

Intra-Articular Antibiotic Therapy for PJI

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Disclosures

- Joint Purification Systems LLC
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Current treatment methods of chronic PJI

- One Stage Exchange
- Two Stage Exchange



How are we *really* doing? Well...

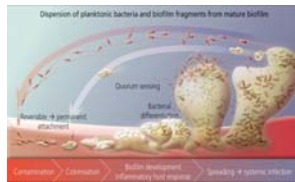
504 cases

- 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



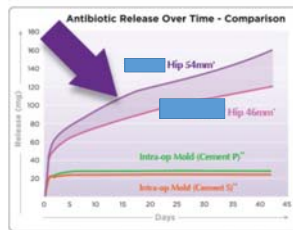
The problem? BIOFILM!!!

- *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)

Treatment of acutely infected arthroplasty with local antibiotics. Davenport K, Perry CR: J Arthroplasty June, 1991

Clinical results of infected total knee arthroplasty treated with intraarticular antibiotics. Melaragno P, Whiteside L: 67th AAOS 2000

Direct exchange treatment of septic total joint arthroplasty with intraarticular infusion of antibiotics: technique and early results. Nayfeh T, Whiteside L: Orthopedics Sept 2004.

- 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

Infusion line



Evacuation line



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."
Minimum biofilm eradication concentration decreases during multi-day anti microbial exposure in vitro. Overstreet D, McLaren A, et al: MSIS 2015 (Cleveland, OH)
- 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 anti microbial longer than 5 days?

MBEC decreases with long-term exposure to antimicrobials. Castaneda P, McLaren A, et al: 2016 MSIS (Charlotte,NC)

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 reimplemented

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!