HYPERTONIC SALINE SOLUTION IN CHILDREN WITH ADENOIDAL HYPERYTROPHY: PRELIMINARY EVIDENCE

G. CIPRANDI, A. VARRICCHIO[1], M. CAPASSO[2], A.M. VARRICCHIO[3], A. DE LUCIA[1], E. ASCIONE[1], F. AVVISATI[1], M. DI GIOACCHINO[4] and U. BARILLARI[5]

Department of Internal Medicine, Azienda Ospedaliera Universitaria San Martino, Genoa; [1]U.O.C. di O.R.L. - Ospedale San Gennaro, ASL Na1, Naples; [2]U.O. Pediatria con Nido, Ospedale Civile di Piedimonte Matese (CE); [3]U.O.C. di O.R.L. - Azienda Ospedaliera Pediatrica Santobono Pausilipon, Naples; [4]Allergy Related Disease Unit, G. d'Annunzio Universtity Foundation, Chieti; [5]Servizio di Foniatria ed Audiologia, Second University of Naples, Italy

Received May 31 2007 – Accepted October 9, 2007

Adenoidal hypertrophy (AH) is a frequent problem in children. A preliminary study evidenced that intranasal hypertonic solutions may exert an anti-inflammatory activity. The aim of the study is to evaluate the effect of intranasal hypertonic or isotonic solutions in children affected with AH. For this purpose, 78 children with AH were evaluated in a 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 hypertonic or isotonic saline solution for 8 weeks. After treatment, endoscopy was performed to evaluate AH degree. Hypertonic treatment was associated with significant ($p<0.05$) reduction of AH degree. There was a consistent reduction of children with III degree of AH. No adverse events were reported. This preliminary study demonstrates that an 8-week treatment with intranasal hypertonic solution is associated with significant reduction of AH. Therefore, this study evidences that hypertonic solution may exert an anti-inflammatory activity and is safe.

Adenoidal hypertrophy (AH) represents one of the most frequent indications for surgery in children (1). Moreover, AH is associated with significant morbidity ranging from nasal airway obstruction, recurrent otitis media and cronic rhinosinusitis to obstructive sleep apnea and cardiorespiratory syndrome (2-7).

It was recently reported that treatment with corticosteroids can decrease the size of AH, both using beclomethasone (8) and fluticasone (9-13). It has also been demonstrated that nasal beclomethasone is capable of decreasing the frequency of adenotonsillectomy (14-17). On the other hand, these preliminary trials are not conclusive as there is no indication of the real effectiveness and overall duration of adenoidal size reduction. Moreover, corticosteroids may also induce side effects.

Recently, preliminary evidence suggested that hypertonic saline nasal sprays alone are effective in treating nasal symptoms in children with seasonal allergic rhinitis (18). Therefore, the present study aimed at evaluating the effect of intranasal hypertonic solution among children affected by AH.

Key words: adenoidal hypertrophy, children, intranasal hypertonic solution

Mailing address: Giorgio Ciprandi, M.D.
Semeiotica Medica I - Padiglione 3,
A.O.U. San Martino,
Largo R. Benzi 10,
16132 Genoa, Italy
Tel: ++ 39 10 35338120 Fax: ++39 10 3537573
e-mail: gio.cip@libero.it

1721-727 (2007)
Copyright © by BIOLIFE, s.a.s.
This publication and/or article is for individual use only and may not be further reproduced without written permission from the copyright holder.
Unauthorized reproduction may result in financial and other penalties

MATERIALS AND METHODS

Study Population

Seventy-eight children, 44 males and 34 females, aged 3 to 6 years (mean age 4.5) and complaining of chronic nasal obstruction, were recruited from two Hospitals in Naples.. Inclusion criteria for the study required a III or IV degree of AH in each patient at the initial endoscopic examination (19-22).

Subjects were excluded if they had used intranasal, topical, or systemic corticosteroids within the last year; had used any intranasal medication within 2 weeks before entering the study; had an active upper respiratory infection within 2 weeks before entering the study; or had a history of chronic epistaxis or immunodeficiency.

Study Design

The study was single blind, randomised, and controlled in design. All children enrolled were individually randomised to receive 8 weeks of either intranasal hypertonic nasal spray or isotonic saline solution. Both intranasal solutions were administered by a Rinowash aerosolizer, as modern therapeutic strategies suggest the use of a device able to administer a correct aerosol therapy, and 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 is able to selectively treat the osteomeatal complex and the rhino-pharynge thanks to the dimension of the nebulized particles. The mass median aerodynamic diameter (MMAD) of the particles is greater than 10 micron, in accordance with the European Resiratory Society Guidelines.

Informed consent for participation in the study was obtained from the children's parents. The study was approved by the Review Committee. Physicians performing visits were blinded from knowing whether children assumed the hypertonic solution or not.

During the 8-week study, the patients administered the saline solutions twice daily.

Evaluation and Patient Management

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

Adenoid size was assessed during rhinolaryngoscopic examination with an Olympus flexible P-2 Rhinolaryngoscope.

AH degree has been extensively described previously (19). Briefly, during the first 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.

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

All 78 children enrolled in the study completed the 8-week trial (39 and 39 in two sections). The use of intranasal hypertonic solution was associated with a significant ($p<0.05$) reduction of AH in 43.5% of them. On the contrary, isotonic saline solution was not associated with significant improvement of AH as reported in 30.7% of children.

Intergroup comparison showed that hypertonic solution-treated children achieved a significantly ($p<0.05$) greater reduction of AH in comparison with isotonic solution-treated patients (Fig. 1).

The analysis of AH degrees showed that 18 children had a reduction of adenoidal size after treatment with hypertonic solution (Table I).

No adverse events were reported in either group.

DISCUSSION

Adenoidal hypertrophy which obstructs the nasal airway in children is associated with numerous symptoms, including: snoring, nasal obstruction, oral breathing, rhinolalia, restsleep, hypersomnolence, and enuresis (2-3, 23-28).

The most common cause of obstructive sleep apnea and the cardiorespiratory syndrome is adenoidal or adenotonsillar hyperplasia (3, 29-31). Moreover, AH plays a major role in the pediatric syndromes of chronic rhinosinusitis and chronic otitis media.

Adenoidectomy has been the definitive treatment for relief of upper airway obstruction and diseases complicated by or attributable to AH (2, 24). The most common complication of adenoidectomy is post-operative bleeding (2). Sometimes, re-growth of the adenoid after surgical removal may occur (32).

Table I. *Number and percentage of children belonging to different AH degrees before and treatment with flunisolide or saline solution.*

Hypertonic Solution	**At baseline**	**After treatment**
IV degree	**4 (10.2%)**	**3 (7.7%)**
III degree	**35 (89.7%)**	**19 (48.7%)**
II degree		**12 (30.7%)**
I degree		**5 (12.8%)**
Isotonic Solution	**At baseline**	**After treatment**
IV degree	**6 (15.4%)**	**5 (12.8%)**
III degree	**33 (84.6)**	**24 (61.5%)**
II degree		**10 (25.6%)**
I degree		

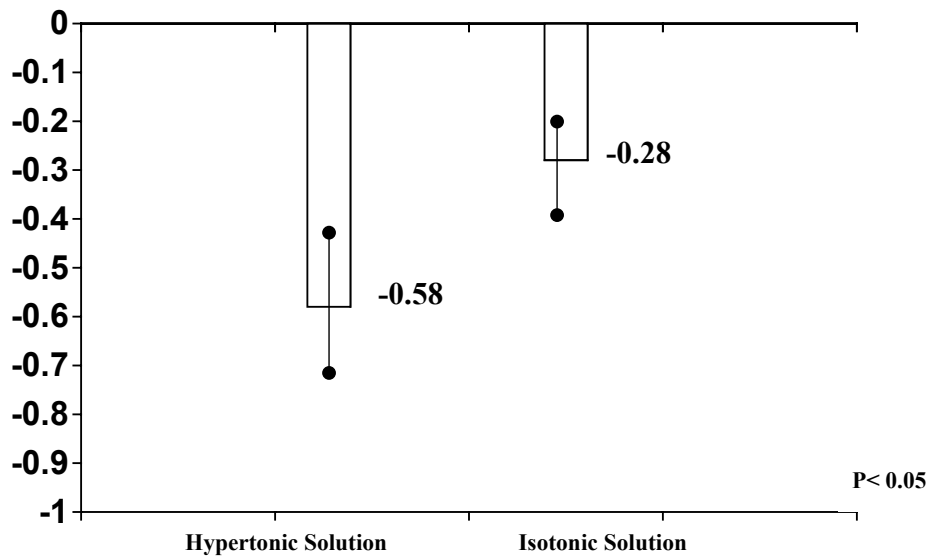

Fig. 1. *Mean values (SD) of AH reduction in the two treated groups. Hypertonic solution-treated children achieved a significantly greater reduction of AH in comparison with isotonic solution-treated patients: p<0.05 (Wilcoxon signed-rank).*

In non-life-threatening AH, medical alternatives to adenoidectomy are usually directed toward treatment of symptoms and concurrent infections.

Systemic corticosteroids may produce a prompt, but temporary, decrease in adenoid size. However, significant side effects preclude their prolonged employment to suppress AH. Recent trials demonstrated that intranasal corticosteroids, such as beclomethasone and fluticasone, were capable of reducing AH (8-9). Moreover, a very recent study provided evidence that treatment with nasal corticosteroids could represent, for some children,

an effective means for avoiding adenoidectomy (14).

However, no definitive indication for their use exists. On the other hand, hypertonic solution may exert symptomatic activity in children with seasonal allergic rhinitis (18).

Thus, this study is aimed at evaluating the possible effect of intranasal hypertonic solution in the treatment of children with III or IV degree of AH. The results provide preliminary evidence that hypertonic solution alone may reduce adenoidal size. An anti-inflammatory activity, due to osmolar effect, may explain the effectiveness of hypertonic solution. Even though this treatment is not resolutive, it is completely devoid of side effects. Therefore, hypertonic solution may be used for long periods as an adjunctive treatment to active drugs, such as topical corticosteroids, and might be used for long periods as an alternative to a short course of corticosteroids.

In conclusion, this study demonstrates that an 8-week treatment with intranasal hypertonic solution is associated with significant reduction of AH and is safe.

REFERENCES

1. **Ratkow I.M.** 1986. Ear, nose, and throat operations in the United States. *Arch. Otolaryngol. Head Neck Surg. 112:873.*
2. **Gates G.A., H.R. Muntz and B. Gaylis.** 1992. Adenoidectomy and otitis media. *Am. Otol. Rhinol. Laryngol. 101:24.*
3. **Potsic W.P. and R.F. Wetmore.** 1990. Sleep disorders and airway obstruction in children. *Otolaryngol. Clin. North Am. 23:651.*
4. **Grundfast K.M. and D.J. Wittich.** 1982. Adenotonsillar hypetrophy and upper airway obstruction in evolutionary perspective. *Laryngoscope 92:650.*
5. **Choucair N., V. Laporte, R. Levy, C. Tranchant, J-P. Gies, P. Poindron and Y. Lombard.** 2006. The role of calcium and magnesium ions in uptake of β-amyloid peptides by microglial cells. *Int. J. Immunopathol. Pharmacol. 19:683.*
6. **Castellani M.L., V. Salini, S. Frydas, J. Donelan, M. Tagen, B. Madhappan, C. Petrarca, K. Falasca, G. Neri, S. Tetè and J. Vecchiet.** 2006. The proinflammatory interleukin-21 elicits anti-tumor response and mediates autoimmunity. *Int. J. Immunopathol. Pharmacol. 19:247.*
7. **Mayilyan K.R., J.S. Presanis, J.N. Arnold and R.B. Sim.** 2006. Discrete MBL-MASP complexes show wide inter-individual variability in concentration: data from UK vs. Armenian populations. *Int. J. Immunopathol. Pharmacol. 19:567.*
8. **Demain J.G. and D.W. Goetz.** 1995. Pediatric adenoidal hypertrophy and nasal airway obstruction reduction with aqueous nasal beclomethasone. *Pediatrics 95:355.*
9. **Brouilette R.T., J.J. Manoukian and F.M. Ducharme.** 2001. Efficacy of fluticasone nasal spray for pediatric obstructive sleep apnea. *J. Pediatr. 138: 838.*
10. **Serra A., G.C. Schito, G. Nicoletti and G. Fadda.** 2007. A therapeutic approach in the treatment of infections of the upper airways: thiamphenicol glycinate acetylcysteinate in sequential treatment (systemic-inhalatory route). *Int. J. Immunopathol. Pharmacol. 20:607.*
11. **Papoff P., M. Mancuso, C.S. Barbàra and C. Moretti.** 2007. The role of terlipressin in pediatric septic shock: a review of the literature and personal experience. *Int. J. Immunopathol. Pharmacol. 20: 213.*
12. **Deepak P., S. Kumar and A. Acharya.** 2007. IL-13 neutralization modulates function of type II polarized macrophages *in vivo* in a murine T-cell lymphoma. *Eur. J. Inflamm. 5:37.*
13. **Karagiannis V., A. Daniilidis, N. Klearhoy, A. Mamopoulos, V. Garipidou, S. Vakalopoulou and H. Zaboulis.** 2007. Acute leukemia and pregnancy. *Eur. J. Inflamm. 5:47.*
14. **Criscuoli G., S. D'Amora, G. Ripa, G. Cinquegrana, N. Mansi, N. Impagliazzo and A. Pisacane.** 2003. Frequency of surgery among children who have adenotonsillar hypertrophy and improbe after treatment with nasal beclomethasone. *Pediatrics 111:236.*
15. **Burastero S.E., C. Paolucci, D. Breda, J. Ponti, B. Munaro and E. Sabbioni.** 2006. Chromium (VI)-induced immunotoxicity and intracellular accumulation in human primary dendritic cells. *Int.*

J. Immunopathol. Pharmacol. 19:581.

16. **Di Trolio R., G. Di Lorenzo, M. Delfino and S. De Placido.** 2006. Role of pegylated lyposomal doxorubicin (PLD) in systemic Kaposi's sarcoma: a systematic review. *Int. J. Immunopathol. Pharmacol. 19:253.*
17. **Scuderi N., M. Mazzocchi and C. Rubino.** 2007. Effects of zafirlukast on capsular contracture: controlled study measuring the mammary compliance. *Int. J. Immunopathol. Pharmacol. 20:577*
18. **Garavello W., M. Romagnoli, L. Sordo, G. Sambataro and R.M. Gaini.** 2003. Hypersaline nasal irrigation in children with symptomatic seasonal allergic rhinitis: a randomized study. *Ped. Allergy Immunol. 14:140.*
19. **Cassano P., M. Gelardi, M. Cassano, M.L. Fiorella and R. Fiorella.** 2003. Adenoid tissue rhinopharyngeal obstruction grading based on fiberendoscopic findings: a novel approach to therapeutic management. *Int. J. Pediatr. Otorhinolaryngol. 67:1303.*
20. **Lakota K., K. Mrak-Poljšak, B. Rozman, T. Kveder, M. Tomšič21. and S. Sodin-Semrl.** 2007. Serum amyloid A activation of inflammatory and adhesion molecules in human coronary artery and umbilical vein endothelial cells. *Eur. J. Inflamm. 5:73.*
22. **Stassi G., A. Cascio, C. Iaria, D. Gazzara, G.B. Costa, D. Iannello and A. Arena.** 2007. Modulation of GRO-α and TNF-α production by peripheral blood mononuclear cells treated with killed *helicobacter pylori*. *Eur. J. Inflamm. 5:83.*
23. **Lo Muzio L., A. Santarelli, M. Emanuelli, F. Pierella, D. Sartini, S. Staibano, C. Rubini and G. De Rosa.** 2006. Genetic analysis of oral squamous cell carcinoma by cDNA microarrays focused apoptotic pathway. *Int. J. Immunopathol. Pharmacol. 19:675.*
24. **Brodsky L.** 1989. Modern assessment of tonsils and adenoids. *Pediatr. Clin. North Am. 36:1551.*
25. **Tankel J.W. and A.D. Chessman.** 1986. Symptom relief by adenoidectomy and relationship to adenoid and post-nasal airway size. *J. Laryngol. Otol. 100: 637.*
26. **Muthusamy A.S.R., A. Vaidya and P.J. Friend.** 2006. Clopidogrel associated acute migratory arthritis following kidney-pancreas transplantation. *Int. J. Immunopathol. Pharmacol. 19:443.*
27. **Ammendolia M.G., F. Superti, L. Bertuccini, F. Chiarini, M.P. Conte, D. Cipriani, L. Seganti and C. Longhi.** 2007. Invasive pathway of *Listeria Ivanovii* in human amnion-derived WISH cells. *Int. J. Immunopathol. Pharmacol. 20:509.*
28. **D'Onofrio F., L. Miele, M. Diaco, L. Santoro, G. De Socio, M. Montalto, A. Grieco, G. Gasbarrini and R. Manna.** 2006. Sjogren's syndrome in a celiac patient: searching for environmental triggers. *Int. J. Immunopathol. Pharmacol. 19:445.*
29. **Vena G.A., N. Cassano, G. Alessandrini, D. Fai, M. Gabellone, P. Ligori, C. Malvindi, A. Mancino, S. Pellè, F. Rinaldi and M.R. Sodo.** 2007. Treatment of mild to moderate plaque psoriasis with calcitriol ointment applied with or without a dosing device. *Eur. J. Inflamm. 5:89.*
30. **Yonkers J.W. and R.C. Spaurc.** 1987. Upper airway obstruction and the pharyngeal lymphoid tissue. *Otolaryngol. Clin. North Am. 20:235.*
31. **Falasca K., C. Ucciferri, M. Manzoli, P. Mancino, E. Pizzigallo, P. Conti and J. Vecchiet.** 2007. Metabolic syndrome and cardiovascular risk in HIV-infected patients with lipodystrophy. *Int. J. Immunopathol. Pharmacol. 20:519.*
32. **Marasini B., L. Belloli and M. Massarotti.** 2007. Interstitial lung disease in systemic sclerosis. *Int. J. Immunopathol. Pharmacol. 20:223.*
33. **Rasmussen N.** 1987. Complications of tonsillectomy and adenoidectomy. *Otolaryngol. Clin. North Am. 20:383.*