BY STEPHEN I. PELTON, M.D.

ID CONSULT

Recalcitrant Otorrhea 'After the Tubes'

Novel approaches are necessary to address the emerging problem of the child who fails conventional therapy for acute otorrhea following tympanostomy tube insertion.

We've seen an increase in the number of children with otorrhea through a tympanostomy tube lasting more than 10 days in the past few years, primarily due to the emergence of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA). Another contributing factor is the increased use of quinolone ear drops, which are thought to promote the occurrence of fungal infections.

Approximately 30% of children who undergo tube placement develop acute otorrhea. *Haemophilus influenzae* and *Streptococcus pneumoniae* are responsible for 40%-45% of these cases, particularly in children under 2 years of age and in those who develop symptoms during the winter months. It's hypothesized that these children have ongoing eustachian tube dysfunction that permits nasopharyngeal pathogens to ascend to the middle ear, resulting in acute otorrhea through the tympanostomy tube.

The other 55%-60% of cases are caused by pathogens from the external canal, most commonly *Staphylococcus aureus* and *Pseudomonas aeruginosa*. These patients tend to be older, to develop symptoms during the warmer months, and to have a malodorous discharge (in contrast to the nasopharyngeal pathogens, which are odorless).

There appears to be a contribution from water in the ear, which triggers an inflammatory response.

In the past, standard treatment for ear drainage in children was oral antibiotics aimed at *H. influenzae* and pneumococcus, such as amoxicillin, amoxicillin-clavulanate, or a cephalosporin.

More recently, there has been a shift to greater use of topical fluoroquinolones—particularly ofloxacin and ciprofloxacin—with the increased recognition that the staphylococcus and pseudomonas pathogens also contribute to the microbiology of this disease.

Even in young children, otic preparations are often considered superior to oral antibiotics because they are active against all four of the main pathogens, safely achieve high concentrations in the middle ear, and are less likely to contribute to the emergence of resistance because they are not given systemically.

And of course, they eliminate the bad taste problem.

Now, however, we're starting to see clinical failures with both oral and topical antibiotics, primarily due to CA-MRSA. Among otherwise healthy children, the risk for the development of otorrhea due to MRSA appears to increase with the number of acute otitis media episodes prior to tube placement, as well as with the number of courses and duration of treatment prior to tube placement (Arch. Otolaryngol. Head Neck Surg. 2005;131:868-73).

It's hypothesized that these children have ongoing eustachian tube dysfunction that permits nasopharyngeal pathogens to ascend to the middle ear.

For MRSA-associated skin and soft tissue infections, drugs such as trimethoprim-sulfamethoxazole, linezolid, or even intravenous vancomycin are usually effective. However, these agents are often ineffective or associated with relapse as soon as therapy is discontinued when a foreign body such as a tympanostomy tube is involved, because of the lack of blood supply and the formation of biofilm.

What does appear to work, at least in small case reports, is the use of either topical vancomycin or combination topical plus oral treatment.

In one report, a group in Thailand combined a 500-mg vial of vancomycin powder with 20 mL of sterile distilled water to create a 25-mg/mL vancomycin solution. Two 0.8-mg drops were placed into the ear three times daily for 10 days in 35 patients with MRSA otorrhea. A control group of 20 patients was treated with the same regimen of gentamycin 0.3% drops (J. Laryngol. Otol. 2004;118:645-7).

Clinical cure was achieved in 30 (86%) of the vancomycin recipients, compared with 2 (10%) of those treated with gentamycin. Failures occurred in just 2 (6%) patients given vancomycin versus 16 (80%) given gentamycin.

Of course, this is a small study, but it is based on sound biologic principles and there appear to be no adverse effects. We certainly need more long-term data, but I think topical vancomycin may represent a good alternative to removal of the tubes in some patients. If your pharmacy is able to make this formulation, I think it offers an option to tube removal if CA-MRSA is cultured and the child fails initial oral or topical therapy.

In another small study, successful eradication of MRSA was achieved using a combination of oral trimethoprim-sulfamethoxazole plus topical gentamycin sulfate or polymyxin B sulfate-neomycin sulfate-hydrocortisone (Cortisporin) in six children (five with prior tympanostomy tube placement and one with perforation of the tympanic membrane) who had failed either oral antibiotics or fluoroquinolone ear drops alone (Arch. Otolaryngol. Head Neck Surg. 2005;131:782-4). However, I'd be less apt to use this approach because of concerns about potential ototoxicity of the gentamycin/neomycin on the vestibular system.

In addition to CA-MRSA, otorrhea due to fungal organisms is now being seen increasingly in children who have been treated previously for bacterial infections following tube placement.

In a retrospective review conducted at a pediatric otolaryngology clinic, out of a total 1,242 patients who underwent ear culture between 1996 and 2003, 166 patients (119 with otitis media, 41 with otitis externa, and 6 with both) aged 16 days to 18 years (mean 4 years) were found to have fungal organisms. The proportion of fungus-positive cultures increased dramatically in the years following the availability of the fluoroquinolone drops, from just 4.2% of 356 cultures obtained during 1996-1998 to 18.2% of the 457 cultures done during 1999-2001 (Int. J. Pediatr. Otorhinolaryngol. 2005;69:1503-8).

The most common of the fungi were *Candida albicans* (43% of the 166), *Candida parapsilosis* (23.5%), and *Aspergillus fumigatus* (21%). Although reporting of medications was inconsistent, the authors estimated that the patients had previously received an average of 1.7 oral antibiotics and 1.1 ototopical agents before the culture was taken. Infection resolved in all the patients with treatment, which included clotrimazole topical and tolnaftate topical in 27 patients each, fluconazole in 25, acetic acid alone in 14, and topical plus fluconazole in 10. The thinking is that the use of broad-spectrum quinolone drops may be promoting the emergence of fungus by eliminating the colonizers in the external ear canal, thereby allowing the fungus to grow. This doesn't imply we should stop using quinolone-containing otic solutions, but I do think we need to be aware of the possibility and culture the middle ear in a child who still has otorrhea after 5-7 days of treatment.

Of course, we all know that prevention is the best medicine.

A group from Turkey recently published a comparison of 1 mL intraoperative isotonic saline irrigation, postoperative antibiotic treatment (sulbactam/ampicillin 25 mg/kg for 5 days), postoperative ofloxacin drops (twice a day for 5 days), or placebo in 280 children (mean age 5.9 years) undergoing bilateral ventilation tube insertion because of serous otitis media during 2000-2004 (Am. J. Otolaryngol. 2005;26:123-7).

At 2 weeks post surgery, purulent otorrhea was observed in 15.7% of the saline group, 14.2% of those who received prophylactic oral antibiotics, and 8.6% of the topical antibiotic group, all significantly lower than the 30% rate among the controls. It appears that saline irrigation of the middle ear prior to tube placement offers a low-cost intervention for reducing early post–tympanostomy tube otorrhea. ■

DR. PELTON *is chief of pediatric infectious disease and also is the coordinator for the Maternal-Child HIV Program at Boston Medical Center.*

Review Highlights Need for More Data on CSOM Treatment

BY SHARON WORCESTER
Southeast Bureau

Available data, though limited, suggest topical quinolone antibiotics are better than systemic antibiotics for treating chronic suppurative otitis media, according to a new Cochrane review of systemic antibiotic and topical treatments for the condition.

For the review, Dr. Carolyn A. Macfadyen of the Liverpool School of Tropical Medicine (England), and her colleagues searched the literature and identified nine relevant randomized controlled trials, including four that enrolled children under age 16 years. The trials involved a total of 833 randomized participants and 842 analyzed participants or ears.

Findings from the studies, which had short follow-up and were regarded by the authors as poorly reported, suggest that quinolone antibiotic drops such as ciprofloxacin had better ear-drying effects than either systemic quinolone antibiotics (relative risk 3.18) or systemic nonquinolone antibiotics (relative risk 3.21) at 1-2 weeks after the start of treatment. This finding was based on pooled data from two trials involving 116 patients with chronic suppurative otitis media (CSOM).

Systemic antibiotics plus topical quinolones were superior to systemic quinolones alone (relative risk 2.75), according to pooled data from two trials involving 90 CSOM patients.

Limited evidence from one trial with 31 patients suggested there was no significant benefit for topical nonquinolones or antiseptics, compared with systemic antibiotics at 2-4 weeks, and limited evidence based on three trials with 204 participants suggested there was no benefit to adding systemic treatment to topical treatment at 1-2 weeks, the investigators reported (The Cochrane Database of Syst. Rev. 2006;DOI:10.1002/14651858.CD005608).

Good evidence regarding long-term outcomes—such as ear-drying, complication prevention, healing of eardrum perforations, and hearing improvement—was lacking, as were data defining the role of topical nonquinolones and antiseptics, data on treating complicated CSOM, and data on safety. These matters should be addressed in future studies, the authors recommended. The lack of safety data and information on the risk of ototoxicity with alternative treatments, which is of particular concern, warrants regular medical follow-up, clinical vigilance, and monitoring for adverse treatment effects and disease complications in patients being treated for CSOM, they said. ■