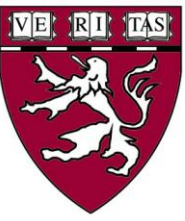




Feasibility study of the RenalGuard™ balanced hydration system: a novel strategy for prevention of contrast induced nephropathy in high risk patients



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ABSTRACT

Background: Contrast-induced nephropathy (CIN) is a common and significant complication following angiographic procedures. Multiple preventive approaches have been studied but have shown no definite benefits. The RenalGuard™ automated hydration matching system was developed in order to achieve a precise, real-time fluid balance using a closed loop hydration monitoring and infusion system. **Methods:** This prospective, non-randomized, multi-center feasibility study was designed to evaluate the safety and the performance of the system. Between October 2006 and November 2007, twenty-three subjects at high risk for CIN (baseline impaired renal function with an estimated glomerular filtration rate < 50mL/min) undergoing diagnostic or therapeutic catheterization were treated with the system. **Results:** The primary efficacy endpoint of the study defined as the ability of the system to effectively match fluid ins and outs, showed a mean effectiveness rate of 99.9% over the length of therapy. Two subjects (8.5%) developed CIN as defined by >0.5mg/dl or >25% rise in serum creatinine at 48-60hrs post contrast administration when compared with the baseline. This was much lower than the 17.9% predicted risk of CIN in this population according to the literature. There were no other complications for any patient during the study. **Conclusion:** The study confirmed that the RenalGuard™ system as a strong potential for preventing CIN in a high-risk population.

DISCLOSURES: The study was supported by PLC Medical Systems Inc., makers of RenalGuard™

Background:

- Contrast-induced nephropathy (CIN) is a common complication following diagnostic and interventional angiographic procedures with an incidence between 3.3-18.9%
- Multiple preventive approaches have been evaluated but few have been prospectively validated
- The cornerstones of prevention remain limiting contrast and pre-procedure hydration
- The PRINCE study demonstrated that no pre-contrast patient with a mean urine flow rate above 150 mL/hr developed acute renal failure with the need for dialysis
- The RenalGuard™ system was developed for precise, real-time automated fluid matching by continuously measuring urine excretion, replacing it with infused fluid, milliliter for milliliter
- We sought to evaluate the safety and the performance of the RenalGuard™ system in patients at high risk for CIN undergoing diagnostic or therapeutic catheterization

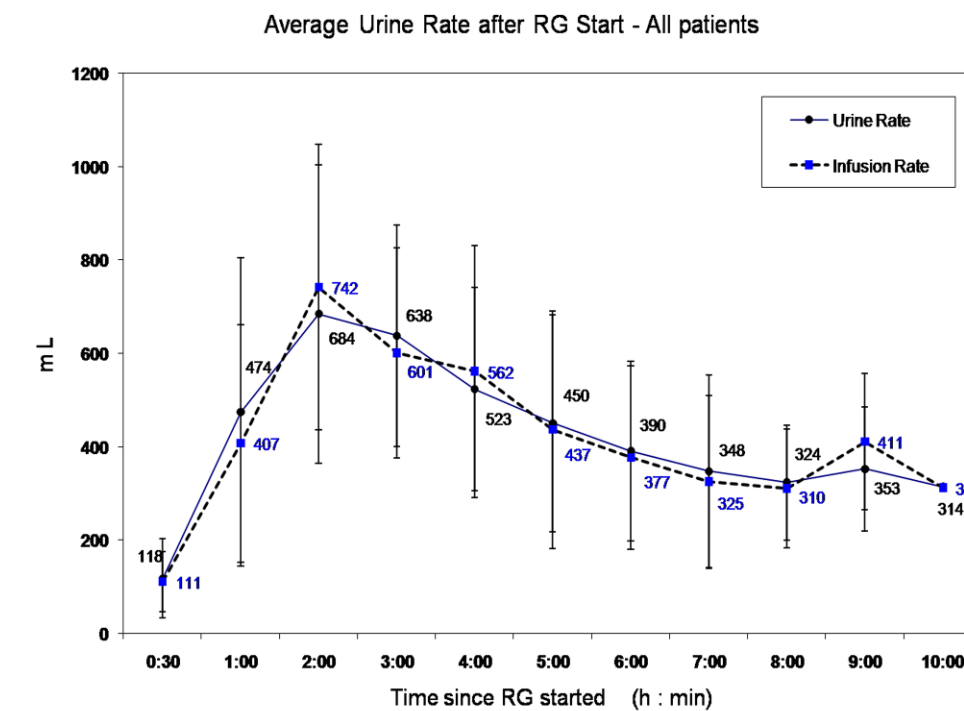
Methods:

- 23 subjects were recruited between October 13th, 2006 and November 22nd 2007
- All patients completed RenalGuard™ Therapy along with their previously scheduled catheterization procedure and were followed for the duration of the study (72 hours)
- Within a minimum one hour prior to the first dose of contrast a 250ml bolus of 0.9% normal saline and a 0.5mg/kg bolus of furosemide were given intravenously
- Additional doses of furosemide could be given if, during and/or up to 3 hours after the catheterization, the urine output fell below 300mL/h (max dose of 2.0 mg/kg)
- RenalGuard therapy continued throughout the procedure, and for 4 hours after the last dose of contrast; fluid replacement was performed with 0.9% sterile normal saline
- Efficacy endpoints:**
 - The ability of the system to effectively match volume infusion and urine production
 - The percentage of patients who developed CIN, defined as a >0.5 mg/dl or >25% rise in serum creatinine at 48-60h post contrast administration
 - The percentage of patients that reached the target urine output of 300 mL/hr or greater over at least 2 hours of treatment
- Safety endpoints:**
 - The proportion of patients experiencing symptomatic hypotension (sBP<90 mmHg)
 - The need for renal replacement therapy, symptomatic pulmonary edema, clinically significant arrhythmias, frequency of significant electrolyte abnormalities, infection

1. Baseline characteristics

Variable	Percentage (n)
Gender - Percent Male	65% (15/23)
History of Diabetes	35% (8/23)
History of Heart Failure	13% (3/23)
History of Renal Insufficiency	91% (21/23)
GFR < 30	3 subjects eGFR<30, 11 subjects eGFR <40
Variable	Value ± STD (range)
Age(years)	78 ± 6 (68 - 87yrs)
Serum Creatinine (mg/dl)	1.80 ± 0.67 (1.2 - 4.1)
Screening eGFR(MDRD)	39.1 ± 9.3 (15.5 - 49.9)
Type of Procedure	
Left heart cath without stent	5 (22%)
Left heart cath with stent(s)	4 (17%)
Left and right heart cath without stent	7 (30%)
Left and right heart cath with stent(s)	4 (17%)
Peripheral diagnostic procedure	3 (13%)

2. Urine flow rate with corresponding infusion rate over time



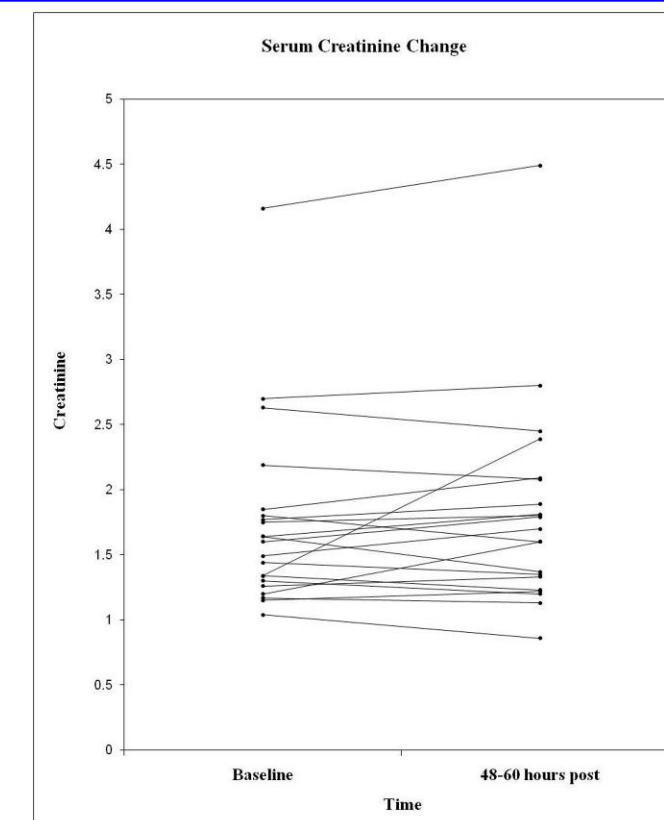
3. Procedural factors

Total contrast (ml) Mean ± STD Range	176 ± 105ml (35 - 470m1)
Duration of Procedure (hrs) Mean ± STD Range	1.04 ± 0.58hr (0.2 - 2.3hr)
Duration of RenalGuard Therapy Mean ± STD Range	7.58 ± 1.85hr (5.07- 10.12hr)
Hourly urine rate at time of first dose of contrast (ml/hr) Mean ± STD Range	620 ± 400ml/hr (136 - 1984m1/hr)

4. Efficacy of the RenalGuard system

RenalGuard System Fluid Matching Pre-Cath through Post Cath (n=23)	
Total Fluid Infused (includes 250 ml bolus)	3825 ml (3264 - 4385)
Total Urine Output	3579 ml (3022 - 4136)
Total Fluid Gain (250ml bolus)	246 ml (190 - 301)
Percent Fluid Matched	99.9% (98.8 - 101.1)

5. Serum creatinine at baseline and follow-up for all patients



6. Secondary efficacy endpoint data

	Number of Events (%)	95% Confidence Interval
Develop CIN*		
Yes	2 (8.7%)	1.2 - 30.4
No	19 (82.6%)	
Unknown	2 (8.7%)	
Creatinine - Baseline compared to 48 - 60 hr (mg/dL)		0.1- 23.8
≤0.25 rise	18 (78.3%)	
>0.25 and ≤0.50 rise	2 (8.7%)	
>0.50 rise	1 (4.3%)	
Unknown	2 (8.7%)	
Creatinine - Baseline compared to 48 - 60 hr (%)		1.2 - 30.4
≤ 12.25% rise	17 (73.9%)	
>12.25% and ≤25.0% rise	2 (8.7%)	
>25.0% rise	2 (8.7%)	
Unknown	2 (8.7%)	
Met Target Urine Output		72.0 - 98.9
Did not meet Target Urine Output	2 (8.7%)	

* defined as a >0.5 mg/dl or >25% rise in serum creatinine at 48 - 60 hours post contrast administration

Results:

- The 23 subjects at high risk for CIN enrolled had a mean±SD eGFR of 39±9.3
- The patients achieved an hourly urine flow rate of 620±400 ml/hr
- The system showed that it had a mean effectiveness rate of 99.9% over the duration of therapy with an average saline volume infused of 3825ml closely matched, minute to minute, to urine output of 3579ml
- Two subjects (8.5%) developed CIN as defined by >0.5mg/dL or >25% rise in serum creatinine at 48-60hrs post contrast administration when compared with the baseline
- The predicted risk of CIN in this population was 17.9%
- There were no device related complications in any patient during the study

Conclusions:

- The study confirmed that the RenalGuard™ system is safe and effectively balances aggressive volume hydration with urine production with an incidence of CIN 50% less than predicted for such a population
- Further randomized studies are needed to confirm the efficacy of the system in reducing the incidence of CIN

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