Development of a Direct Peritoneal Sodium Removal Technique with Salt Free Solution

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Background

- Retention of sodium and fluid drives volume overload and congestion in heart failure (HF)
- Current therapies to relieve volume overload primarily rely on antagonism of renal sodium transporters but cardio-renal limitations pose an obstacle to maintaining compensation of HF via renal routes
- The concept of sodium and fluid removal via non-renal routes in heart failure (HF) has gained interest, with use of the peritoneal membrane representing one such method
- Commercially available peritoneal dialysis solutions are optimized for dialysis rather than fluid and sodium removal

Hypothesis

- Utilization of zero sodium peritoneal salt removal solution will result in removal of a clinically significant amount of sodium and fluid

Methods

- N = 20 endotracheally intubated anesthetized pigs underwent surgical implantation of peritoneal dialysis catheters via mini-laparotomy and direct sodium removal with 10% dextrose in water (D10)
- In 5 pigs, a 6 hour dwell time with zero sodium 1L D10 solution was administered to determine the kinetics of sodium and fluid removal over time
- 10 pigs underwent a 2 hour dwell with 1L D10 solution
- In order to test the extreme of titratability of this approach, 4 of the above pigs then underwent four 90 minute cycles of 2.5L of D10 solution. In these pigs, plasma volume was measured directly with I-131 radiolabeled albumin (Daxor Corp., New York, NY) prior to and after cycling
- In 5 pigs, an acute congestive HF model was created by inducing cardiac tamponade. Elevated central venous pressure (CVP) was attained and maintained with pressurization of the pericardium and IV fluid administration (goal CVP 20-22.5 mmHg). After a stable HF model was created, these pigs underwent a 2 hour dwell with 1L D10 solution

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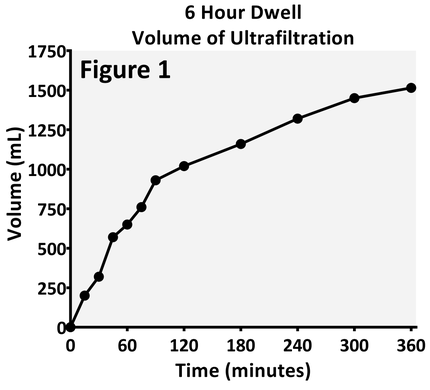
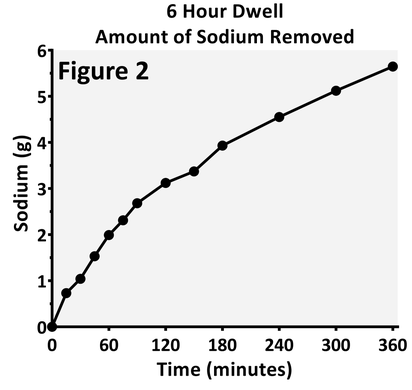
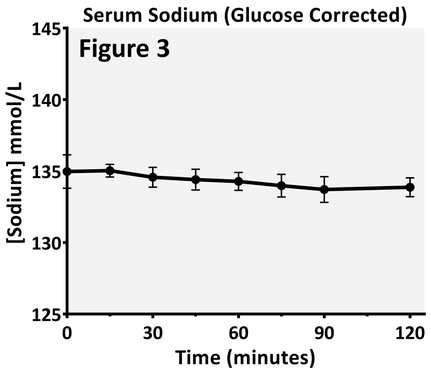
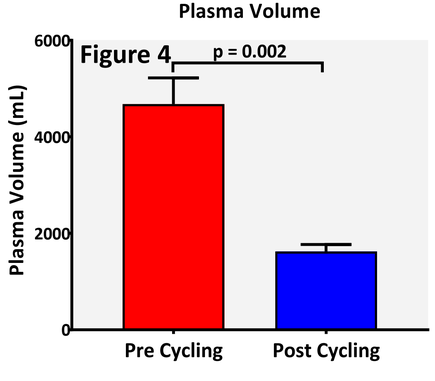
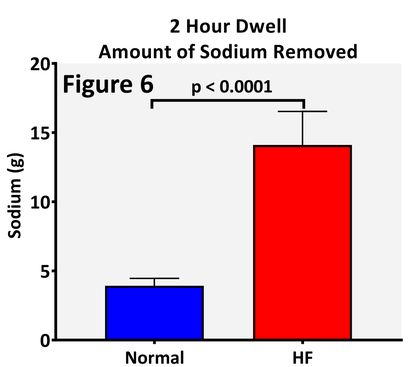
Results

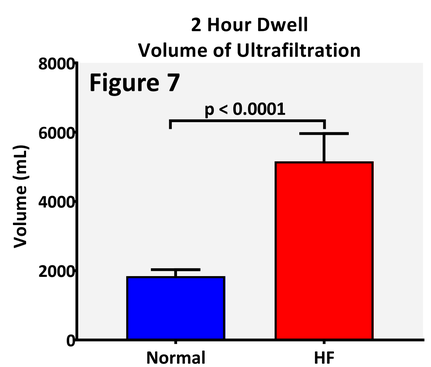




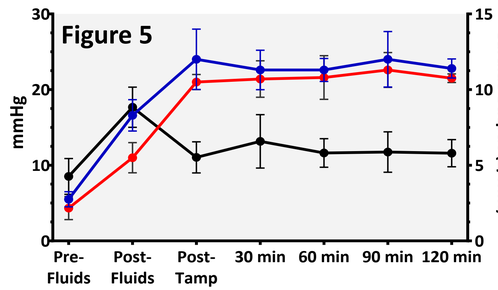








- Fluid **(Figure 1)** and sodium **(Figure 2)** removal was substantial and sustained throughout the entire 6 hour dwell, but with a larger proportion in the first 2 hours
- Due to sustained ultrafiltration and sodium diffusion down a large concentration gradient (zero in the D10 and ~135 mmol/L in plasma), the net ultrafiltrate had similar sodium content as plasma resulting in a stable serum sodium concentration (**Figure 3**)
- In the pigs that underwent 10L of D10 cycling, plasma volume exhibited a dramatic decrease from baseline to completion of cycling **(Figure 4)**, with a net sodium removal of 19.4 +/- 3.6 grams
- The pericardial tamponade HF model recapitulated a warm and wet phenotype typical of human decompensated HF with stable cardiac output and increased CVP (**Figure 5**) throughout the experiment
- In the setting of elevated filling pressures in the HF model, sodium removal (**Figure 6**) and the volume of ultrafiltration (**Figure 7**) was dramatically increased as compared to normal pigs



Hemodynamics during experimental HF at baseline (pre-fluids), after fluid loading (post-fluids), after induction of cardiac tamponade (post-tamp) and during the 2 hour dwell

Conclusion

- The direct peritoneal sodium removal approach is capable of removing large quantities of fluid and sodium with a relatively small volume of peritoneal infusate
- Additional research is required to understand the safety/tolerability of this approach in humans and for development of optimal solutions and protocols for fluid instillation and removal from the peritoneum