

Background

- *Staphylococcus aureus* is the most common pathogen isolated in cases of injection drug use-associated infective endocarditis (IDUaIE).
- In our centre, *S. aureus* causes 77% of all cases of first episode IE in PWID¹
- Our incidence of IDUaIE is high with 56% of all cases of IE occurring in PWID¹
- The local drug of choice in persons who inject drugs (PWID) in London, Ontario is Hydromorph contin (HCR), a controlled-release opioid.
- Due to its formulation and low solubility, HCR is often washed and injected multiple times to fully extract the opioid.

Hypothesis

Extensive manipulation of HCR can result in multiple chances for bacterial contamination and that excipients within HCR increase *S. aureus* survival in the drug preparation.

Methods and Results

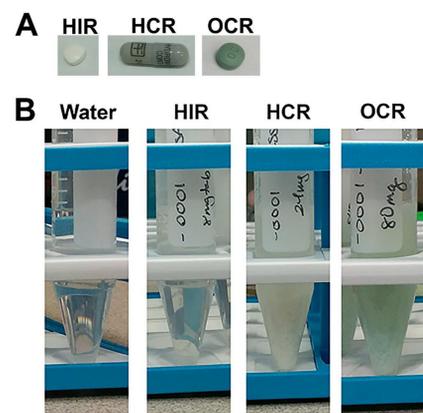


Figure 1. The controlled-release opioids are not water-soluble. (A) HCR comes in a capsule formulation which PWID open to extracts the beads contained inside. Hydromorphone immediate-release (HIR) and Oxycodone controlled-release (OCR) comes in an a pill formulation that is easily crushed by PWID. (B) HIR is the most easily dissolvable of the opioids testing with HCR being the least as a result of residual bead fragments.

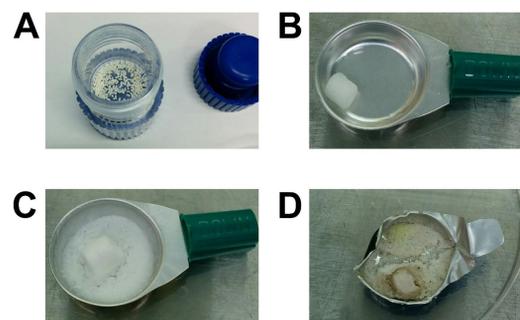


Figure 2. Low water solubility of HCR results in PWID crushing HCR and washing it multiple times to extract the drug. (A) HCR is removed from the capsule and crushed in a pill crusher before being transferred to a cooker. (B) Unused cooker with filter, which is a part of a provincial harm-reduction initiative. (C) HCR-containing sterile cooker and filter after a single wash in controlled laboratory environment. (D) Used injection drug preparation equipment (IDPE) after three washes (donated by a local PWID) with large amount of residual HCR. Multiple “washes” (addition of water with subsequent aspiration of residual drug for injection) are performed over hours to days.

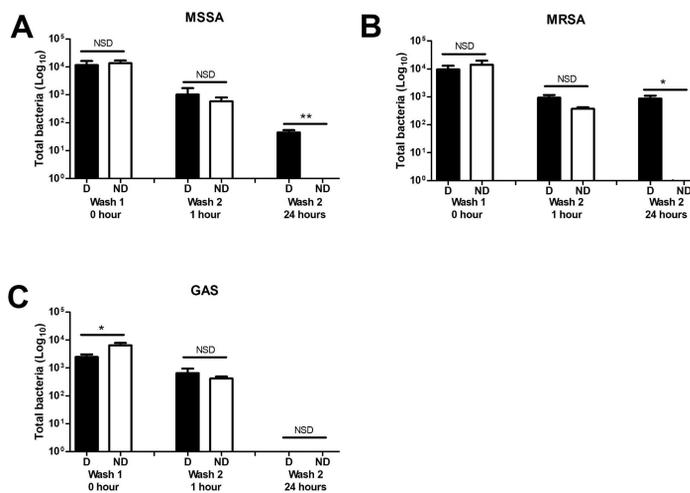


Figure 3. *S. aureus* survived significantly better in HCR than water when the second wash of IDPE was performed at 24 hours. All IDPE underwent an initial wash with bacteria-spiked water for 5 minutes and were subsequently left to dry at room temperature before a second five minute wash was performed at both 1 hour and 24 hours. Both (A) MSSA and (B) MRSA survived significantly better in the HCR solution than in the water vehicle control when the second wash happened after 24 hours. (C) *S. pyogenes* did not survive on drug equipment at 24 hours. Significance assessed by paired t-test *P<0.05, **P<0.01. D=Drug, HCR, ND=No drug.

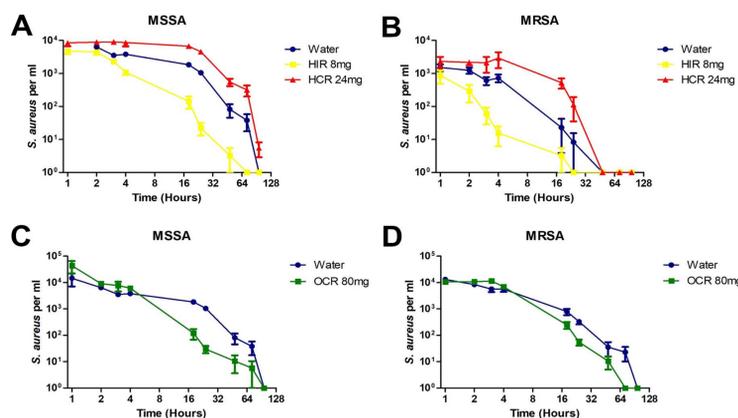


Figure 4. *S. aureus* persists longer over time on unused IDPE containing HCR compared to HIR or water, the same thing was not observed in OCR. (A-B) Clinical strains of *S. aureus*, both MSSA and MRSA, persist longer in HCR solution compared to both HIR solution or sterile water control. (C-D) Both MSSA and MRSA persist longer in sterile water control when compared to OCR solution.

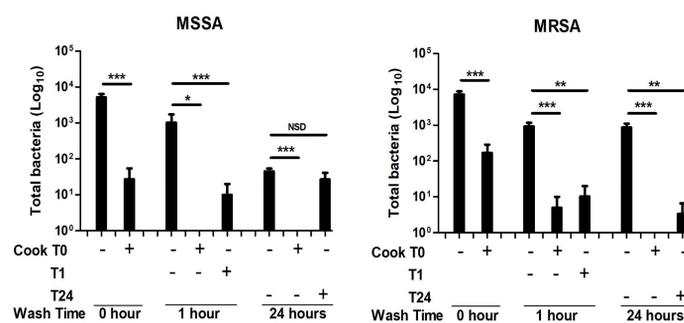


Figure 5. *S. aureus*-spiked IDPE had a decrease in the overall bacterial burden when heated with a cigarette lighter prior to sampling. *S. aureus* was recovered in cooked samples at Time 0, and after cooking at 1 hour and 24 hours in MRSA and MSSA preparations. *S. aureus* was also recovered in samples that had been cooked at T0 and washed at 1 hour in the MRSA preparation. Significance assessed by paired t-test *P<0.05, **P<0.01, ***P<0.001

Collection of Samples of Used Cookers and Filters from PWID

- PWID donated used cookers/filters after use of Hydromorphone controlled release at a local needle/syringe exchange clinic.
- A 5\$ coffee card was provided as reimbursement.
- A “wash” with sterile water using the used equipment was performed (simulating PWID routine use) and cultured on Mannitol salt agar.
- *S. aureus* was detected in 20/87 (23%, 95%CI 15-33%) cookers. 7 were MRSA, 11 were MSSA, 2 were Borderline Oxacillin Resistant (BORSA)

Conclusions

- Preparation of HCR for injection requires a significant amount of manipulation and increases risk for contamination
- ~1/4 of solutions for injection prepared with cookers previously used to inject HCR are contaminated with *S. aureus*
- In vitro HCR delays the death of the *S. aureus* so that it may persist longer on IDPE, HIR and OCR do not do this
- “Cooking” (heating with cigarette lighter for <10 sec) HCR during preparation reduced the number of *S. aureus* on the equipment by 99%. It was most efficacious if done shortly after contamination.
- In June 2017, a “Cook Your Wash” campaign was launched in London to encourage PWID to “cook” their HCR before each injection. The goal is to reduce the local incidence of IE and HIV/HCV in the community.
- Studies to assess the efficacy of the campaign are ongoing.

References

1. Rodger L et al. Clinical Characteristics and Factors Associated with Mortality in First Episode Infective Endocarditis Among Persons Who Inject Drugs. ID Week 2018. Poster #1024

Support

This work is funded by the Iain Mackie Foundation Grant from St. Joseph's Health Care in London, Ontario.

This work is also made possible by the continued support of the London Regional HIV/AIDS Connection who run the used IDPE collection program.