DATIPO: Antibiotic Therapy for 6 or 12 Weeks for Prosthetic Joint Infection

Reviewer: Candra Hubbard, PharmD

Peer Reviewers: Anne Cetto, PharmD and Andrea Donaldson, PharmD, BCPS, BCGP, FASCP

Background:

Prosthetic joint infections are a serious complication of prosthetic joint implantation that requires surgical intervention and prolonged courses of antibiotic therapy. The Infectious Diseases Society of America (IDSA) published guidelines on the diagnosis and management of prosthetic joint infections recognizing that data supporting specific recommendations are limited and often based on expert opinion. Depending on the surgical intervention and pathogen identified, IDSA recommends 2 to 6 weeks of intravenous antibiotic therapy in combination with rifampin followed by rifampin plus oral antibiotics for 3 to 6 months. The DAIR Trial, a multi-center retrospective study, evaluated the effect of antibiotic duration (6 vs. 12 weeks) on remission rates in 87 patients with prosthetic joint infections treated with debridement and implant retention. After a mean follow-up of 52 months, 69% of patients remained in remission with no significant difference between patients receiving 6 weeks versus 12 weeks of antibiotic therapy. However, the trial authors concluded prospective randomized trials would be needed to confirm their results. Therefore, based on the results of the DAIR trial, along with the limited data available, risk of adverse effects associated with antibiotics, and the risk of antibiotic resistance with long courses of therapy, the DATIPO trial was conducted to evaluate shorter courses of antibiotic therapy.

What They Did:

- Determine the efficacy and safety of short term (6 weeks) versus long term (12 weeks) antibiotic therapy in patients with prosthetic joint infections following appropriate surgical procedures
- Randomized, multi-center, open-label, controlled, noninferiority trial
- Conducted at 28 sites in France, including 14 university hospital sites
- 410 patients were randomized in a 1:1 fashion to receive antibiotic therapy for either 6 or 12 weeks

Outcomes:

- Primary:
    - Persistent infection within 2 years of completing antibiotic therapy
- Secondary:
    - Treatment failure due to new infection
    - Probable treatment failure
    - Hospital length of stay
    - Functional outcome
    - Safety outcomes

Inclusion:

- 18 years or older
- Prosthetic joint infection with appropriate surgical management

- At least 2 bacterial cultures obtained during surgical procedure that yielded the same pathogen

Exclusion:

- Effective antibiotic therapy initiated more than 21 days prior to screening
- Received more than one prosthesis replacement strategy due to septic joint infection
- Infection due to mycobacterium, actinomyces, a fungal pathogen, or brucella
- Life expectancy of less than 2 years

Results:

- Primary outcome of persistent infection within 2 years of completing antibiotic therapy
    - 6 week therapy: 18.1%
    - 12 week therapy: 9.4%
    - Risk difference = 8.7; 95% CI (1.5-15.6)
- Treatment failure
    - 6 week therapy: 6.8%
    - 12 week therapy: 10.6%
    - Risk difference = -3.8; 95% CI (-9.7-2.0)
- Probable treatment failure
    - 6 week therapy: 4.2%
    - 12 week therapy: 3.7%
    - Risk difference = 0.5; 95% CI (-3.8-4.8)
- Hospital length of stay
    - 6 week therapy: 14 days
    - 12 week therapy: 13 days
- Safety outcomes
    - Serious adverse event
        - 6 week therapy: 38.4%
        - 12 week therapy: 35.3%
    - Nonserious adverse event
        - 6 week therapy: 47.3%
        - 12 week therapy: 59.7%

Strengths:

- High completion rate among trial participants
- Good adherence to assigned antibiotic therapy
- Treatment success is consistent with previous trials
- Multiple treatment locations improves the generalizability

Limitations:

- Open-label trial
- Majority of the 6-week treatment failures occurred in the debridement with implant retention group

- Duration of intravenous antibiotics varied between patients and was shorter than the US standard
- Between group differences related to the infectious pathogen

Discussion:

- Authors' Conclusion: "Among patients with microbiologically confirmed prosthetic joint infections that were managed with standard surgical procedures, antibiotic therapy for 6 weeks was not shown to be noninferior to antibiotic therapy for 12 weeks and resulted in a higher percentage of patients with unfavorable outcomes."
- Clinical Take Home Point: Data from this study does not support the use of a shorter antibiotic treatment duration (6 weeks) versus a longer antibiotic treatment duration (12 weeks) in patients with prosthetic joint infections who have undergone appropriate surgical interventions. Due to the limited data, along with the results of this trial and the DIAR trial, best practice would be to continue following the recommendations published by IDSA and treat for at least 3 to 6 months depending on the pathogen.

References:

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