Can frequent replacement of showerheads reduce the frequency of *Pseudomonas aeruginosa (PA)* infections in cystic fibrosis (CF) patients? – Research Proposal

Seb Gray, Paediatric Trainee Contact details: sebastiangray@hotmail.com; @SebJGray

Background

Cystic fibrosis (CF) affects 100,000 globally with approximately 8,000 patients in the UK alone. It is caused by a defect in the CF transmembrane regulator (CFTR) gene located on the long arm of chromosome 7. The net result of a dysfunctional (or absent) CFTR is impaired muco-ciliary clearance leading to chronic lung infection and inflammation resulting in irreversible bronchiectasis and reduced life expectancy.

PA is the infecting organism most implicated in this process. It is a low virulence bacteria with various strains associated with accelerated lung function decline in CF. It may be acquired from the environment or from person-to-person contact. Segregation of CF inpatients and careful planning of outpatient reviews to avoid mixing has reduced transmission of infective strains and is now incorporated into CF management guidelines. However, there has been minimal work looking at both initial transmission from the environment and potential repeat environmental infection.

Environmentally, PA is widely present on plants, soil, wet surfaces and in water. In large pools of water concentrations are low ranging from 10 to >1,000 colony forming units (CFUs) per 100ml. The concentration in drinking water increases up to 230,000CFUs/ml but with a low risk of colonisation. Dose response studies established that even with doses large enough to cause colonisation, subjects remained asymptomatic. In contrast, mice studies showed aerosol inhalation doses of 10^7 CFUs induced symptoms and 10^9 CFU doses caused death.

Despite standardised disinfectant and pH regimes, PA was identified by PCR from 59% of swimming pools in Atlanta, USA. An Irish study found PA in 73% of Jacuzzis and spas. Both pools and spas have been implicated as sources for various PA infections including folliculitis, urinary tract infections, otitis externa, mastitis as well as pneumonia. With PA seemingly hydrophilic, and showers providing the warmth optimal for bacterial growth, it leads on that shower heads could potentially harbour PA.

Various studies have looked at showers as a source of PA both in the home and clinical environment. In Belgium, a study looked at matching first infective PA genotypes to isolates from the home environment. PA was isolated from the home environment in 18 of the 50 patient sample size with 72% of these isolated from the bathroom. A German study by Regnath et al detected PA in 71.6% of CF households with the drains of showers the most common site (39.6%). This is higher than the detection rate in an ICU setting in Tehran which isolated PA in 11.4% of samples from showers, baths or taps. However, in a less intensive ward-based setting, Ferroni et al found PA in 23% of shower samples following washing of hospitalised CF children.

There have also been reports of outbreaks of multi-drug resistance PA from 2 English hospitals. Waste water systems were found to be the only environmental source. One postulated cause was “faulty sink, shower and toilet design” and reducing the flow rate of the shower combined with various other interventions, was found collectively to reduce transmission. Following another outbreak of PA infection in a PICU, the source was linked back to humanitarian workers staying at a non-governmental organisational residential setting. Shower heads were not sampled in this study but PA was isolated from 70% of the sink and shower drains. Another American study quantified the potentially pathogenic bacteria in shower water and aerosol at a stem cell unit. Shower water was found to have 2.2 x 10^7 bacterial cells/ litre & shower aerosol 3.4 x 10^4 cells/m^3. PA was identified via quantitative PCR, gene sequencing and culture in 99.3%. The presence of PA within the shower drains invokes the ‘chicken and egg’ argument where it is unclear whether the PA in the drain came from the patient or vice versa. The shower head was therefore chosen as the focus of this study as it comes before the patient in the flow of water.

Ulrich et al in Germany looked at the understanding of both medical professionals and parents of children with CF of risk factors associated with PA infection. 51% of CF physicians recommended that the child should not be the first to use the bathroom in the morning and 9% advised not using public showers. Parents appeared to place more onus on these hygienic measures with 75% and 25% respectively viewing these as measures to prevent PA infection.

PA is characteristically able to produce biofilms whereby cells adhere to each other and embed themselves with a matrix of extracellular polymeric substance (EPS). Bacteria within a biofilm can develop increased antibiotic resistance due to the protective role of the dense outer layer of the EPS. In some cases this has been reported to increase resistance a thousand fold. One of the key factors in disease progression with CF is the evolution of PA into a mucoid phenotype. Mucoid strains overproduce the exopolysaccharide, alginate which stabilises the biofilm. It has been postulated due to the scarcity of environmental strains, that there are specific features of the CF lung that promote this phenotypic adaptation. It does seem plausible that whilst existing within an environmental biofilm prior to CF lung infection, the initial stages of this process could have been triggered. Oxidative stress has been identified as an initiator of increased conversion to the mucoid strain. Other stressor such as the shear stress from flowing water could potentially have similar effects.

Hypothesis

Regular changing of shower heads reduces the frequency of PA infections in CF

Aims

Primary outcome: incidence of *PA* on cough swabs obtained at 4, 8 & 12 months.
Secondary outcomes:

- The incidence of any other positive microbiological growth from the cough swabs at 4, 8 & 12 months.
- Spirometry (FEV_1 and FVC) at 0 (baseline), 4, 8 & 12 months.

Protocol

Inclusion Criteria:
All CF patients who use a shower head as their primary washing method & able to provide cough swabs/ sputum & perform spirometry.

Exclusion Criteria:

- Patients who cannot accurately perform spirometry or provide cough swabs/ sputum either due to age or co-morbidities.
- Patients who require continuous oxygen or who are awaiting lung transplant.
- Patients who do not use a shower-head as their primary washing method.
- Participation in other CF-related research studies.
- Specialist showers not compatible with replacement with standard shower-heads.

Study Design:
Randomised controlled trial running over 2 years from a large tertiary CF centre (patients recruited & randomised at annual review).
Intervention arm: will have their shower heads replaced by the study clinician on a 2-monthly basis for 12 months. All shower heads will be cultured for the presence of PA (2-monthly in intervention arm and end of 12 months in control arm). Standard CF management would continue in both arms and any infections or positive microbiology results would be managed as per standard CF guidelines.
Baseline spirometry and previous microbiology results would be recorded at randomisation. To address potential confounders, baseline swabs would be taken and cultured from the toilet basin, toilet seat, wash basin (drain and tap) and shower drain. Cough swabs and lung function testing would then be performed at 4, 8 and 12 months. Those performing the lung function testing and analysing the cough swabs would be blinded.
Demographics and baseline details would be statistically analysed (chi-square) to ensure homogeneity. For results analysis, patients would be stratified into those with or without previous PA microbiological growth (at point of randomisation). The incidence of positive microbiology would then be compared between the 2 groups and statistically analysed using the Student’s t test with a p value of <0.05 considered significant. Spirometry (FEV_1 and FVC) would be expressed as a percentage of the baseline lung function and analysed in the same way.

Potential Implications

The antibiotic policies in CF walk a tight-rope between killing bacteria and breeding resistant strains. To prove such a simple intervention reduces the infection rate of PA in CF patients would be ground-breaking for the CF community. A reduced infection rate could reduce inflammation, remodelling and eventual bronchiectasis. This in turn would prevent the decline in lung function and delay the need for transplant. With showerheads available cheaper than a course of ciprofloxacin, a modest reduction in infections would make this economically attractive.

The lack of new antibiotic development and increasingly resistant bacterial strains suggests focus should be targeted at preventing both primary and recurrent infection. CF research is currently focused on cutting edge genetics and work at the molecular level. This obviously needs to continue, but pending breakthrough advances more work should focus on antibiotic-sparing measures such as that described in this study.

Full reference list available on request