

## A New Method of Conservative Residual OME Treatment

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**ABSTRACT.** Nonsurgical conservative therapy was used for residual OME (otitis media with effusion) treatment. In this article OME is considered as chronic secretory *salpingootitis*. Secretory salpingootitis in all patients studied developed in consequence of acute otitis media (AOM). Patients were distributed in 4 groups and were treated by instillation of Sinuforte/Nasodren spray (standardized Cyclamen tuber sap, S/N) in both nostrils once daily for 10 days. The results of S/N monotherapy were compared with outcomes of combined S/N/antibiotic, and standard antibiotic/decongestant therapy. Results indicate that treatment based on administration of S/N as a constituent of the therapy is associated with a significant clinical benefit. Outcomes in S/N monotherapy group and combined S/N/antibiotic group were obviously more favorable than in the group to which the standard method of conservative OME treatment was applied. Clinically proved curative outcomes of *salpingootitis* in humans treated with S/N could be explained by prompt reflex discharge from hyperplastic/hypertrophic glands, resulting reduction in edematous state of the mucosal lining in the auditory tube, opening of the pharyngeal orifice of the tube and consequent facilitated propulsion of exudates out of tubar, and respectively, middle ear cavities. In other words, beneficial outcome is achieved due to effective draining of middle ear cavity by inherent, natural way. These results permit to consider topically applied S/N as an adequate stimulus for physiologic reflex discharge of inflammatory secretions out of the auditory tube and for its frequent opening. © 2010 Bull. Georg. Natl. Acad. Sci.

**Key words:** OME, salpingootitis, conservative treatment, Nasodren, reflex response.

Otitis media with effusion (OME) or secretory otitis media is defined as the presence of fluid in the middle ear without signs or symptoms of acute ear infection. OME may occur spontaneously, or as an inflammatory response following acute otitis media (AOM) because of poor eustachian tube function and abnormal middle ear pressures due to residual inflammatory alterations in the auditory tube proper, such as adenoid hypertrophy, abnormal secretion and swelling of mucous membrane. Therefore, this residual OME could be considered as *chronic salpingootitis with effusion*. Many episodes of residual OME resolve spontaneously: for example, about

75% to 90% of residual OME after an AOM episode resolves within 3 months. Nevertheless, among patients which improve within 3 months, one third will have OME relapse within the next 3 months [1-4].

Chronic middle ear effusion may persist for several months and 5% to 10% of episodes last 1 year or longer. Chronic effusions may produce a degree of conductive hearing loss that requires treatment by the placement of pneumatic equalisation tubes, because persistent middle-ear fluid from OME results in decreased mobility of the tympanic membrane and serves as a barrier to sound conduction. When a patient becomes a surgical

candidate, tympanostomy tube insertion is the preferred initial procedure. However, it is assumed conventionally that surgery should be withheld for 3 or more months to permit the highest rate of spontaneous resolution. Nevertheless, prolonged watchful waiting of OME is not appropriate when regular surveillance is impossible or when the child is at risk for developmental sequelae of OME.

Tympanostomy tubes are recommended for initial surgery because randomized trials show a mean 62% relative decrease in effusion prevalence. Unfortunately, about 20% to 50% of children who have had tympanostomy tubes have OME relapse after tube extrusion that may require additional surgery [5].

Nonsurgical therapies that are used in the OME treatment include antihistamines and decongestants but recently are considered ineffective for OME and are not recommended for treatment. Antimicrobials and corticosteroids do not have long-term efficacy and are not recommended for routine management. Really, antimicrobial therapy, with or without steroids, has not been demonstrated to be effective in long-term resolution of OME, but in some cases this therapy can be considered an option because of short-term benefit in randomized trials, when the parent or caregiver expresses a strong aversion to impending surgery. In this circumstance a single course of therapy for 10 to 14 days may be used [6]. Other nonsurgical methods include autoinflation of the eustachian tube, oral or intratympanic use of mucolytics, and systemic use of pharmacologic agents other than antimicrobials, steroids and antihistamine-decongestants. Insufficient data exist for any of these therapies to be recommended in treating OME [7].

In this respect *Cyclamen tuber sap* and extract that have been standardized by Hartington Pharma LTD as nasal spray Sinuforte/Nasodren (S/N) for rhinosinusitis (RS) treatment seems to be of particular interest. High percentage of curative outcomes of RS was proved by several clinical trials using S/N. In Ukraine, Russia and Georgia a large number of clinical trials have been carried out that have established its effectiveness and safety in the treatment of acute and chronic RS, and also for postoperative care [8,9] According to the "Prosinus" study, a pioneering multicentre, prospective, epidemiological study performed in Spain, addition of S/N to any other treatment provides, in all cases added benefit in terms of cure. Moreover, in most cases of acute RS, antibiotics do not provide any added benefit if S/N is given. Curative outcomes were proved clinically even when patients were treated with S/N only [10, 11]. Interestingly, curative outcomes were proved clinically

also in acute OM cases when patients were treated with intranasal S/N only [12].

This article deals with conservative treatment of residual OME after AOM episodes using S/N monotherapy. The results were compared with outcomes of combined S/N/antibiotic and standard antibiotic/decongestant therapy.

## Material and Methods

Diagnosing of residual AOM was based on acute onset of signs and symptoms, the presence of middle-ear effusion, and signs and symptoms of middle-ear inflammation. Residual OME persisting for more than 3 months after AOM episode was diagnosed by means of microotoscopy, audiometry and tympanometry in 56 patients aged 6-12 years. As mentioned above, secretory OME in all studied patients developed in consequence of AOM. According to audiometric data conductive hearing loss appeared in all cases, and mean speech frequency threshold did not exceed 40 db. Bilateral effusion was observed in 38 patients, but 18 had unilateral effusion. Patients were distributed in 4 groups. Group I (15 patients) was treated by instillation of S/N spray in both nostrils once daily; group II (15 patients) was treated by instillation of S/N, and amoxicillin orally; group III (16 patients) was treated with oral amoxicillin and xilometasoline as decongestant. In all these groups patients were treated for 10 days. In group IV patients (10) were left without treatment, but under observation. On the 7<sup>th</sup> day of treatment and 4<sup>th</sup> day after cessation of treatment the patients were examined repeatedly for quality status of hearing according to audiometry and tympanometry. The patients were observed for additional 3 months.

## Results

After irrigation of nasal cavity in all patients nasal discharge and frequent deglutition could be observed for approximately 30-40 min. The majority of patients in groups I and II confirmed hearing improvement already from 3-4<sup>th</sup> day of treatment. Audiometric examination on 7<sup>th</sup> day in group I verified recovery of normal hearing in approximately 66% cases and improvement in 9%, respectively. In group II such outcomes comprised 75% and 10%, respectively. In group III on 7<sup>th</sup> day normal hearing was recorded in 38% only and improvement only in 16%, but in control group normal hearing was observed in 30% and improvement in 24% respectively. In group I, at the second audiometric examination, on the 4<sup>th</sup> day after the cessation of treatment, only one patient had sustained type B (flat curve) in tympanogram; in this particular case after 3 months of observation

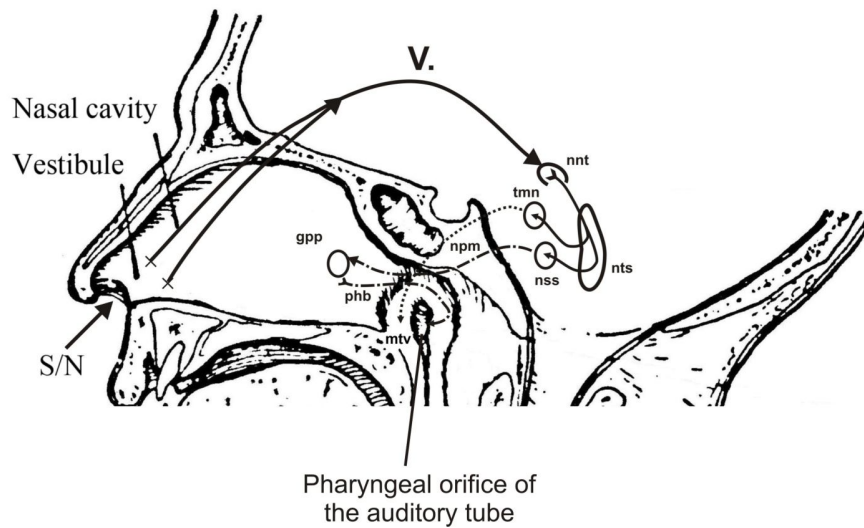


Fig. Secretomotor reflexes elicited in auditory tube by irrigation of anterior nasal cavity

**Heavy arrow:** afferent branch of the reflex arc

**Dotted arrows:** efferent branches of the reflex arc

**V:** trigeminal nerve (afferent fibers); **nnt:** trigeminal sensory nucleus; **nts:** solitary tract nucleus; **tmn:** trigeminal motor nucleus; **nss:** superior salivatory nucleus; **npm:** greater petrosal nerve (from n. intermedius of VII); **gpp:** pterygopalatine ganglion; **phb:** pharyngeal branch of maxillary nerve (parasympathetic secretory fibers); **mtv:** tensor veli palatini muscle.

typanostomy tube insertion was performed. In two other cases of this group negative pressure in tympanic cavity was detected, but it resolved spontaneously within 2 weeks. In group II in 3 patients audiometry revealed conductive hearing loss confirmed by C type curve in tympanogram and hearing depression in low frequency; however, hearing recovered spontaneously. In 4 patients of group III persistent effusion was detected after completion of treatment, and respectively ventilation tubes were inserted. In control untreated group IV - 2 patients complained of worsened hearing, other 3 patients had persistent effusions in tympanic cavity, and again in 3 cases persistent low pressure in tympanic cavity was detected. After 3 months observation 4 patients within this group were inserted with tympanostomy tubes, but in one case it appeared ineffective, and antromastoidotomy was performed.

## Discussion

Results indicate that treatment based on administration of S/N as a constituent of the therapy is associated with a significant clinical benefit. The curative outcomes of conservative residual otitis media with effusion (OME) treatment can be considered equally effective in groups treated with S/N or S/N- amoxicillin combined, despite that in the monotherapy group 1 case was negative, because actually the number of patients in either group was inadequate for comparison of results. Outcomes in groups I and II were obviously more favorable than in group III, when the standard method of conservative OME treatment was applied.

The physiological and/or pathophysiological grounds of conservative treatment of OME, which is considered otitis media with effusion in this clinical investigation, may be explained by mechanisms of therapeutic efficacy of S/N also in RS treatment. Actually, this is important for understanding the curative outcomes observed in the present investigation. Main pharmacologically active principles of S/N are triterpene glycosides – saponins. Saponins at intranasal administration evoke typical “emergency acute airway defense response” [13], which is a reflex positively controlled by cholinergic mechanisms [14, 15]. That specific reflex-eliciting effect of S/N depends directly on its constituent saponins was evidenced by similar properties of a group of purified saponins obtained from other plant species (e.g. *Quilaja*, *Thea*, *Aesculus*) which also evoke nasal reflex secretion in the range of 0.1-1.0 % concentrations [16]. Initial action of S/N is confined to limited area of anterior portions of inferior nasal meatus and of inferior concha, where it stimulates the “nociceptive” endings of *ethmoidal* nerve (branch of N. *trigeminus*, V); as a result, cholinergic reflex responses are elicited from *superior salivatory nucleus*, and cholinergic impulses are conveyed to *pterygopalatine ganglion*, and thereafter to nasal and paranasal cavities via *nasopharyngeal nerves*. It was supposed that reduction in oedematous state could be achieved by prompt discharge of secretions from hyperplastic/hypertrophic sero-mucous glands in nasal and paranasal cavities leading to effective dehydration of swollen mucosa. Actually, statistically significant differences were obtained in the improvement of the nasal oedema as determined

by endoscopy confirming a “*detumescent*” effect clinically [11], predicted on the basis of histophysiological experiments in healthy rabbits [17, 18]. Similarly, while the auditory tube is lined with typical pseudostratified respiratory epithelium with numerous goblet cells, and while submucosal glands are also abundant in this region, i.e. in the lower 2/3 of the tube, and are innervated by parasympathetic fibers originating from *pterygopalatine ganglion* (assembled in *pharyngeal nerve*), irritation of nasal mucosa could trigger secretion also in this part of the auditory tube, eliciting the physiological mechanism of draining and expulsion of effusions out of its lumen. Additionally, afferent impulses from *ethmoidal nerve* (branch of V) integrated in the nucleus of *tractus solitarius* are conveyed also to, and trigger the reflex contraction of *tensor veli palatini* muscle (innervated by motor fibres of V), which pools the wall of tube laterally during contraction and opens the pharyngeal orifice of the tube. Therefore opening of the tube is added to the secretory draining counterpart creating integrated physiologic cleansing conditions (Fig. 1).

Actually, clinically proved curative outcomes of *salpingoitis* in humans treated with S/N could be explained by active reflex discharge from hyperplastic/hypertrophic glands in the mucosal lining of the tube and consequent facilitated propulsion of exudates out of tubar, and respectively, middle ear cavities. In other words, beneficial outcome is achieved due to effective draining of middle ear cavity in the inherent, natural way. Positive secretion and drainage effect not only avoids surgical interventions, but also does so without increasing the incidence of side effects, which were not observed in the present study.

These results permit to consider topically applied S/N as an adequate stimulus for physiological reflex discharge of secretions out of the auditory tube and for its active opening.

Oral and nasal decongestants could be expected to lower the intensity of evoked secretion and respectively therapeutic efficacy in these circumstances through *vasoconstriction*, and therefore are incompatible with S/N intranasal administration.

სამედიცინო მეცნიერებანი

## სეკრეციული ოტიტის კონსერვატიული მკურნალობის ახალი მეთოდი

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სტატიაში აღწერილია ქრონიკული სეკრეციული ოტიტის კონსერვატიული მკურნალობის ახალი მეთოდი. შუა ყურის მწვავე ჩირქოვანი ანთების შედეგად განვითარებული სალპინგოოტიტის სამკურნალოდ სინუფორტე/ნაზოდრენი (S/N) იყო გამოყენებული. მონოთერაპიის (S/N) ეფექტურობა შედარებული იყო კომბინირებული S/N ანტიბიოტიკით და, აგრეთვე, სტანდარტული ანტიბიოტიკ/დეკონგესტანტით მკურნალობის შედეგებთან. S/N მონოთერაპიის ჯგუფში, ისევე როგორც S/N/ანტიბიოტიკით ნამკურნალებ ავადმყოფთა ჯგუფში მკურნალობის გამოსავალი გაცილებით უკეთესი აღმოჩნდა, ვიდრე სტანდარტული მკურნალობის შემთხვევაში. მიღებული შედეგები შუა ყურის ღრუს ბუნებრივი, ფიზიოლოგიური გათავისუფლებითაა განპირობებული.

კლინიკური გამოკვლევის შედეგებმა დაადასტურა, რომ S/N ადგილობრივი გამოყენება შეიძლება განვიხილოთ როგორც ვესტაქის მილში რეფლექსური სეკრეციისა და სანათურიდან ექსუდატის აქტიური გამოძევების ადეკვატური სტიმული.

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