Background: The use of 7% hypertonic saline (7%HS) has proven useful as a mechanism of airway clearance in individuals with CF. A number of studies have demonstrated improved lung function, accelerated mucus clearance, fewer pulmonary exacerbations and a higher percentage of patients without exacerbations. The majority of currently available 7%HS solutions follow USP guidelines and have a pH between 4.5 and 7.0. The average is pH 6.2, although there can be variability between each batch produced by an individual company. A recently released 7%HS solution is pH controlled with a pH of 7.4, which is within the NIH range for physiologic pH in the human lung (pH 7.38 to 7.42), although not within USP guidelines.

Hypothesis: Based on data in the literature reporting that CF airway surface liquid is acidic, which may contribute to the poor clearance of P. aeruginosa, we hypothesized that addition of a 7%HS solution that was physiologic pH would decrease P. aeruginosa density over time more than acidic 7%HS solutions.

Methods: We tested this hypothesis by performing 24-hour killing curves in sterilized CF sputum that was “spiked” with P. aeruginosa and diluted 10% wt/vol in commercial saline products of differing pH. We used three different 7%HS products: sterilized CF sputum that was “spiked” with P. aeruginosa, and diluted 10% wt/vol in each of 3 tubes:
- 7% Generic saline solution (Nephron Pharma NDC: 0487-0307-60)
- 7% Hyper-Sal (PARI NDC: 83490-0307-60)
- 7% PulmoSal pH+ (PharmaCaribe NDC: 50190-0307-60)

Results: In the laboratory strain, PA01, the data show approximately 5 log decrease in bacterial density in the pH 7.4 solution compared with approximately 2 log decrease in the pH 5.86 and pH 6.6 solutions at 24 hours. The density difference between solutions is even more dramatic at 8 and 12 hours. Additional experiments with CF patient isolates demonstrated no difference in bacterial density over 24 hours with an initial colonizing isolate, but similar differences as PA01 with a late mucoid isolate from the same patient.

Conclusions: Given the dosing frequency of 7%HS in CF these findings suggest the use of physiologic pH solution could have a marked impact on bacterial density. A clinical trial designed to determine the microbiological and clinical impact of a pH+ hypertonic saline solution may be warranted.

Supported by PharmaCaribe LLC, Punta Gorda, FL, W. Randolph Warner, Werner Gutmann Scientific Advisory: Preston Campbell, Daniel Klein, CF Foundation, Bethesda, MD, Clinical isolates provided by Seattle Children’s Research Institute Center for Global Infectious Disease Research, CF Isolate Core (NIH P30 DK089507)

Conclusions

P. aeruginosa viability in 7% hypertonic saline appears to vary with pH of the solution and with characteristics of the organism:
- PA01 (original source non-CF, chronic infection):
  - ~5 log decrease at pH 4.4, ~1.5 log decrease in pH 5.68 and ~2 log decrease in pH 6.6
  - Early and late isogenic patient isolates showed disparate results:
    - Early: ~0.5 log decrease in all pH tested
    - Late: ~3 log decrease pH 7.4, ~1.5 log decrease pH 5.68 and pH 6.6

Given dosing frequency of 7% hypertonic saline these findings suggest the use of physiologic pH could have a marked impact on bacterial density.
- A clinical trial designed to determine the microbiological and clinical impact of a pH 7.4 hypertonic saline solution may be warranted.