assessment of relief of sleep-related obstructive symptoms. Analyses of patient records included measurements of operative time, estimated blood loss, and incidence of delayed postoperative complications, such as bleeding and tonsil regrowth. Partial tonsillectomy was performed by using a microdebrider to remove the bulk of the tonsil tissue while leaving the surrounding capsule intact. Standard tonsillectomy was performed by using electrocautery to remove the palatine tonsils and their capsules in their entirety.

Results. The children who underwent partial tonsillectomy were younger than those who underwent standard tonsillectomy (mean age: 6.1 years vs 9.1 years; P < .001). The children who were treated with the new technique experienced significantly less postoperative pain, fewer days to normal activity and diet, and less analgesic use, compared with the children who underwent standard tonsillectomy. Partial tonsillectomy was associated with small but significantly greater intraoperative blood loss, after adjustment for patient age, and the new procedure required a slightly longer time to perform (an average of 3 minutes longer for experienced surgeons). The microdebrider instrumentation was more expensive than that used for conventional tonsillectomy. The frequency of delayed postoperative bleeding appeared lower with partial tonsillectomy (4.7% and 1.7% for standard and partial tonsillectomy, respectively), but this difference was not statistically significant. Quality of life measurements showed similar rates of improvement for children treated with the 2 procedures, with >93% of the parents in both groups reporting marked improvements after surgery. Tonsillar regrowth after partial tonsillectomy was not observed for any patient during the 2-year follow-up period.

Conclusions. Partial tonsillectomy is a safe reliable technique that results in less postoperative pain, more rapid return to normal function, and equivalent improvements in sleep-related airway obstruction and quality of life, compared with standard tonsillectomy, among children.

Reviewers’ Comments. The most common indication for adenotonsillectomy among children is an obstructive sleep disorder. Tonsillectomy is associated with considerable postoperative discomfort and a small but finite risk of perioperative bleeding. The authors support the concept that subtotal tonsil removal (usually combined with adenoidectomy) may be curative, with less postoperative pain and other morbidities. This study has the limitations of all retrospective analyses. The study groups may not be directly comparable, because of selection biases. Additional
bias may occur with telephone surveys of patients and families after a surgical procedure. Finally, the diagnosis of obstructive sleep-disordered breathing on the basis of history findings, with similar assessments of improvement after surgery, does not have the quantitative accuracy of preoperative and postoperative polysomnographic evaluations. Despite these limitations, this study succeeded in showing that intracapsular tonsillectomy (partial tonsillectomy) shows great promise as a safe effective treatment for children with obstructive sleep-disordered breathing and appears to cause less morbidity than standard tonsillectomy. Additional studies with more long-term follow-up monitoring are required to assess the recurrence rates for both obstructive and infectious tonsillar disease, after this procedure is performed among young children.

Matthew E. Wolpoe, MD
David E. Tunkel, MD
Baltimore, MD

Asthma

PATHOPHYSIOLOGY

EARLY THICKENING OF THE RETICULAR BASEMENT MEMBRANE IN CHILDREN WITH DIFFICULT ASTHMA


Purpose of the Study. To determine whether reticular basement membrane (RBM) thickening is present among children with difficult-to-control asthma and to compare the findings with those for adults with asthma.

Study Population. Subjects were 19 children (6–16 years of age) with difficult-to-control asthma. Control subjects were 10 children (7–16 years of age) without asthma, 10 adults with mild asthma, 6 adults with severe asthma, and 8 healthy adults.

Methods. The 19 asthmatic children underwent bronchoscopy and endobronchial biopsy as part of an asthma evaluation. Patients were treated with oral prednisolone therapy (40 mg/day) for 2 weeks before the biopsy. Exhaled nitric oxide levels were measured before and after the course of corticosteroids. Endobronchial samples were obtained from third-order or higher bronchi on either side of the lung. The control subjects were pediatric patients undergoing bronchoscopy because of other indications. The adults with mild asthma were corticosteroid-naïve. Adults with severe asthma underwent biopsy while intubated because of a severe asthma attack. The 8 adult control subjects were nonsmokers. Three biopsy specimens for each patient were fixed immediately and stained for light-microscopic evaluation.

Results. Children with asthma had an average RBM thickness of 8.2 μm (range: 5.4–11.2 μm). Adults with mild asthma had a mean RBM thickness of 8.1 μm (range: 5.8–10.0 μm); adults with severe asthma had a mean RBM thickness of 7.2 μm (range: 2.8–10.0). Adult control subjects had an average RBM thickness of 4.4 μm (range: 3.2–6.3 μm; P < .01); pediatric control subjects had an average RBM thickness of 4.9 μm (range: 3.7–8.3 μm; P < .01). There was no correlation of RBM thickness with duration of asthma or age. The exhaled nitric oxide concentrations before and after prednisolone treatment were 16.9 ppb (range: 1.2–33.4 ppb) and 8.1 ppb (range: 1.3–24.5 ppb), respectively (normal values at the study center: <12.5 ppb). There was no correlation between RBM thickness and exhaled nitric oxide levels.

Conclusions. The authors concluded that RBM thickening is a feature of childhood asthma that is not present among normal control subjects. RBM thickening is a common feature of asthma among adults and children but is not correlated with age, severity, or duration.

Reviewers’ Comments. This study demonstrated that histologic changes in the airways of children with severe asthma, as evidenced by RBM thickening, are similar to those seen among adults. This is one of the few such studies among children and is novel for the inclusion of child and adult control subjects. The authors were unable to show a link between RBM thickness and severity of asthma or a marker of inflammation (exhaled nitric oxide). This information raises questions regarding the timing and appropriateness of antiinflammatory treatment delivered with the hope of preventing airway remodeling among children with asthma. Clinical trials are needed to establish whether it is possible to prevent these changes and whether such prevention is important.

David W. Hauswirth, MD
Larry W. Williams, MD
Durham, NC

LIPOPOLYSACCHARIDE-ENHANCED, TOLL-LIKE RECEPTOR 4-DEPENDENT, T HELPER CELL TYPE 2 RESPONSES TO INHALED ANTIGEN


Purpose of the Study. To evaluate the dose-dependent effects of lipopolysaccharide (LPS) (endotoxin) inhalation and LPS-induced activation of toll-like receptor 4 (TLR4) on the generation of T helper (Th) cell type 2-dependent allergic inflammatory responses to an inhaled antigen, ovalbumin (OVA).

Study Population. Wild-type or TLR4-deficient, 6- to 10-week-old, female mice were studied.

Methods. Mice were sensitized with intranasal exposure to LPS-depleted OVA or OVA with either a low (0.1 μg) or high (100 μg) dose of LPS. After intranasal OVA challenge, pulmonary inflammatory responses were assessed through enumerating bronchoalveolar lavage cells, performing histopathologic analyses, measuring OVA-dependent cytokine production by lung-draining lymph node cells, and determining OVA-specific serum antibody levels. Dendritic cell responses to OVA with LPS were evaluated in cytokine production, activation marker expression, and cell migration studies.

Results. After antigen challenge, mice sensitized to OVA with low-dose LPS exhibited a Th2-associated response, with pulmonary eosinophilia, airway mucus secretion, Th2 cytokine (interleukin-5 and -13) production by lymph node cells, and production of high levels of OVA-specific immunoglobulin E and immunoglobulin G1. In contrast, mice sensitized to OVA with high-dose LPS developed a Th1-associated response, with a predominance of neutrophils, no airway mucus secretion, Th1 cytokine (interferon-γ) production by lymph node cells, and production of high levels of OVA-specific immunoglobulin G2a. No pulmonary inflammatory responses were observed with mice sensitized to LPS-depleted OVA. OVA sensitization of TLR4-deficient mice with either low- or high-dose LPS failed to generate inflammatory responses. However, treatment with tumor necrosis factor, which is secreted by LPS-stimulated dendritic cells, compensated...
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Matthew E. Wolpoe and David E. Tunkel

*Pediatrics* 2004;114;526

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