Intra-Articular Antibiotic Therapy for PJI

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Disclosures

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Current treatment methods of chronic PJI

• One Stage Exchange
• Two Stage Exchange
How are we really doing? Well...

- 504 cases
- 82.7% achieved reimplantation
- 81.4% of these (at least one yr f/u) were successful
- 4.2 mo mean duration between stages (range 0.7 to 131.7 mo)
- 11.9% required additional spacers
- 17.3% did not undergo reimplantation
- 36 patients died between stages

The problem? BIOFILM!!!

- *Planktonic* state
  - MIC (Minimal Inhibitory Concentration)
- *Biofilm based* state
  - MBEC (Minimal Biofilm Eradication Concentration)
  - MBEC may be 100-1,000x MIC

Traditional two stage utilizing a spacer

- PMMA elutes antibiotics typically above MIC
- Combined w/ systemic antibiotics (limited by toxicity)
- AKI 5%
- Local antibiotic levels below MBEC
- Duration 6-12 weeks
The solution to biofilm?: Intraarticular antibiotic delivery (IAA)

Clinical results of infected total knee arthroplasty treated with intraarticular antibiotics. Melarango P, Whiteside L: 67th AAOS 2000
• 34 cases; 94% success rate
• Intraarticular levels reported 100-500x higher than spacer + systemic

2005: Novel treatment concept of IAA combined with NPWT for a 7 day exchange

Why NPWT?
• Edema reduction reduces pressure compressing capillaries allowing increased O2 delivery
• Tension applied to cells stimulates replication and neovascularization, thereby promoting granulation tissue
• Allows high fluid turnover

Stage one technique

Debridement complete NPWT sponge placement
Local intraarticular antibiotic delivery device

Protocol: IAA/ NPWT for 7 day duration

- Tobramycin 80 mg/50 ml NS infused once daily. Soak time 2 hrs
- Vancomycin 3000 mg/1200 ml NS; infused 50 ml aliquots hourly. Soak time 30 min, VAC time 30 min. Total time 22 hrs.
- Total antibiotic load delivered over 7 days: tobramycin 560 mg, vancomycin 21,000 mg
- Concentration: tobramycin 1600 ug/ml, vancomycin 2500 ug/ml

In vitro studies supporting dose and duration

- "Although local delivery can achieve MBEC levels, the duration for which they must be sustained is unknown."
- Staph epi, S. aureus, MRSA, E. coli, P. aeruginosa
- Staphylococcal strains had MBEC 8,000 ug/ml or higher after one day abx exposure. After five days exposure, MBEC 2,000 ug/ml or less
- Similar findings for gram (-) organisms exposed to tobramycin
Does the MBEC decrease with in vitro exposure to antimicrobial longer than 5 days?

S. Aureus and MRSA biofilms were exposed to vancomycin, tobramycin, and combo for 2, 4, 6 and 8 weeks in vitro
Conclusion: Even when exposure time is 8 weeks, MBECs do not fall within systemically achievable levels

My early experience with 7 day two stage: 2005-2009

Seven day abbreviated two-stage exchange arthroplasty for treatment of peri-prosthetic joint infection: 2-6 year results. de Beaubien B, Ekpo T, Parvizi J: 2012 EBJIS, (Montreux, Switzerland)
• Retrospective, one surgeon, IRB approved
• 73 consecutive patients with chronic PJI
• 10 patients excluded
• 63 patients, 64 joints
• 37 knees, 27 hips

Results 2005-2009

• Failure defined as recurrence of infection requiring revision
• Follow up 2-6 yrs (mean 4y)
• Success rate 89.1% (57/64)
• 7 failures; 4 knees, 3 hips
• 6 patients underwent further surgery; all considered infection free
Most recent cohort: March 2014 - present

- Treatment protocol updated regarding dosing and timing of antibiotic infusion. Also, automated infusion/evacuation system started

- Pre 2014, vanc/tobra infused together q 4 hrs manually, with equal soak time/VAC time
- Post 2014, automated infusion schedule with separate infusion of vanc/tobra to take advantage of different mechanisms of action

Most recent cohort

- Preliminary results 3/14-9/15
- IRB application submitted
- Minimum 1 yr f/u
- MSIS PJI diagnostic criteria for inclusion
- Success rates based on Delphi criteria

Results

- 35 patients had vanco/tobra protocol
- 8 didn’t meet MSIS diagnostic criteria for PJI
- 27 patients, 28 joints (12 hips, 16 knees)
- 4 failures (Delphi), including one death from PE
- 39% of patients previously failed medical or surgical intervention
- 7.25 days average between stage I and II
- 7.6 days average length of IAAT
- No dose adjustments, AKI
- All patients reimplanted
Results con’t

• Success achieved in 24/28 of patients (85.7%)
• Infection free at one year
• One of four failed cases had IAAT repeated successfully for cumulative success rate 89.3%
• Two amputations
• One death due to PE

Conclusions

• Biofilm eradication is key to eliminating chronic PJI
• Local delivery is necessary, systemic therapy is not capable
• MBEC levels maintained for 5 days duration
• NPWT is helpful as adjunct therapy
• Patient, surgeon, economic benefit to shorter duration between stages

Thank you!