Effectiveness of the 10-Valent Pneumococcal NTHi Protein D Conjugate Vaccine Against AOM

Written by Phil Vinall

Acute otitis media (AOM) is a common medical condition with high incidence in children <5 years of age. [Monasta L et al. *PLoS One* 2012]. The incidence in Europe is ~299 cases/1000 person-years in children under the age of 2 years [Liese J et al. ESPID 2011 Abstract 366]. Accurate diagnosis is difficult and may partially explain differences in incidence rates in different studies and countries [Toll EC, Nunez DA. *J Laryngol Otol* 2012]. *Streptococcus pneumoniae*, nontypeable *Haemophilus influenzae* (NTHi), and to a lesser extent *Moraxella catarrhalis* and *Streptococcus pyogenes* are the bacterial pathogens mainly responsible for AOM [Leibovitz E et al. *Pediatr Infect Dis J* 2004]. A trial with the 11-valent predecessor protein D conjugate vaccine demonstrated efficacy against AOM episodes caused by *S. pneumoniae* and NTHi [Prymula R et al. *Lancet* 2006].

Timo Vesikari, MD, University of Tampere, Tampere, Finland, presented preliminary data showing a trend toward positive vaccine effectiveness against AOM episodes for 10-valent pneumococcal nontypeable *H. influenzae* protein D conjugate vaccine (PHiD-CV) in infants.

This was a Phase 3/4, cluster-randomized, double-blind controlled study in Finland [NCT00839254] nested within a large invasive pneumococcal disease effectiveness study [NCT00861380; Palmu A. ESPID 2012 Abstract 1340]. Infants <7 months of age were randomized to receive 1 of 2 dose schedules of PHiD-CV (1 dose at age 3, 4, and 6 months *or* 1 dose at age 3 months and a second dose at 5 months; both groups received a booster dose at ~12 months) or a control vaccine (hepatitis B) using the same schedules. The study participants were followed for 18 months. AOM surveillance was based on parental reporting of physician diagnosed AOM using an AOM questionnaire. AOM was diagnosed according to the 2004 Finnish national consensus guidelines (abnormal tympanic membrane+presence of middle ear fluid+sign(s) of acute infection). Vaccine effectiveness was calculated as 1 minus rate ratio with 95% CI for subjects reporting ≥1 AOM.

The total vaccinated cohort for effectiveness comprised 4117 infants allocated into 50 clusters with 4019 infants included in the per protocol cohort. Participants were mean age 2.3 months at first dose, about 50% female, and almost exclusively of white European heritage.

At least 1 AOM was reported in 63% of subjects in the PHiD-CV group and 67% in the control group. Both dose schedules reduced the number of reported cases of AOM; however the results were not statistically significant (Table 1). The results showed a trend toward positive vaccine effectiveness as shown by a reduction in number of subjects reporting ≥1 AOM following PHiD-CV administration. The trend for effectiveness against AOM was stronger using a 3 plus 1 vaccination schedule compared with a 2 plus 1 vaccination schedule. Vaccine effectiveness was similar for OM cases treated with antibiotics (97% of cases).

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Table 1. Results: Vaccine Effectiveness in Reducing the Number of Subjects Reporting ≥1 AOM.

	n (C)	n	IR	FU	n/FU (per 1000)	Vaccine Effectiveness (95% CI)
PHiD-CV						
3+1 schedule	1846 (16)	1163	0.63	4407	264	14 (–10.6-33.3)
2+1 schedule	942 (17)	589	0.63	2041	289	5.0 (–25.8-28.2)
Control						
3+1 schedule	1329 (17)	892	0.67	3084	289	14 (–10.6-33.3)
2+1 schedule	1327 (17)	892	0.67	3084	289	5.0 (–25.8-28.2)

C=number of clusters; IR=incidence rate; FU=follow-up expressed in years; n/FU (per 1000)=incidence of subjects reporting ≥AOM expressed in 1000 child-years.

CABP Due to MRSA and Treatment with Ceftaroline: Experience from the CAPTURE Study

Written by Phil Vinall

There is a need for new antibiotics to treat the rising incidence of community-acquired bacterial pneumonia (CABP) and acute bacterial skin and skin structure infections (ABSSSI) caused by Gram-positive bacteria such as *Streptococcus pneumoniae* and *Staphylococcus aureus*, including the multidrug resistant (MDRSP) and methicillin-resistant (MRSA) forms of these bacteria. Ceftaroline (CPT) fosamil is an injectable novel cephalosporin antibiotic approved by the FDA to treat CABP and ABSSSI. Alena Jandourek, MD, Cerexa, Inc., Oakland, California, USA, presented a poster [Jandourek et al. ICAAC 2012 L1-300c] with results from the Clinical Assessment Program and Teflaro® Utilization Registry cohort [CAPTURE] study that showed CPT produced good clinical outcomes when used as monotherapy to treat CABP due to MRSA.

CAPTURE was a multicenter, retrospective chart review conducted to document outcomes in patients with CABP due to MRSA isolated from sputum and/or blood after CPT treatment. A successful outcome was defined as clinical improvement resulting in either a change to oral agents or end of antibacterial therapy. Men and women ≥18 years of age, diagnosed with CABP, and receiving ≥2 consecutive IV doses of CPT per the institution's standard of care between January 2011 and 2012 were included. Data collected included pathogens cultured, concomitant antibacterials, comorbid conditions, and relevant past medical history, admission, and discharge information.

Out of 70 patients enrolled with CAPB, 10 patients (mean age 68.5 years; range 52 to 85 years) had MRSA CABP. Nine patients had MRSA only and 1 patient had methicillin-sensitive *Staphylococcus aureus* (MSSA) and MRSA. All patients had comorbidities, including structural lung disease, prior pneumonia, history of smoking, cancer, congestive heart failure, gastroesophageal reflux disease, and cerebrovascular accident. Eight patients were treated with other antibacterial therapy prior to CPT. CPT was dosed at 600 mg every 12 hours for a median duration of 6.5 days (range 4 to 30); 3 patients received adjunctive antibacterial therapy. Clinical success was reported in 7 patients. The patient with MSSA and MRSA was discharged home after 9 days. Two of the 3 patients with treatment failure had end-stage cancer and both were transitioned to palliative care. The third patient was treated with multiple antibacterials, then changed to CPT, and later switched to clindamycin.

Limitations of this study include the bias associated with a retrospective cohort study and imprecise reporting of prior antimicrobial therapy dates and dates of cultures collection/results. Dr. Jandourek concluded by noting that despite the presence of significant comorbidities and severe disease, the good clinical outcomes in this study suggest that the use of CPT in MRSA CABP warrants further investigation.

One-Step 2% CHX-OH Compared to 4-Step Povidone Iodine Scrub, Rinse, Dry, and 5% PVI-OH for Preventing Central Line-Associated Bloodstream Infection

Written by Phil Vinall

The Center for Disease Control guidelines recommend that clean skin be prepared with >0.5% chlorhexidine in 70% isopropyl alcohol (CHX-OH) before invasive procedures. Similar preparation is recommended by the American Society of Anesthesiologists in preparation for a central venous catheter. However, to date there has been insufficient data to evaluate CHX-OH compared with povidone iodine in alcohol (PVI-OH).

Jean-Jacques Parienti, MD, PhD, Centre Hospitalier Universitaire de Caen, Caen, France, presented results from a late-breaking clinical trial suggesting that the use of 1-step 2% CHX-OH without scrubbing was more effective