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OTOLOGY

The rationale for preventive treatments for early post-tympanostomy tube otorrhea in persistent otitis media with effusion

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Abstract Some studies have shown that post-tympanostomy tube otorrhea (PTTO) is a common complication after tympanostomy tube insertion. There are wide range of controversies about the incidence of PTTO and different methods of preventive treatment. The aim of this study was to determine the incidence of early PTTO in persistent otitis media with effusion in our centers. We also investigated the effect of preventive treatments on the incidence of early PTTO in children with persistent otitis media with effusion. This multi-central study comprised 536 ears belonging to children with otitis media and effusion for at least 3 months, referred for complications arising from post-tympanostomy tube insertion. The patients were randomly divided into three treatment and control groups. In the first group of patients, the middle ear cavity was irrigated with isotonic saline after myringotomy. The second group received oral amoxicillin three times a day for 7 days postoperatively. The third group had similar treatment as the second group, in addition to topical ciprofloxacin drop, 4 drops three times a day for 3 days after operation. The control group did not undergo any treatment. Early post-tympanostomy tube otorrhea was detected in 6 ears (1.1 %), including 3 (2.2 %) from the control group and 3 (2.3 %) from the first group. There was no statistically significant difference in early PTTO between integrated treatment groups and control group ($P = 0.111$). As the total rate of early post-tympanostomy tube otorrhea was very low, there was no significant difference between the 3 treatment groups and control group. Our study did not support the routine use of preventive therapy. A period of at least 3 months watchful waiting before tympanostomy tube insertion may help reduce the incidence of PTTO.

Keywords Otitis media with effusion · Tympanostomy tube · Otorrhea

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Introduction

Otitis media with effusion (OME) is defined as the effusion in the middle ear that is usually related to poor Eustachian tube function or occurring after acute middle ear infection. Chronic OME is characterized by persisting middle ear effusion for more than 3 months [1]. Risk factors for OME include craniofacial abnormalities, cleft palate, acute otitis media with early onset, Trisomy 21, asthma, allergy, genetic predisposition, lack of breastfeeding, environmental factors such as exposure to tobacco smoke, lower socioeconomic status and day care attendance [2–8].

Usual surgical intervention to treat recurrent episodes of acute otitis media or the persistence of OME is tympanostomy tube (TT) insertion [9]. This is the most common surgical operation in children in the United States of America [10]. However, there are great differences in surgical rates of TT between countries [11]. But at least

3 months of watchful waiting is an acceptable surgical practice [11–16].

Although TT insertion is a minor procedure, up to 83 % of patients develop post-tympanostomy tube otorrhea (PTTO), which is the most common complication of this surgery [17]. Other researchers reported the incidence of PTTO to be 10–50 % [18]. Some studies also explore the role of bacterial biofilm not only in the pathogenesis of OME but also its association with refractory PTTO [18–21]. Some researchers found that local antibiotic drops are only helpful to partially neutralize bacterial biofilm [12, 19]. Other reports indicated that the shape or the type of TT material may play a role in PTTO, which led to designing tubes with various configuration, lumen diameters, composition, and coating materials [22]. Recent study has shown that polyvinylpyrrolidone and silver coatings decrease formation of biofilm by *Pseudomona aeruginosa* on silicone TTs. But combining polyvinylpyrrolidone with silver coatings had no additional effect on elimination of biofilm [23]. On the contrary, Licameli et al. found that there was no clear distinction, in the incidence of PTTO, between uncoated and phosphorylcholine-coated fluoroplastic Armstrong tubes [22]. Kisser et al. showed that the incidence of PTTO was 18 % in fluoroplastic tubes but only 4 % in titanium tubes [24].

The procedures suggested to prevent PTTO include preparing the external canal with povidone iodine or 70 % alcohol before operation, using postoperative oral antibiotic, local otic antibiotic or steroid drops, and irrigation of the middle ear cavity with isotonic saline after myringotomy [25, 26]. In view of wide range of controversy about different methods of preventive treatment reported in previous studies, the present study attempted to determine the incidence of early PTTO in persistent OME in our centers. We also sought to explore the impact of preventive treatment on the incidence of early PTTO.

Materials and methods

This multi-centered randomized clinical trial registered in Iranian registry of clinical trial under code number of 2013112315496N1.

A total of 560 ears belonging to 291 patients underwent TT insertion, for persistent OME, from March 2006 to May 2014 at Khalili and Dastgheib Hospitals, affiliated with Shiraz University of Medical Sciences; Besat Hospital, affiliated with Hamedan University of Medical Sciences, and Shahid Sadoughi Hospital affiliated with Yazd University of Medical Sciences. The research protocol was approved by the Ethics Committee of Shiraz University of Medical Sciences. Written informed consent was obtained from parents of all children before starting the study. Inclusion criteria were children undergoing TT placement for persistent OME for at least 3 months without concurrent adenoidectomy, children not using preoperative antibiotic at least 2 weeks before surgery, children without upper respiratory infections for at least 2 weeks before surgery and lacking active allergic rhinitis or nasal and paranasal sinus infection. Exclusion criteria were children having allergy to penicillin, chronic sinusitis, having had previous myringotomy and/or tube insertion, children with Down syndrome, cleft palate, sensory neural hearing loss, complications of otitis media, craniofacial dysmorphism, mucociliary clearance disorders, immune deficiency and those aged more than 15 years. A total of 560 ears were randomized into four groups using blocked randomization method regarding the type of preventive therapy. In first group, the middle ear cavity was irrigated with isotonic saline to cleanse the sticky fluid. In second group, the patients received oral amoxicillin, 50 mg/kg three times daily for 7 days postoperatively. The third group had similar treatment as the second group, in addition to topical ciprofloxacin drop (ciplex, Sinadarou Company) 4 drops three times a day for 3 days after operation. Finally, control group did not undergo any treatment. All surgical interventions were performed by four academic otolaryngologists and a consistent operative technique was used throughout. Following general anesthesia, irrigation of the ear canal with povidone iodine was carried out, and myringotomy incision was made on the antero-inferior quadrant. The middle ear had either congested mucosa with no fluid or was secretory with mucoid, serous, or purulent exudates. The same type of TT (Shepard Grommet, Network Company) was used for all groups. Clinical follow-up regarding early PTTO was carried out by an independent blinded otolaryngologist, guided by microscopic otoscopy in outpatient departments on 7 and 14 postoperative days.

The data were analyzed using Chi square test using SPSS version 15 software. P value <0.05 was considered statistically significant.

Results

Of total 560 ears, 24 ears from 14 children were excluded from the study because of inadequate follow-up. Finally, 536 ears from 277 patients in 4 groups were evaluated for early PTTO 2 weeks after surgery. Of these, 135,134, 134, and 133 ears were from first, second, third and fourth groups, respectively.

The respective mean age $\pm$ standard deviation of patients were 6.18 ± 2.52, 6.22 ± 2.55, 5.56 ± 3.57 and 5.45 ± 2.74, but the differences between these groups were not statistically significant ($P = 0.535$).

Female to male ratios were 43:92, 52:82, 49:85, and 37:96 in the first, second, third and fourth groups, respectively, but the differences between these groups were not statistically significant ($P = 0.236$).

Middle ear status after myringotomy between groups (Table 1) was not statistically significant ($P > 0.05$).

Early PTTO was detected in 6 ears (1.1 %), 3 of which (2.2 %) belonged to the control group and 3 (2.3 %) to saline group; the difference between early PTTO treatment and control groups was not statistically significant ($P = 0.111$). The evaluation of middle ear status of the aforementioned 6 ears revealed congested mucosa in two and mucous fluid in four ears.

Discussion

An important strong point of this study was that it was a multi-central randomized clinical trial with a relatively large sample size, which detected very low early PTTO rate of 1.1 %. Although myringotomy and TT placement are among the most common surgical procedures performed in children, the best management of early PTTO in children is currently an issue of debate. In Rosenfeld's meta-analysis, based on 134 articles, late PTTO was reported in 26 % of the patients versus 16 % for early PTTO [27]. Many trials have studied the impact of oral antibiotic therapy on the rate of PTTO with controversial results. Luxford and Sheehy found that a 10-day postoperative oral antibiotic therapy had no effect on incidence of PTTO [28]. Also, Balkany et al. reported lack of efficacy of preoperative ampicillin administration [29].

There is currently no consensus on the use of most appropriate choice of antibiotic drop. However, several studies using ototopical agents have shown a reduction in postoperative otorrhea [25, 26, 30–34]. Two meta-analyses showed reduction in early PTTO rates following administration of prophylactic antimicrobial drops [30, 34]. Baker and Chole reported a significant reduction in early PTTO using topical gentamicin solution [31]. Giles et al. found that combination of ciprofloxacin 0.3 % and dexamethasone 0.1 % (Ciprodex) reduced early PTTO compared with no treatment group [34]. In this regard, Roland et al. indicated that topical (Ciprodex) for 7 days is superior to treatment with ciprofloxacin 0.3 % [26]. On the contrary, Morpeth et al. suggested that topical Cortisporin offers no benefit over Ciprofloxacin for PTTO prophylaxis [35]. Poetker et al. revealed approximately 7 % reduction in PTTO in ofloxacin otic drop group and a 10 % reduction in the Neomycin–Polymyxin B otic drop group [32]. Other studies have shown no beneficial effect of prophylactic ear drops [31, 36–38].

Goldblatt et al. compared the effect of topical ofloxacin drops on preventing otorrhea with that of oral amoxicillin clavulanate with respective PTTO rates of 23.7 and 31 %, and the difference was not statistically significant [39].

Regarding intra-operative irrigation of the middle ear with isotonic saline, our study showed three ears (2.3 %) with early PTTO, after irrigation with isotonic saline, compared with three ears (2.2 %) in the control group. Following isotonic saline irrigation, the rates of PTTO as reported by Balkany et al. and Gross et al., were 4 and 19.2 %, respectively [29, 40]. Gross et al. found that the rate and degree of drainage were significantly reduced in both the saline irrigation and antibiotic drop groups [40]. Kocaturk et al. had 15.71 % early PTTO in patients with isotonic saline irrigation and the difference was significant as compared with the control group [25]. Finally, they reported that all their treatment groups including the patients receiving either isotonic saline, oral sulbactam ampicillin or ofloxacin otic drops were statistically different from the control group, although there was no statistically significant difference between treatment groups. Consequently, they concluded that the efficacy of these 3 methods seemed to be similar and advocated irrigation with isotonic saline due to its lower cost [25]. On the contrary, we found no statistically significant difference between the treatment and control groups.

Table 1 Frequency of middle ear status and the type of effusion in 4 groups of patients

Assessment variables	Control group ($n = 133$)	Antibiotic drop group ($n = 134$)	Oral antibiotic group ($n = 134$)	Saline group ($n = 135$)	P value
Middle ear status					
Congested	31 (23.3)	17 (12.7)	25 (18.7)	20 (14.8)	0.107
Secretory	102 (76.7)	117 (87.3)	109 (81.3)	115 (85.2)	
Effusion types					
Mucoid	94 (70.7)	108 (80.6)	98 (73.1)	104 (77)	0.895
Serous	6 (4.5)	7 (5.2)	6 (4.5)	8 (5.9)	0.973
Purulent	2 (1.5)	2 (1.5)	5 (3.7)	3 (2.2)	0.571

Although, the majority of studies showed a higher rate of PTTO [22], other investigations reported a low early PTTO incidence which was consistent with our findings. Kinsella et al. and Kalcioglu et al. reported only 1.67 % (66 cases) and 0.8 % (366 cases) early PTTO in their studies [31, 41]. Our assumption on such wide range of PTTO rates reported in different studies may be due to various characteristics of patients such as, age, sex, race, immune deficiency, and socioeconomic condition, or different inclusion and exclusion criteria, such as surgery in active phase of infection (recurrent acute otitis media) where the middle ear cavity is under inflammation and heavily infected with bacteria. We believe that the status of the middle ear mucosa in recurrent acute otitis media is different from persistent OME which accounts for the most significant predictive factor for early PTTO. The higher rate of early PTTO in some studies is related to short time interval between surgery and active otitis media [34]. Although the authors found that early insertion of TT had no effect on language development or behavior [42–45], according to the study of Keyhani et al. in New York, it was found that many children with OME had shorter durations of effusions before surgery. In other words, many operations were inappropriate according to criteria in guidelines which most of surgeons did not follow [9]. We believe that shorter duration of effusions before TT may play a major role in higher rates of PTTO reported in some studies.

Also, in our study, the prevalence of mucous aspiration from the middle ear cavity was about 75.37 % (404 ears), compared to 50 % reported by Kocaturk et al. [25]. This was due to our longer preoperative waiting for resolving the acute phase and higher rate of mucous formation. This time period can be sufficient for the immune system to control the infection by decreasing fluid and increasing the viscosity of secretions to limit the acute inflammation, resulting in decreased rate of early PTTO. Some studies found that pattern of cytokines profiles may be related to different phases of middle ear infection [46, 47]. In addition, a higher cytokine concentration was detected in ears with more than 3 months duration of OME [46]. Recently, Rosenfeld et al. have developed a new practical guideline and recommended that children who suffer from single episode of OME, the insertion of TT should be postponed to at least 3 months [48].

Conclusion

An important clinical lesson learnt from the current study is that routine use of preventive therapy is not supported in this group of patients. Interestingly, the incidence of early PTTO was lower than those reported by most previous studies. This may have been related to our inclusion criterion, which was consist of at least 3 months watchful waiting before TT insertion.

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