مجموعه مقالات نشست بینالمللی «همرأیی» درباره عفونت مفاصل مصنوعی

رؤسای جلسه:

دکتر جواد پرویزی، دکتر تورستن گرک

Proceedings of the International
Consensus Meeting on Periprosthetic Joint Infection

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قسمت پنجم

Question 8: Is there a role for routine prophylactic use of dual antibiotics (cephalosporins and aminoglycosides or cephalosporins and vancomycin)?

Consensus: Routine prophylactic use of dual antibiotics is not recommended.

Delegate Vote: Agree: 85%, Disagree: 14%, Abstain: 1% (Strong Consensus)

Justification: Clinical studies have used pre- and post-intervention periods to assess the effect of switching to vancomycin for surgical prophylaxis in patients undergoing cardiothoracic surgery. Walsh et al. implemented a compre-hensive MRSA bundle program in which vancomycin was added to the routine cefazolin prophylaxis regimen for patients who tested positive for nasal MRSA carriage. Other components of the program included decoloni-zation of all cardiothoracic staff who screened positive for nasal MRSA, application of nasal mupirocin ointment for 5 days in all patients starting one day before surgery, application of topical mupirocin to exit sites after removal of chest and mediastinal tubes, and rescreening of patients for MRSA colonization at the time of hospital discharge. This program resulted in a significant reduction in the SSI rate (2.1% to 0.8%, p<0.001) as well as a 93% reduction in postoperative MRSA wound infections (from 32 infections/2,767 procedures during the 3-year pre-intervention period to 2 infections/2,496 procedures during the 3-year post-intervention period).[79] Dhadwal et al. conducted a double-blind RCT to compare the efficacy of a 48 hour, weight-based dosing of vanco-mycin plus gentamicin and rifampin versus a 24 hour cefuroxime regimen for antibiotic prophylaxis of sternal wound infections in a high-risk group of patients undergoing CABG surgery. The infection rates significantly decreased from 23.6% (25/106) in the cefuroxime group to 8.4% (8/95) in the combination vancomycin group (p=0.004).[80] Patrick et al. conducted an RCT to compare cefazolin and combinations of cefazolin and either

vancomycin or daptomycin in 181 low-risk patients undergoing vascular surgery. Only 6 postoperative MRSA infections were reported (2 in the cefazolin group, 4 in the vancomycin plus cefazolin group, and 0 in the daptomycin plus cefazolin group), making the interpretation of the differences between antibiotic regimens difficult.[81]
Sewick et al. retrospectively reviewed 1,828 primary TJAs that received either a dual antibiotic regimen of cefazolin and vancomycin or received cefazolin alone in order to determine the rate of SSI as well as the microbiology of subsequent SSI. There was a total of 22 SSIs (1.2%) with no significant difference in the infection rate between the dual antibiotic prophylaxis group compared to the single antibiotic regimen (1.1% and 1.4% respectively, p=0.636), while the prevalence of subsequent MRSA infection was significantly lower (0.002% vs 0.08%, p=0.02).[82]Ritter et al. administered a single prophylactic dose of vancomycin and gentamicin in a cohort of 201 consecutive TJA patients and documented bactericidal blood concentrations during and for 24 hours after surgery with no postoperative infections.[83] Elliot et al. developed an economic model to explore the cost effectiveness of vancomycin and/or cephalosporin for surgical prophylaxis in patients undergoing THA. Combination therapy (such as vancomycin plus a cephalosporin) was recommended when the rate of MRSA SSIs is ≥0.25% and the rate of non-MRSA SSIs is ≥ 0.2%).[78] Thus, based on the available literature, this workgroup feels that dual antibiotics may be utilized to allow broad coverage in institutions or regions where there is a high rate of MRSA infection for which prophylactic vancomycin use is deemed appropriate under question 6 above.

Question 9: What should be the antibiotic of choice for patients with abnormal urinary screening and/or an indwelling urinary catheter?

Consensus: The presence of urinary tract symptoms should trigger urinary screening prior to TJA. Asympto-

matic patients with bacteriuria may safely undergo TJA provided that routine prophylactic antibiotics are administered. Patients with acute urinary tract infections (UTI) need to be treated prior to elective arthroplasty

Delegate Vote: Agree: 82%, Disagree: 12%, Abstain: 6% (Strong Consensus)

Justification: There is sparse literature on the risk of deep joint infection in patients with abnormal perioperative urinalysis. While several case reports in the 1970s linked postoperative UTIs to PJI,[84 85] the literature supporting the correlation between preoperative UTIs and PJI following TJA is inadequate.[86] Only 3 studies have directly addressed the relationship between preoperative bacteriuria and PJI following TJA, none of which observed a positive correlation.[87-89] To our knowledge there are no studies of patients with symptomatic UTI undergoing TJA with routine perioperative prophylactic antibiotics. There is no evidence either in support of or against proceeding with surgery in this cohort of patients.

The presence of UTI symptoms should serve as a preliminary screening tool for surgical clearance of the TJA candidate. Symptoms can then be classified as either irritative or obstructive. Irritative symptoms (such as dysuria, urgency, or frequency) may or may not be related to bacteriuria and a noncentrifuged clean catch midstream urine sample should be evaluated for white blood cells (WBCs) in these patients. In patients with>10^4 WBC/mL, a bacterial count and culture should be obtained and in patients with>4 WBC/high power field and bacterial count >10^3/mL, surgery should be postponed until an appropriate course of microbe-specific antibiotics is administered and repeat urinalysis is obtained. On the other hand, asymptomatic patients with bacteriuria may safely undergo TJA provided routine prophylactic antibiotics are administered. Patients with obstructive symptoms should undergo urologic evaluation before arthroplasty, as postoperative urinary retention has been shown to be a risk factor for PJI.[86,90,91]

In a prospective, multicenter study of 362 knee and 2,651 hip arthroplasty cases, the authors reported a deep joint infection rate of 2.5% for knee and 0.64% for hip cases at one year follow-up. While univariate analysis showed no association between deep joint infection and preoperative UTI (>10^5 CFU/mL), multivariate regression analysis indicated that postoperative UTI increased the risk of hip PJI.[88]

Of 1,934 surgical cases (1,291 orthopaedic surgeries) performed at a Veterans Administration hospital, a preoperative urine culture was obtained in 25% (489) of cases. Of these, bacteriuria was detected in 54 (11%) patients, of which only 16 received antimicrobial drugs. The incidence of SSI was similar between those with bacteriuria and those without (20% vs 16%, p=0.56), while the rate of postoperative UTI was more frequent among patients with bacteriuria than those without (9% vs 2%, p=0.01). Among the 54 patients with a positive

urinary culture, treated and untreated patients were compared. Unexpectedly, a greater proportion of treated patients developed an SSI (45% vs 14%, p=0.03). This effect was greatest among patients with high count bacteriuria (>10^5 CFU/mL), with SSI occurring in 4 of 8 (50%) of treated vs 1of 15 (7%) of untreated (p=0.03). These results led the authors to conclude that in this system preoperative urinary cultures were inconsistently ordered and that when they were, they were rarely positive for bacteriuria. Even when bacteriuria was detected, it was usually not treated. The authors noted that treating bacteriuria associated with SSI is likely confounded by factors that contributed to the initial decision to administer antimicrobials in the first place.[92]

A retrospective study of 274 THAs found that 5 patients with PJI had perioperative UTIs. However, the same organism was isolated from the urinary tract and hip in only 3 patients. Of these, only one had a documented preoperative urinalysis.[93] A retrospective analysis of 277 patients (364 TJAs) showed that 35 patients had evidence of preoperative or perioperative UTI with colony counts greater than 10^5 CFU/mL on preoperative clean-catch urine specimens. Only 3 patients (1.1%) developed joint infections at 9, 19, and 45 months respectively, and none was thought to be due to perioperative UTI.[87] Another retrospective analysis found 57 (55 asymptomatic, 2 symptomatic) of 299 arthroplasty patients had bacteriuria on admission. Twenty of the 57 patients went to surgery before the routine culture results were available, but postoperatively received appropriate antibiotics for treatment of the UTI. Another 18 patients underwent surgery during their treatment course for preoperatively-diagnosed UTI, while the other 19 patients completed an appropriate antibiotic course prior to surgery. None of the patients developed a PJI, which led the authors to conclude that a treatment course of antibiotics can be implemented at any time perioperatively once culture data are obtained.[89]

The incidence of bacteriuria rises from 0.5% to 1% for a single in-and-out catheterization, 10% to 30% for catheters in place for up to 4 days, and up to 95% for catheters in place for 30 days or more.[94,95]

Question 10: Should the preoperative antibiotic choice be different in patients who have previously been treated for another joint infection?

Consensus: The type of preoperative antibiotic administered to a patient with prior septic arthritis or PJI should cover the previous infecting organism of the same joint. In these patients, we recommend the use of antibiotic-impregnated cement, if a cemented component is utilized.

Delegate Vote: Agree: 84%, Disagree: 10%, Abstain: 6% (Strong Consensus)

Justification: There is no evidence that septic arthritis or a PJI can be completely cured. Jerry et al. conducted a

study of 65 patients who underwent TKA and had a history of prior sepsis or osteomyelitis around the knee. They reported rates of deep PJI of 4% and 15% respectively.[96]

Lee et al. studied a consecutive series of 20 primary TKAs in 19 patients with a history of prior septic arthritis or osteomyelitis around the knee. They performed a preoperative workup to evaluate for infection that included serologies and plain radiographs in all patients, while 8 patients additionally had tagged WBC scans and 7 patients had a knee aspiration. Intraoperatively, frozen section for evidence of acute inflammation was used to guide decisions on whether the procedure was done as a single or staged procedure. All TKA components were implanted with antibiotic cement containing 1g of vancomycin and 1.2g of tobramycin/batch of Simplex bone cement. Of the 17 patients with a minimum of 2 years follow-up, only one developed a PJI approximately 3.5 years from the index arthroplasty. Of note, this was one of the two patients that had been treated in a staged manner and additionally had immunosuppressive comorbidities, including rheumatoid arthritis, insulin-dependent diabetes mellitus, and was taking daily doses of prednisone.[97]

Larson et al. performed a retrospective matched case control study to review the clinical results of 19 patients who underwent TKA after infected tibial plateau fractures, comparing them to 19 control subjects matched for age, gender, and arthroplasty year, who underwent TKAs for tibial plateau fractures without a history of infection. Of the 19 case patients, 13 underwent one-stage TKA, while the remainder underwent a staged TKA with either an antibiotic spacer or debridement and intravenous antibiotic therapy. Antibiotic cement was used in the majority of patients. Previously infected knees were 4.1 times more likely to require additional procedures for complications compared with knees with no previous infection (95% CI 1.2-18.3, p=0.02). The 5 year infection-free survival was 73%±10% in the case group compared with 100% in the control group (p=0.023). The authors recommended that in patients at high risk less than one year since active evidence of infection, a two-stage TKA be performed, with antibiotic therapy and a 4 to 6 week delay between procedures.[98]

Question 11: Should postoperative antibiotics be continued while a urinary catheter or surgical drain remains in place?

Consensus: No. There is no evidence to support the support the continued use of postoperative antibiotics when urinary catheter or surgical drains are in place. Urinary catheters and surgical drains should be removed as soon as safely possible.

Delegate Vote: Agree: 90%, Disagree: 7%, Abstain: 3% (Strong Consensus)

Justification: Short-term use of an indwelling catheter after surgery reduces the incidence of urinary retention and bladder over-distension without increasing the rate of UTI and is therefore common practice in many hospitals.[99] However, it has been shown that there is an increased risk of UTIs when a catheter is employed for more than 48 hours.[100,101] Urinary retention as well as catheterization can both lead to bacteriuria,[101-103] which increases the risk of deep PJI from 3 to 6 times.[87,88,104,105]

Literature in the field of surgical oncology demonstrates that bacterial colonization of surgical drains used in breast and axillary procedures is a significant risk factor for the development of SSI and the microorganisms that caused SSIs were the same as those that colonized the drainage tube in 83% of cases.[106] Other studies have demonstrated that there is an association between longer duration of drain use and increased incidence of SSI.[107]

The AAOS recommendations for the use of IV antibiotic prophylaxis in primary TJA, recommendation 3, states that the "duration of prophylactic antibiotic administration should not exceed the 24 hour postoperative period. Prophylactic antibiotics should be discontinued within 24 hrs of the end of surgery. The medical literature does not support the continuation of antibiotics until all drains or catheters are removed and provides no evidence of benefit when they are continued past 24 hours."[2]

Colonization of drains by skin organisms can certainly occur, but in only 10% of cases with positive drain tip culture does overt infection develop.[108] Michelson et al. conducted an RCT of 100 TJA patients using two methods of bladder management: short term (<24 hour) indwelling catheters and intermittent catheterization. All patients received the same perioperative cefazolin prophylaxis. The authors reported a lower incidence of urinary retention in the indwelling catheter group (27% vs 52%, p<0.01) and a lower rate of bladder distension (7% vs 45%; p<0.01). Moreover, patients who had an indwelling catheter for more than 48 hours had a significantly higher rate of bladder infection (35%) than patients who were straight catheterized and/or who had an indwelling catheter for fewer than 48 hours (6%, p<0.01).[99]

Van den Brand et al. performed a prospective RCT to determine whether an indwelling catheter for 48 hours or intermittent catheterization leads to less postoperative bacteriuria or a UTI with a single dose of cefazolin prophylaxis in primary hip and knee arthroplasties. In their protocol, patients received 48 hours of IV prophylactic cefazolin during the postoperative period. Patients who had an indwelling catheter in place after the IV antibiotics were completed were treated with oral antibiotic prophylaxis (nitrofurantoin) until catheter removal. Of the 99 patients who completed the study, 14 patients (5 men, 9 women) developed postoperative bacteriuria. The indwelling catheter group had a bacteriuria rate of 24% (11/46) compared with 6% (3/53) in the intermittent catheterization group (p=0.018).[109]

Similar findings were reported by Oishi et al., who reviewed 95 consecutive patients who had been managed with either an indwelling catheter (72 hours) or intermittent catheterization. Patients who were treated with an indwelling catheter had significantly lower incidences of urinary retention (7% vs 84% respectively; p<0.005) and bladder distension (7% vs 41%; p<0.005) than those who were treated with straight catheterization. While not statistically significant, though no patient in the indwelling catheter group developed infection, in the intermittent catheterization group one patient (2%) had bacteriuria and one patient (2%) had a UTI (p>0.1).[110]

Koulouvaris et al. performed a retrospective case control study to determine whether a treated preoperative or postoperative UTI or asymptomatic bacteriuria increases the risk of deep PJI and whether the organisms are the same for the UTI and PJI. The authors matched 58 patients who had wound infections with 58 patients who did not develop wound infection based on age, gender, surgeon, joint, year of surgery, and length of follow-up. The authors found no association between preoperative UTI and wound infection (OR 0.34; 95% CI 0.086-1.357, p=0.13), and no association between postoperative UTI and wound infection (OR 4.22; 95% CI 0.46-38.9, p=0.20). Only one patient had the same bacteria (*E. faecalis*) cultured in the urine and the wound.[111]

In a survey of the members of the American Society of Breast Surgeons regarding the use of perioperative antibiotics for breast operations requiring drains, respondents continued antibiotic prophylaxis for 2-7 days or until all drains were removed (38% and 39% respectively) in cases without reconstruction, while in reconstruction cases 33% of respondents continued antibiotic prophylaxis for 2-7 days or until all drains were removed.[112] A similar study surveying the American and Canadian societies of Plastic Surgeons regarding drain use and perioperative antibiotic prophylaxis in cases of breast reconstruction found that 72% of plastic surgeons prescribed postoperative outpatient antibiotics in reconstruction patients with drains, with 46% continuing antibiotics until drains were removed.[113]

Question 12: What is the evidence for the optimal duration of postoperative antibiotics in decreasing SSI or PJI?

Consensus: Postoperative antibiotics should not be administered for greater than 24 hours after surgery.

Delegate Vote: Agree: 87%, Disagree: 10%, Abstain: 3% (Strong Consensus)

Justification: Many studies across surgical specialties have been performed to compare durations of antibiotic prophylaxis and the overwhelming majority have not shown any benefit in antibiotic use for more than 24 hours in clean elective cases.[114-116] Prolonged postoperative prophylaxis should be discouraged because of the possibility of added antimicrobial toxicity, selection of resistant organisms, and unnecessary expense.[24]

The AAOS recommendations for the use of IV antibiotic prophylaxis in primary TJA, recommendation 3, states that "duration of prophylactic antibiotic administration should not exceed the 24 hour postoperative period. Prophylactic antibiotics should be discontinued within 24 hours of surgery."[1]

Mcdonald et al. performed a systematic review across surgical disciplines to determine the overall efficacy of single versus multiple dose antimicrobial prophylaxis for major surgery. They included only prospective RCTs which used the same antimicrobial in each treatment arm whose results were published in English. Regardless of fixed models (OR 1.06, 95% CI 0.89-1.25) or random effects (OR 1.04; 95% CI 0.86-1.25), there was no significant advantage of either single or multiple dose regimens in preventing SSI. Furthermore, subgroup analysis showed no significant differences in the type of antibiotic used, length of the multiple dose arm (>24 hr vs ≤24 hr), or type of surgery (obstetric-gynecological vs other).[117]

Mauerhan compared the efficacy of a one-day regimen of cefuroxime with a 3-day regimen of cefazolin in a prospective, double-blinded, multicenter study of 1,354 patients treated with arthroplasty and concluded that there was no significant difference in the prevalence of wound infections between the two groups. In the group treated with primary THA, the prevalence of deep wound infection was 0.5% (1/187) for those treated with cefuroxime compared with 1.2% (2/168) for those who had received cefazolin. In the group treated with a primary TKA, the rate of deep wound infection was 0.6% (1/178) for those treated with cefuroxime compared with 1.4% (3/207) for those who had received cefazolin.[22]

Heydemann and Nelson, in a study of hip and knee arthroplasty procedures, initially compared a 24-hour regimen of either nafcillin or cefazolin with a 7-day regimen of the same and found no difference in the prevalence of infection. They then compared a single preoperative dose with a 48-hour regimen and again found no difference in infection prevalence. A total of 466 procedures was performed during the 4-year study. No deep infections developed in either the one-dose or 48-hour antibiotic protocol group. A deep infection developed in one (0.8%) of the 127 patients in the 24-hour protocol group and in two (1.6%) of the 128 patients in the 7-day protocol group for an overall infection rate of 0.6% (3/466). The authors recognized that as a result of the small sample sizes, the study lacked the power to compare the one dose and the more than one dose categories.[118]

Stone et al. performed two separate prospective, placebo RCTs of variable-duration antibiotic prophylaxis in patients undergoing elective gastric, biliary, or colonic surgery and then in patients undergoing emergency laparotomy and found that in both cases no significant difference was seen in the rate of SSI. Specifically, in a prospective RCT of 220 patients undergoing elective general surgery who were randomized to either periope-

rative cefamandole plus 5 days of placebo or perioperative plus 5 postoperative days of cefamandole, there was no significant difference in the rate of wound infection (6% and 5% respectively). In a second prospective RCT of patients undergoing emergent laporatomy in which cephalothin was utilized perioperatively, there was no significant difference in the rate of peritoneal infection between those who received perioperative therapy only (8 and 4% respectively) compared to those who had 5 to 7 days of additional postoperative therapy (10% and 5% respectively).[119]

In a retrospective review of 1,341 TJAs, Williams and Gustilo found no difference in deep infection rates between a 3day and 1day course of prophylactic antibiotics, but emphasized the importance of the preoperative dose, which was 2g of cefazolin.[120]

Clinical studies have used pre- and post-intervention periods to assess the effect of antibiotic duration for

surgical prophylaxis. One institution launched a surgical wound infection surveillance program to monitor all orthopaedic surgeries and changed the prophylactic antibiotic regimen from intravenous cefuroxime (one preoperative and 2 postoperative doses every 8 hours) to one single preoperative dose of intravenous cefazolin for all clean orthopaedic surgeries. The authors of this study found no significant difference in the superficial and deep wound infection rates in 1,367 primary arthroplasties performed with a single preoperative dose of cefazolin versus 3 doses of cefuroxime. The deep wound infection rate for THA was 1.1% (95% CI, 0%-3.3%) in the cefuroxime group and 1.1% (95% CI, 0%-2.2%) in the cefazolin group (p=1.0). The deep wound infection rate of TKA was 1.6% (95% CI, 0%-3.8%) in the cefuroxime group and 1.0% (95% CI, 0.3%-1.7%) in the cefazolin group (p=0.63).[121]

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