Urea in the Treatment of Hyponatremia: The First Reported US Inpatient Experience

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Background

- Hyponatremia is associated with increased morbidity, mortality, and health resource utilization.
- Most therapies for hyponatremia have not been systematically studied, while vasopressin antagonists have safety risks and cost limitations.
- Small European studies suggest urea is safe and effective.
- A commercial formulation of urea for hyponatremia has recently become available in the US.

Objectives

- To report the first US experience with the use of a novel formulation of oral urea for the treatment of hyponatremia and describe its efficacy, safety and tolerability in the inpatient setting.

Materials & Methods

- All patients hospitalized between July 2016 and August 2017 with the diagnosis of hyponatremia [plasma sodium concentration (PNa) < 135 meq/L] treated with ≥ 1 doses of new formulation of oral urea were identified.
- Patients who received urea as the sole drug therapy for hyponatremia were also identified within the above group (cases).
- Hyponatremic patients admitted the year prior who did not receive urea (controls) were also identified.
- Cases and controls were matched 1:1 on sex, etiology and degree of hyponatremia.

Materials & Methods

- Wilcoxon signed-rank test was used to analyze PNa changes at 24h and at the end of therapy in entire cohort, within cases, and between cases and controls.
- McNemar's test was used to compare the achievement of normal PNa between cases and controls.
- A discrete proportional hazard model was used to compare length of hospital stay (LOS) between cases and controls.
- All patient-reported adverse events associated with urea use were recorded.

Results: Changes in PNa with Urea

- A total of 58 patients received urea for hyponatremia. 14 were 'urea-only' cases.
- Median age was 67.5 yrs [IQR 55-79] and 35 (60%) were males.
- SIADH was the most common cause of hyponatremia (81%) in cases.
- Patients received urea 7.5-90 g/day for a median duration of 4.5 [IQR 3-7] days.
- Urea therapy was associated with an increase in median PNa from 124 meq/L [IQR 122-126] to 130.5 meq/L [IQR 127-133] meq/L, p<0.001.
- Table 1 and figure 1 show changes in PNa and other laboratory parameters in cases.

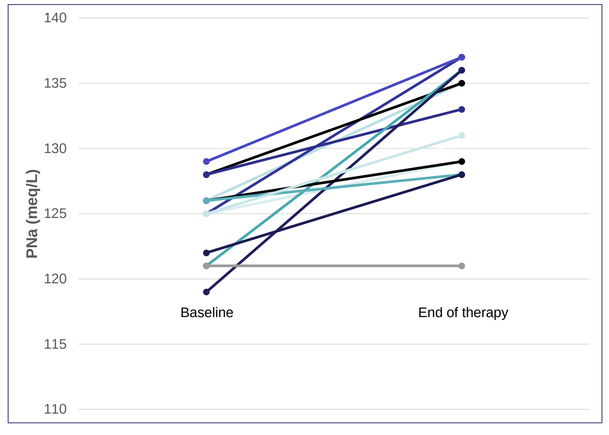
Table 1. Laboratory parameters before and at the end of therapy in cases

Plasma Na (meq/L)		BUN (mg/dl)		Urine Osm (mOsm/kg)		Urine Na (meq/L)	
Baseline	**End**	**Baseline**	**End**	**Baseline**	**End**	**Baseline**	**End**
125 [IQR 121-126]	132 [IQR 129-136]	16.5 [IQR 10-19]	41.5 [IQR 26-48]	431 [IQR 319-561]	574 [IQR 542-639]	66 [IQR 38-94]	43.5 [IQR 10-76]
	p<0.001		p<0.001		p=0.06		P=0.03

Results: Cases vs. Controls

- There was a trend towards a larger median ΔPNa at 24h in cases compared to controls: 2.5 meq/L [IQR 0-5] vs. 0.5 meq/L [IQR -2-3] respectively, p=0.10.
- There was no difference in median ΔPNa at the end of therapy in cases compared to controls: 6.5 meq/L [IQR 4-12] vs. 6.5 meq/L [IQR 3-8] respectively, p=0.22.
- A greater proportion of cases achieved a normal PNa compared to controls (43% vs. 7% respectively, p=0.03).
- There was no difference in LOS between cases and controls: 6 days [IQR 4-7] vs. 6 days [IQR 4-6] respectively, p=0.76.

Figure 1. Changes in PNa among cases



Results: Safety of Urea

- Overcorrection of PNa was not observed in the entire cohort of patients.
- No adverse events associated with the use of urea were observed.
- One patient discontinued urea due to poor palatability.

Limitations

- Retrospective nature
- Small sample size
- Relatively short duration of urea therapy

Conclusions

- A novel formulation of oral urea is well tolerated, safe, and effective for the treatment of inpatient hyponatremia.
- Randomized control trials comparing the effects of urea to other therapies on patient-centered clinical and economical outcomes are needed.

References

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