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CORR Insights

CORR Insights®: Premature Therapeutic Antimicrobial Treatments Can Compromise the Diagnosis of Late Periprosthetic Joint Infection

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Where Are We Now?

Lacking definitive standards, the Musculoskeletal Infection Society (MSIS) created a definition for the diagnosis of periprosthetic joint infection (PJI), which was subsequently modified during the International Consensus meeting on PJI in 2013 [4]. The diagnostic criteria are based on both clinical and laboratory findings, and are considered more helpful than any single test might be in terms of reaching the diagnosis of PJI. However, the diagnostic picture may be confounded in cases when patients are on antibiotic therapy, which previous research has shown to be a risk factor for culture-negative PJI [3]. The recommendations by the American Academy of Orthopaedic Surgeons (AAOS) in their clinical practice guidelines discourage the use of antimicrobial treatments in patients with suspected PJI until after aspiration samples for intraoperative cultures are obtained. The AAOS also recommends withholding antibiotics for at least 2 weeks before intraarticular sample collection for culture if antibiotics have already been given [2]. However, in spite of these guidelines, some patients present for evaluation of suspected PJI having already been exposed to antibiotics. Unfortunately, we have no data to guide our interpretation of laboratory parameters such as serologic results and synovial fluid analysis in patients who had antibiotics prior to completion of a thorough workup for PJI.

In the current study, Shahi and colleagues retrospectively evaluated the prospectively maintained PJI databases of three institutions and identified patients with late PJI (as per MSIS criteria) after TKA during a 12-year period. A total of 161 patients out of 1100 infected patients fit their criteria with 53 patients (33%) having received antibiotics before aspiration. The median erythrocyte sedimentation rate, C-reactive protein, synovial white blood cell count, and synovial polymorphonuclear neutrophil percentage

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were lower in patients who received antibiotics compared with those who did not. When using the MSIS-determined PJI thresholds for the diagnostic markers (erythrocyte sedimentation rate, C-reactive protein, synovial polymorphonuclear neutrophil percentage), a larger percentage of the values were below the threshold in patients receiving antibiotics. There was no difference in rates of false-negatives in synovial white blood cell count for patients with and without antibiotics but higher rates of culture negative infection in patients with preaspiration antibiotic administration.

Where Do We Need To Go?

The current study is the first to investigate the relationship between antibiotic use and the most-common laboratory parameters used for PJI diagnosis. Though this study establishes association and not causation between therapeutic use of antibiotics and lower likelihood of diagnosing PJI, it sends a strong message to the medical community to abstain from administration of therapeutic antibiotics to patients with suspected PJI before obtaining samples. The study is limited by its retrospective nature, which likely resulted in some variability in data collection as well as some selection bias. Enrolled patients were already diagnosed with PJI, therefore the true-rate of false-negatives may be even higher as patients who received antibiotics but did not meet enough criteria may have been overlooked. Due to incomplete data capture, the study authors could not report on variables such as the type and virulence of microorganisms, duration of infection, and reasons for administration of antibiotics, its route, and dosage. All of these factors might have influenced the outcome of the study. Shahi et al. included patients who received antibiotics within 2 weeks prior to joint aspiration. But certain antibiotics, such as quinolones, which have longer half-lives, can potentially influence these parameters and such cases could have been missed.

A recent study [1] has highlighted the role of biomarkers such as alpha-defensin and synovial C-reactive protein with high sensitivity and specificity in diagnosing PJI—even while including patients with immunosuppressive conditions and concurrent antibiotic therapy. These biomarkers could potentially serve as useful tools in diagnosing PJI regardless of whether the patient is on antibiotics or not. However, these tests may not be available to all institutions or in different parts of the world for many years to come. Therefore, the role of basic laboratory parameters such as erythrocyte sedimentation rate, C-reactive protein, synovial fluid analysis in PJI diagnosis cannot be undermined. ROC curves for a cut-off of the values of erythrocyte sedimentation rate, C-reactive protein, synovial fluid white blood cell count could be useful to establish new thresholds for diagnosis of PJI in patients who receive antibiotics.

How Do We Get There?

Since infection is a low-frequency event, future research should include larger, multicenter studies involving high-volume institutions in order to reach appropriate power to make meaningful comparisons. Future studies should focus on complete data capture to evaluate the role of the type of antibiotic, duration of administration, timeline, and virulence of organism on diagnostic criteria for PJI, as well as defining new thresholds for these criteria in diagnosis of PJI for patients who receive antibiotics. Arthroplasty registries can also play an important role by tracking infection data into their databases. Studies based on such large numbers would then be able to hopefully tease out various variables influencing interpretation of laboratory parameters in patients with PJI on antibiotics.

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