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Bacterial Conjunctivitis and Resistance

The treatment of bacterial conjunctivitis has become more challenging in this era of increasing antimicrobial resistance.

Conjunctivitis in children is extremely common, accounting for an estimated 1%-4% of all pediatric office visits. Yet, with so much focus on otitis media, the impact of antimicrobial resistance on conjunctivitis treatment has been widely overlooked. This is despite that approximately one-third of children with bacterial conjunctivitis have concurrent otitis media, most commonly caused by *Haemophilus influenzae*. In fact, my interest in conjunctivitis stems from its connection with otitis media.

Many of the traditional topical ocular agents we've used in the past to treat bacterial conjunctivitis—including those of the aminoglycoside, polymixin B combination, and macrolide classes—are less effective than they once were, thanks to increasing resistance. At the same time, many of these agents have tolerability issues, which render them even less effective. After all, if a child won't allow the medicine to be placed in her eyes, it most certainly won't work.

Fluoroquinolones, while remaining highly effective with far less resistance, are about 10 times as expensive as older agents available generically. Is it worth the cost to speed up the cure and reduce the contagion of a self-limited disease by a day or two at the most? The answer to that depends on a variety of factors, including the degree of the child's discomfort, the potential burden to the parent of missing days from work, and whether the child attends day care. It's not a simple decision.

Of course, it's important to determine whether the conjunctivitis is bacterial. Acute bacterial conjunctivitis begins

abruptly with early symptoms of irritation or foreign body sensation and tearing. Mucopurulent or purulent discharge, morning crusting, swelling, and comorbid otitis media are common indicators. In contrast, viral conjunctivitis is characterized by watery discharge and conjunctival injection, while allergic conjunctivitis is more likely to involve itching, stringy or ropy discharge, lid edema, red/hyperemic conjunctiva, and comorbid allergic rhinitis.

The age of the child is also predictive. Conjunctivitis in preschool children is most likely bacterial, usually either *H. influenzae* or *Streptococcus pneumoniae*. In a newborn, the cause is most likely chemical irritation (from silver nitrate), while in older children the conjunctivitis is usually viral or allergic.

Oral antibiotics are recommended for any child who has concurrent otitis media. But for uncomplicated bacterial conjunctivitis, topical ocular agents are recommended over systemic agents because they achieve a greater concentration of antibiotic to the eye while avoiding systemic side effects. Most of the topicals discussed below are approved for children 1 year of age and older.

Aminoglycosides, including gentamicin, tobramycin, and neomycin, are most active against gram-negative bacteria such as *Pseudomonas aeruginosa* (except neomycin) and methicillin-sensitive *Staphylococcus aureus* (MSSA). However, they do not cover streptococci or methicillin-resistant *Staph. aureus* (MRSA), and studies have shown increasing resistance of *Streptococcus pneumoniae* to these agents, reaching 65% by 2006 in the Ocular TRUST (Tracking Resistance in

U.S. Today) 1 survey (Am. J. Ophthalmol. 2008;145:951-8).

Polymixin B is active only against gram-negative bacteria and therefore is given in combination with other antibiotics, including trimethoprim, bacitracin, and neomycin/bacitracin, which broaden the coverage to include staphylococci, streptococci, and some gram-negative bacteria including *H. influenzae*. While most *H. influenzae* strains remain susceptible to polymixin B alone or in combination, there is high resistance among *Strep. pneumoniae* and MSSA isolates.

The macrolide erythromycin—used as a 0.5% ointment—is one of the oldest ocular antibiotics, but now is rarely effective in bacterial conjunctivitis because of the high resistance among *Staphylococcus* species and poor activity against *H. influenzae*. The newer topical macrolide azithromycin is also hampered by high levels of resistance. In the TRUST survey, resistance to azithromycin was 22% for *Strep. pneumoniae* isolates, 46% among MSSA bacteria, and 91% among MRSA isolates. Other studies have shown significant resistance among *H. influenzae* as well.

Fluoroquinolones offer broad-spectrum coverage against both gram-positive and gram-negative organisms. The older topical agents ofloxacin and ciprofloxacin have largely been replaced by the newer agents levofloxacin, moxifloxacin, gatifloxacin, and now besifloxacin, which was approved by the U.S. Food and Drug Administration in May 2009. Numerous randomized, double-masked, controlled clinical trials in children and adults with bacterial conjunctivitis have demonstrated clinical cure

rates of approximately 66%-96% and microbial eradication rates ranging from 84% to 96% for the newer fluoroquinolones.

There has been almost no resistance to fluoroquinolones among *Strep. pneumoniae* or *H. influenzae* organisms, but there is some fluoroquinolone resistance among MSSA isolates and a high level for MRSA, reaching 85% in Ocular TRUST 1.

Although most topical ophthalmic antibiotics used for the treatment of bacterial conjunctivitis are generally safe and well tolerated, ocular adverse events can cause discomfort that leads to noncompliance. Topical aminoglycosides have been associated with corneal and conjunctival toxicity, especially when used frequently, as well as ocular allergic reactions. Bacitracin has been associated with cases of contact dermatitis in the conjunctival area, and the polymixin B combinations can also cause local irritation. Macrolides, too, can cause minor ocular irritation, redness, and hypersensitivity.

In contrast, the fluoroquinolones have been well tolerated and associated with less toxicity than the other ophthalmic antibacterial classes, although crystalline precipitates have been seen with ciprofloxacin when it is administered frequently.

The ideal treatment for acute bacterial conjunctivitis should be a well-tolerated, broad-spectrum, highly potent, and bactericidal agent with a high concentration on the ocular surface and a rapid kill time. Convenience in dosing is also an important consideration. The newer fluoroquinolones, with potent efficacy against *H. influenzae* and *Strep. pneumoniae*, may best fulfill those requirements. But of course, cost remains a problem for many. ■

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Adenotonsillectomy for Sleep-Disordered Breathing Increased

BY HEIDI SPLETE

ORLANDO — Both the indications for, and the incidence of, adenotonsillar procedures in children have changed, according to Dr. Laura Orvidas.

"We seem to do more adenotonsillectomies for sleep-disordered breathing than we have in the past," she said at the combined sections meeting of the Triological Society.

To evaluate changes in the incidence and indications for tonsillectomy and adenotonsillectomy, Dr. Orvidas of the Mayo Clinic in Rochester, Minn., reviewed data from the Mayo Clinic's database for a 35-year

period between 1970 and 2005. The study population included 8,106 tonsillectomy and/or adenotonsillectomy patients aged 6 months to 29 years (mean age, 10.5 years).

The most interesting finding was the change in surgical indications for all procedures, said Dr. Orvidas: "Early on we were treating mostly for infection, and now it seems to be mostly for upper airway obstruction." In 1970, treatment of infection accounted for approximately 90% of either adenotonsillectomies or tonsillectomies, while upper airway obstruction accounted

for about 10%. In 2005, upper airway obstruction accounted for more than half of the indications for both procedures,

The indications for all adenotonsillar procedures have changed. 'Early on we were treating mostly for infection, and now it seems to be mostly for upper airway obstruction.'

while infection accounted for about 25% and a combination of both upper airway obstruction and infection accounted for approximately 20%.

The incidence of tonsillectomy or adenotonsillectomy was

369/100,000 person-years during the period from 1970 to 1974, compared with 642/100,000 person-years from 2001 to 2005, Dr. Orvidas said.

Sixty-five percent of the tonsillectomy patients, 48% of the adenotonsillectomy patients, and 55% of the patients for both conditions were female.

"Neither the indication nor the incidence for adenotonsillar surgery has been static," Dr. Orvidas noted at the meeting, jointly sponsored by the Triological Society and the American College of Surgeons.

Adenotonsillectomy incidence increased more than tonsillectomy incidence overall, although there was a high density of tonsillectomies in adolescent females, she said. For tonsillectomy alone, the mean age across the entire study period was 16 years vs. a mean of 7 years for adenotonsillectomy.

Dr. Orvidas also noted an increase in both adenotonsillectomy and tonsillectomy procedures for younger males. The possible reasons for these two trends were not addressed in the Mayo Clinic study. ■

Disclosures: None was reported.