Does all osteomyelitis require prolonged IV antibiotic therapy?

Zaoutis et al. Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children. *Pediatrics* 2009; 123:636-642.

Take Home Message: Early transition to oral antibiotics in the treatment of children with acute, uncomplicated osteomyelitis was not associated with a higher risk of treatment failure, as compared to prolonged intravenous therapy.

Highlights: Acute osteomyelitis has typically been treated with several weeks of intravenous antibiotics. Prior to this study, only small observational studies had demonstrated successful treatment with an early transition to oral antibiotics. Zaoutis et al.[i] performed a retrospective cohort study looking at 1969 children admitted to 29 hospitals over 5 years with acute uncomplicated osteomyelitis and compared treatment failure rates within 6 months among those who were treated with prolonged intravenous therapy with those who were transitioned to oral therapy early. There was a wide variation in treatment strategy across the 29 hospitals, with the proportion of children at each hospital being transitioned to oral therapy ranging from 10 to 95%. With an overall treatment failure rate of 4.7%, they found that there was not an increased risk of treatment failure in those who had been transitioned to oral antibiotics. Additionally, in their secondary outcomes, they found that children who received prolonged intravenous therapy were more likely to be rehospitalized for a central venous catheter-associated complication.

Three years earlier, in 2006, Ruebner et al.,[ii] with Zaoutis as the last author, published a retrospective cohort study looking at complications associated with central venous catheters for the treatment of acute osteomyelitis. 41% of the patients in their trial had at least one CVC-associated complication, including

malfunction or displacement, catheter-associated bloodstream infection, fever, and local skin infection. This study called for clinical trials to evaluate the safety and efficacy of oral antibiotic therapy, and Zaoutis et al. may have provided such evidence.

The Nitty-Gritty:

- **Design:**
    - Retrospective cohort study
    - N= 1969
        - Prolonged intravenous therapy group (n=1021)
        - Oral therapy group (n=948)
    - Setting: 29 freestanding children's hospitals in the United States
    - Enrollment: 2000-2005
    - Primary outcome: treatment failure, defined as rehospitalization within 6 months with either acute osteomyelitis, chronic osteomyelitis, a potential complication of acute osteomyelitis (eg. myositis, arthritis, etc), or a surgical procedure related to the musculoskeletal system
- **Population:**
    - **Inclusion Criteria:**

- § 2 months to 17 years

- § ICD-9-CM diagnosis code for acute osteomyelitis

- **Exclusion Criteria**

  - § Hospitalization for chronic osteomyelitis in the 6 months before index admission

  - § Discharged during time periods when hospital data was deemed invalid or missing according to database overseers

  - § Comorbid conditions: immunodeficiencies, sickle cell disease, trauma, immobilization, pressure ulcers

  - § Osteomyelitis of the head, face and orbits s

  - § Conditions that would predispose to inadequate absorption of oral medications (eg, malabsorption)

  - § Other conditions that may have increased risk of complicated osteomyelitis: cellulits, pyogenic arthritis, sacroiliitis, synovitis, myositis, chronic sinusitis, arthropathy, congenital or acquired diseases of bone, fasciitis, postoperative wounds, or placement of orthopedic devices or prosthesis

  - § <6 months of observation time after initial admission for osteomyelitis

- **Baseline Characteristics –** from the oral therapy group, no significant differences between the two groups

§ **Age:** 8% 0-1year, 34% 1-5 year, 58%>5 year

§ **Length of hospital stay, median (interquartile range):** 4(3-6) days

§ **Gender:** 62% male

§ **Race:** 71% white, 16% black, 8% other

§ **Site:** 30% Pelvic/thigh, 26% lower leg, 19% ankle/foot, 4% upper arm, 4% forearm, 4% hand, 3% shoulder, 3% multiple sites

§ **Organism:** 31% *S.aureus*, 8% > 1 organism, 7% MRSA, 4% Group A streptococcus

§ **Surgical procedure:** 33%

§ **Parenteral antibiootics received:** 54% cefazolin, 26% oxacillin/nafcillin, 34% clindamycin, 9% vancomycin, 1% trimethoprim-sulfamethoxazole, <1% linezolid, 23% other

§ **Proportion of children who had a central venous catheter placed for prolonged intravenous therapy:** varied significantly across hospitals from 10% to 95% ($P<0.001$)

· **Intervention**: Using data from the Pediatric Health Information System (PHIS), children with acute osteomyelitis were classified into either prolonged intravenous antimicrobial therapy group or early transition to oral antimicrobial therapy group. The two groups were then compared.

- **Outcomes:** comparisons are pronged intravenous group vs. oral therapy group, Odds ratios are for those children treated with oral therapy

    - **Primary outcome:** no significant differences

        - Treatment failure rate (defined above) within 6 months: 5% vs. 4%

            - Chronic osteomyelitis: 1.3% v. 0.8%
            - Musculoskeletal surgery: 1.8% vs. 1.6%
            - Complication of osteomyelitis (synovitis, pyogenic arthritis, sacroiliitis, disorders of bone/cartilage NOS, disc disorder): 1.1% vs. 0.6%
            - Acute osteomyelitis: 1.2% vs. 0.9%

    - **Secondary outcomes:**

        - Any hospitalization within 6 months of diagnosis: 10% vs. 5.9%, OR: 0.6 (95% CI 0.38-0.96), P=.017
        - Rehospitalization for catheter associated complication: 3% vs. 0%
        - Rehospitalization for adverse effect of antimicrobials (adverse drug reactions, *C difficile infection*, agranulocytosis): 1.5% vs. 0.4% OR 0.39 (95% CI 0.14-1.1), P=.005

[i] Zaoutis et al. Prolonged intravenous therapy versus early transition to oral antimicrobial therapy for acute osteomyelitis in children. *Pediatrics* 2009; 123:636-642.

[ii] Ruebner et al. Complications of central venous catheters used for the treatment of acute hematogeneous osteomyelitis. *Pediatrics* 2006; 117: 1210-5.