Comparative analysis of the change in the microbiome of diabetic foot ulcers in response to novel therapies

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**Introduction**

Diabetic foot ulcers (DFUs) are a common secondary complication of diabetes. DFUs occur in 15-25% of Diabetic patients of which 40-80% will become infected. Infected DFUs can lead to osteomyelitis, sepsis and gangrene of which amputation is the only possible treatment. Infection of a DFU is typically polymicrobial in nature and primarily features gram positive organisms such as Staphylococci, Group B Streptococci, Anaerococci, Peptoniphilus and Enterococci. Recent research however suggests a evolution in DFU environment in which future DFUs will present with a heavier presence of Gram negative species. This diverse microbiome, coupled with organisms capacity for biofilm production within the wound makes antimicrobial options such as antibiotics unsuitable. Novel treatments such as phages and new irrigant compounds are being investigated as alternatives therapies, such as electrolysed water (Hypochlorous acid).

It is unclear what role the DFU microbiome plays in the chronicity of the wound. Many studies have produced contradictory results showing evidence supporting or disproving microbiome involvement . In addition it is unclear how the DFU microbiome changes during therapies. Further research into these areas may assist in the future treatment of DFUs and improve patient outcomes.

**Aims and Methods**

- Using 16S rRNA sequencing and Qiime 2.0, identify the organisms present in infected DFUs and non diabetic feet and observe the changes that occur within the microbiome of these locations during treatment strategies.
- Compare the efficacy of a novel treatment (Electrolysed water) against a currently used irrigant (Prontosan/PHMB) on common DFU colonisers.

**Average microbial composition of different foot microbiomes**

**Comparison of the efficacy of two irrigants, Electrolysed water (E.W) and PHMB (P) on the biofilm viability of various Staphylococcus aureus strains.**

**Comparison of average alpha diversity indices (Shannon, Simpson and Richness index) of different foot microbiomes**

**Figure A** - The average DFA microbial composition from 7 patients over 4 weeks on 2 different therapies (E.W: N= 3, PHMB – N= 5) and average composition of non diabetic foot microbiome

**Figure B** - The change in the average DFA microbial diversity (Shannon index) and dominance (Simpson index) and genera richness induced by either E.W or PHMB over the 4 weeks of treatment.

**Conclusions**

- Neither the PHMB or Electrolysed water (E.W) therapies have any significant impact on the diversity (Shannon index), dominance (Simpson index) or richness of bacterial genera over 4 weeks of treatment, however both irrigants produced increases in Corynebacterium (a ‘normal’ foot commensal) and reductions in Pseudomonas, Proteus, Streptococcus and Anaerococcus (skin pathogens).
- Against a non diabetic control foot microbiome, there was significant differences in richness for all variables tested and for E.Water in Shannon index.
- Both Prontosan and E.W were equally effective at reducing the biofilm integrity of most the S.aureus strains tested, with exception to Clin-2 where E.Water produced a significantly greater reduction than the PHMB irrigant.