Mon année en 3 papiers
Infections bactériennes chroniques

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GILAR

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PLAN

1 - How We Approach Suppressive Antibiotic Therapy (SAT) Following Debridement, Antibiotics, and Implant Retention for Prosthetic Joint Infection. Nicolas Cortes-Penfield, et al. CID. 2023 August

2 - Suppressive Antibiotic Therapy after Debridement, Antibiotics, and Implant Retention (DAIR) is Well-Tolerated Without Inducing Resistance: A Multicenter Study. Sumon Nandi, et al. *The Journal of Arthroplasty*. 2023 September

3 - Dalbavancin as suppressive antibiotic therapy in patients with prosthetic infections: efficacy and safety. Andrés Ruiz-Sancho, et al. *Front Pharmacol*. 2023 Jun

How We Approach Suppressive Antibiotic Therapy (SAT) Following Debridement, Antibiotics, and Implant Retention for Prosthetic Joint Infection

Nicolas Cortes-Penfield, et al. CID. 2023 August

Rationnel : Recommandations de l'*Infectious Diseases Society of America* (IDSA) 2013 proposent SAT lorsque le traitement medico-chriurgical n'est pas optimal sans indication précise

Méthode :

- Narrative review
- Pubmed -> Avril 2023
- Critères d'inclusion :
    - Infection de prothèse ostéoarticulaire,
    - Synovectomie, lavage et antibiothérapie,
    - Aucune restriction sur indication SAT,
- Définition SAT : poursuite traitement > 6mois

Objectifs :

- Diminution du risque de rechute sous SAT ?
- Evaluation de effets indésirables sous SAT ?

Synthèse de la littérature et proposition d'indications au SAT

How We Approach Suppressive Antibiotic Therapy (SAT) Following Debridement, Antibiotics, and Implant Retention for Prosthetic Joint Infection

Nicolas Cortes-Penfield, et al. CID. 2023 August

1) Risque d'échec du SAT :

Study or Subgroup	SAT Events	SAT Total	No SAT Events	No SAT Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Siquiera 2015	19	54	106	152	89.7%	0.24 [0.12, 0.45]	2015
Bryan 2017	2	69	1	9	6.1%	0.24 [0.02, 2.94]	2017
Renz 2019	0	15	4	12	4.2%	0.06 [0.00, 1.27]	2019
Total (95% CI)		**138**		**173**	**100.0%**	**0.22 [0.12, 0.42]**	
Total events	21		111				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.74$, $df = 2$ ($P = 0.69$); $I^2 = 0\%$

Test for overall effect: $Z = 4.73$ ($P < 0.00001$)

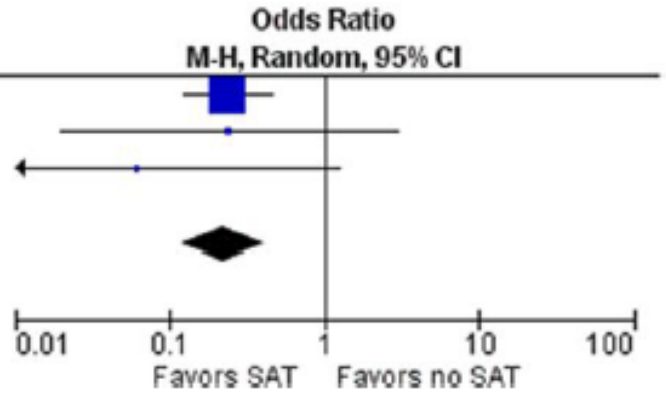

Figure 1. Receipt of SAT is associated with reduced probability of treatment failure following PJI managed with DAIR. Abbreviations: CI, confidence interval; DAIR, debridement, antibiotics, and implant retention; M-H, mantel-haenszel; PJI, prosthetic joint infection; SAT, suppressive antibiotic therapy.

2) Effet indésirable (EI) et arrêt SAT :

- EI : médiane 8,3% (IQR : 0,0-23,1 %)
- Arrêt du SAT : médiane de 3,1 % (IQR : 0,0-15,4 %)

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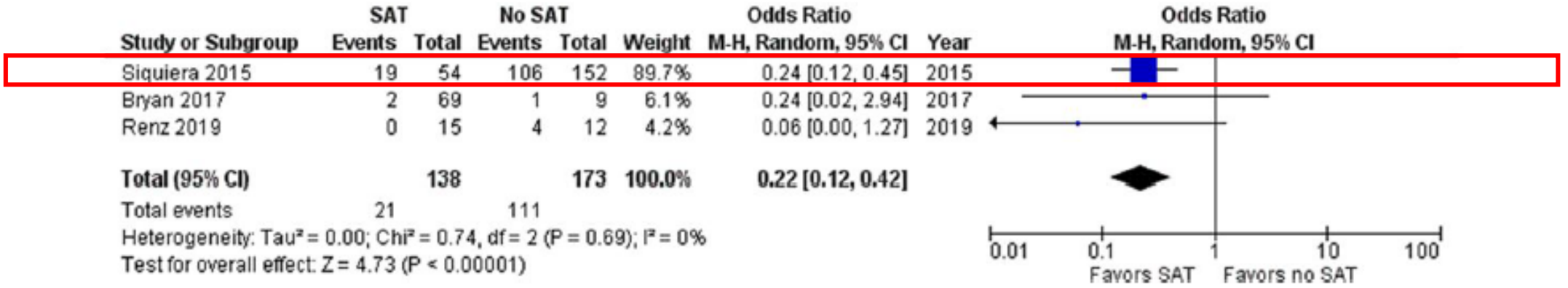

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Nicolas Cortes-Penfield, et al. CID. 2023 August

Proposition indications SAT

Table 3. Factors We Suggest Guide Prescription of Suppressive Antibiotic Therapy Following DAIR

Factors strongly suggesting benefit from SAT after DAIR (the authors would offer SAT to most patients with at least 1 of these factors)
• Limited options for arthroplasty revision (ie, recurrent infection would require amputation, arthrodesis, or difficult wound coverage and likely result in a substantially worse functional outcome)a
• Recurrent PJI/prior PJI treatment failureb
• Infection with difficult-to-treat pathogens (*S. aureus*b and possibly othersa, eg *Pseudomonas aeruginosa* or Candida)
• Severe immunocompromise (ie, solid-organ or stem cell transplant, active chemotherapy, chronic systemic steroid therapy, TNF-inhibitor therapy, advanced HIV)a
• Underwent arthroscopy instead of open DAIR, or polyethylene liner was not exchangedb
Factors that may suggest benefit from SAT after DAIR (the authors would consider SAT in patients with at least 1 of these factors)
• Major end-organ disease predisposing to poor outcome (ie, cirrhosis, ESRD, or heart failure)b
• Age >75 y b or estimated life expectancy <10 ya
• Late hematogenous infection (onset >2 y after initial arthroplasty), particularly if associated with active bacteremiab
• Gram-negative infection that cannot be treated with a fluoroquinoloneb
• Patient strongly values the potential benefits of SAT over the potential risks after both have been explained in an informed shared-decision-making conversationa
Factors suggesting little benefit from SAT (the authors would not offer SAT to most patients with these factors)
• Completion of >6 wk of adjunctive rifampin for susceptible, monomicrobial coagulase-negative *Staphylococcus* spp. infection (as part of a minimum 3–6 mo total antibiotics)b
• Completion of a fluoroquinolone-based regimen for a gram-negative infectionb
• Culture-negative infectionb

Abbreviations: DAIR, debridement, antibiotics, and implant retention; ESRD, end-stage renal disease; HIV, human immunodeficiency virus; PJI, prosthetic joint infection; SAT, suppressive antibiotic therapy; TNF, tumor necrosis factor.

[a]Based on the consensus opinion of the authors, but not directly supported by the data identified in this review.

[b]Based on retrospective data identifying this as a risk factor for treatment failure.

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Suppressive Antibiotic Therapy after Debridement, Antibiotics, and Implant Retention (DAIR) is Well-Tolerated Without Inducing Resistance: A Multicenter Study

Sumon Nandi, et al. *The Journal of Arthroplasty*. 2023 September

Rationnel : Données actuelles sur la tolérance issues d'études avec de faibles effectifs et des données disparates sur la tolérance et l'acquisition de résistance lors des rechutes

Matériel et méthodes :

- Etude rétrospective bi centrique
- 2015-2020
- Population :
    - < 4 semaines de symptômes
    - DAIR
    - 6 semaines de traitement IV
    - > 3 mois SAT

Objectif :

- Décrire les effets indésirables et l'acquisition de résistance

Résultats :

- 115 patients (72 PTG – 43 PTH)
- Microbiologie :
    - *Staphylococcus* spp. - 50%
    - BGN – 3%
    - Polymicrobienne – 10%
    - Culture négative – 13%
- SAT :
    - Bétalactamine 30%
    - Cycline 30%
    - Bactrim 5%
    - Combinaison 25%
- Durée : PTG : 17 mois (3-63) - PTH : 12 mois (2–44)

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Caractéristiques	Effectif
Effets indésirables	
Grade I	**8 (7%)**
Grade II	**7 (6%)**
Gastro-intestinal	7 (6%)
Atteinte cutanée	5% (5%)
Autres	Insuffisance rénale (2), neutropénie (1), Cytolyse (1), hyperkaliémie(1)
Rechute et acquisition de résistances	
Nombre rechutes	47 (40%)
Acquisition résistance	**0**

Conclusion : Définition SAT non consensuelle et patients ne rentrant pas dans les indications d'un traitement suppressif (attention définition SAT). Peu d'effets indésirables et non graves et surtout pas d'acquisition de résistance.

Dalbavancin as suppressive antibiotic therapy in patients with prosthetic infections: efficacy and safety

Andrés Ruiz-Sancho, et al. *Front Pharmacol*. 2023 Jun

Rationnel : Traitement suppressif des infections sur matériel prothétique. Dalbavancine lipoglycopeptide à demi-vie longue IV.

Matériel et méthodes :

- Observationnelle – vie réelle
- Multicentrique : 4 centres espagnols
- Entre 2016 et 2018
- Infection prothèse (vasculaire ou articulaire) avec une prise en charge chirurgicale non optimale et après un traitement d'attaque

Objectif :

- Décrire la population, efficacité, effets indésirables

Résultats : 8 patients

Caractéristiques	
Prothèse	Vasculaire = 6 Articulaire = 2
Micro-organisme	*Staphylococcus* spp. = 3 *Enterococcus faecium* = 2 *Streptococcus gallolyticus* = 1
Posologie/Fréquence	7 jours – 500mg (n = 4) 14 jours – 1500mg (n = 4)
Nombre d'injections	7 à 87 doses
Efficacité	Succès 6/8
Tolérance	Asthénie (1), Insuffisance rénale (1)

Conclusion : Peu de données mais effets indésirables rares et non graves. Efficacité difficile à évaluer sur ce faible effectif - similaire aux précédentes études sur le traitement suppressif

CONCLUSION

- Littérature difficile à interpréter et comparer car différentes définitions SAT et indications (différentes populations)
- En pratique clinique :
  - Discuter collégialement les indications,
  - Peu d'effets indésirables et faible risque d'acquisition de résistance
  - Privilégier le traitement PO mais traitements IV avec longue demi-vie peuvent être utiles dans certaines situations (ex : Dalbavancine)

Merci pour votre attention

Experience Using Adjuvant Bacteriophage Therapy for the Treatment of 10 Recalcitrant PJI: A Case Series,
James B Doub, et al. Clinical Infectious Diseases. February 2023.

Rationnel : Antibiotiques conventionnels : activité limitée contre les phénotypes bactériens et biofilm. Bactériophages : activité anti-biofilm et contre les bactéries métabolisme quiescent.

Matériel et méthodes :
- Etude observationnelle retrospective
- Monocentrique : USA - Baltimore
- Entre 2019 – 2022
- Echec d'un premier traitement malgrés une prise en charge médico-chirurgicale optimale
- Indication théorique à une arthrodèse ou une amputation
- Mono-microbien avec phage réalisable

A **Protocols for Bacteriophage Therapy in PJI**

Protocol 1:
- Intraoperative bacteriophage therapy[1]:

Then
- Intravenous bacteriophage therapy[2]: 1 dose daily for 5 days

Protocol 2:
- Intraoperative bacteriophage therapy[1]:

Plus
- Placement of hickman Catheters[3]

Then
- Intraarticular bacteriophage Therapy[4]: 1 dose daily for 4 days

Plus
- Intravenous bacteriophage therapy[2]: 1 dose daily for 5 days

Both protocols use standard of care antibiotic therapy

[1]Doses given at the end of surgery are diluted in normal saline to create 20 mL solutions.
[2]Intravenous doses are diluted in 50 mL of normal saline and infused over 30 minutes.
[3]Hickman catheters are removed after last dose of intraarticular bacteriophage therapy.
[4]Intraarticular doses are diluted in 20 mL of normal saline.

Conclusion :

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Résultats : 10 patients
- Microbiologie :
  - 8 *Staphylococcus* spp.
  - 1 *Entrococcus faecium*
  - 1 *Klebsiella pneumoniae*
- 6 DAIR / 4 changement en 1 ou 2 temps
- Effet indésirable : Cytolyse hépatique (6/10)
- Absence de récurrence : 9/10 (5 mois -2ans et demi) – 1 Echec : amputation

Conclusion : Bonne tolérance : absence d'effet indésirable grave. Efficacité sur des suivis longs avec patients en échec précédemment. Thérapie à proposer en sauvetage et à évaluer par un essais clinique randomisé.