Cefazolin in Total Knee Arthroplasty Provides Adequate Serum Levels but Insufficient Tissue Protection For All Pathogens: A Prospective Trial

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INTRODUCTION:

Prophylactic administration of intravenous antibiotics prior to skin incision is the most important measure to prevent periprosthetic joint infection (PJI) in arthroplasty surgery. To be effective, the local tissue concentration (LTC) of the antibiotic must exceed the minimum inhibitory concentration (MIC) of the organism. The LTC of Cefazolin in periarticular tissues during total knee arthroplasty (TKA) with and without tourniquet inflation is unknown. The aim of this study was to evaluate the effects of time from infusion to incision, patient weight and length of surgery on the LTC of cefazolin.

METHODS:

The serum and LTC of Cefazolin in 59 consecutive patients undergoing primary TKA with and without tourniquet use were prospectively evaluated. Patients were given 2 grams of cefazolin intravenously (3 grams if weight >120 kg) within 1 hour of the incision. Fat, synovium and bone samples were harvested at regular intervals from the surgery site in addition to blood serum taken from a peripheral IV at the same time intervals. LTC of Cefazolin was quantified using a liquid chromatography–tandem mass spectrometry (LC-MS) technique specifically developed for this study. Student T-Test and regression analysis (ANOVA) were used for repeated measures of cefazolin concentration between groups. Regression analysis was then used to assess the serum and local tissue concentrations of Cefazolin against time from infusion to incision, patient weight, and length of surgery. A p value of <0.05 was considered significant.

RESULTS: Overall, there were no differences in LTC based on the timing of Cefazolin infusion prior to the skin incision. Surgeries that commenced within less than 20 minutes after Cefazolin infusion exhibited blood 95.7ug/g and LTC levels 6.3ug/g comparable to those between 20 to 40 minutes (98.6ug/g, 9.7 ug/g) or those between 40 and 60 minutes (77.1ug/g, 5.2ug/g) (P=0.19). Obesity (BMI>30) had significantly lower LTC compared to their non-obese counterparts at 30 (17.3ug/g vs 11.1ug/g) and 60 (17.3ug/g vs 11.1ug/g) minutes after the incision (p-values of 0.003 and 0.03, respectively). The LTC in both fat and synovium plateaued and dropped after 60 minutes. The use of a tourniquet resulted in significantly lower LTCs in fat, synovium and bone by 60 minutes after cefazolin infusion. (Fat p=0.001, Synovium p=0.03, Bone=0.007).

DISCUSSION AND CONCLUSION:

This study demonstrates that the LTC of Cefazolin depends on numerous factors including patient weight, length of surgery, and use of a tourniquet. Furthermore, the local tissue concentrations are an order of magnitude lower than that of peripheral blood serum and are therefore unlikely to provide sufficient MIC for many common bacteria responsible for PJI. The conventional dosing protocol of Cefazolin is probably not optimal and may need rethinking.