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Evaluation of Therapies for Treatment of Hyponatremia

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OBJECTIVE

- Characterize the use and assess the efficacy of tolvaptan and urea in the treatment of patients who were admitted to the hospital with chronic hyponatremia.

BACKGROUND

- Hyponatremia is one of the most common electrolyte disorders, occurring in 15-30% of patients who are hospitalized.[1] Severe hyponatremia may result in headaches, altered mental status, seizure, and coma.[2]
- Chronic hyponatremia is hyponatremia lasting longer than 48 hours.[2]
- Treatment strategies for hyponatremia include fluid restriction, hypertonic saline infusion, sodium tablets, vasopressin receptor antagonists, and urea.[2]
- In chronic hyponatremia, the maximum correction rate of serum sodium is 8 to 10 mEq/L within the first 24 hours of treatment to reduce the risk of developing osmotic demyelination of cells.[1,3]
- In severe symptomatic hyponatremia, recommendations allow for up to 12 mEq/L correction within the first 24 hours and a total of 18 mEq/L within the first 48 hours.[3]
- Syndrome of inappropriate anti-diuretic hormone (SIADH), is a common cause of chronic hyponatremia.[4]
- Common medication classes may contribute to hyponatremia; these include selective serotonin receptor inhibitors (SSRIs), serotonin-norepinephrine receptor inhibitors (SNRIs), and anticonvulsants.

METHODS

- Retrospective analysis conducted within 2 community hospitals
- This analysis was approved by the Institutional Review Board.
- Inclusion criteria:
  - Admission between January 1, 2020 through December 31, 2021
  - Patients aged 18 or older and having received at least one dose of tolvaptan and/or urea during admission
- Hyponatremia severity was classified via serum sodium levels measured within 24 hours prior to initiation of tolvaptan or urea[5]
  - Mild: serum sodium 130 to 134 mEq/L
  - Moderate: serum sodium 120 to 129 mEq/L
  - Severe: serum sodium less than 120 mEq/L
- Baseline labs were collected to assess liver function
  - Liver dysfunction was defined as aspartate aminotransferase (AST), alanine transaminase (ALT), or total bilirubin more than three times the upper limit of normal
- Patients were analyzed based on subjective and objective diagnosis of SIADH, and prior to admission (PTA) prescriptions were reviewed for any potential contributing medications
- Sodium change was defined as the difference from baseline serum level, and measured serum level 24 +/- 4 hours after first dose of either tolvaptan or urea.

RESULTS

Table 1 – Subject demographics

	Tolvaptan N=68	Urea N=225	Both N=21	Total N=314
Male	39	98	8	145
Average Age (years)	69	70	69.1	69.7
Liver Dysfunction at Baseline	8	21	1	30
Hyponatremia Status				
Mild Hyponatremia	1	31	1	33
Moderate Hyponatremia	48	150	15	213
Severe Hyponatremia	18	34	5	57
No Hyponatremia	1	10	0	11
Received Prior Treatments				
Normal Saline	29	90	10	129
Fluid Restriction	16	53	8	77
Sodium Tablets	33	92	9	134
Hypertonic Saline	18	30	3	51
Loop Diuretics	36	81	9	126
PTA Hyponatremia Treatment				
Urea	0	13	1	14
Salt Tablets	2	21	4	27

Figure 1 – Contributory PTA medications (N=314)

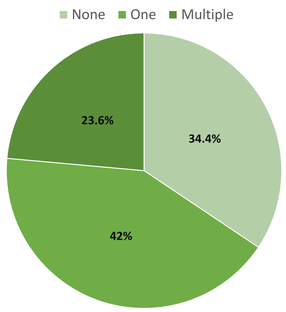

Figure 2 – Change in serum sodium based on treatment

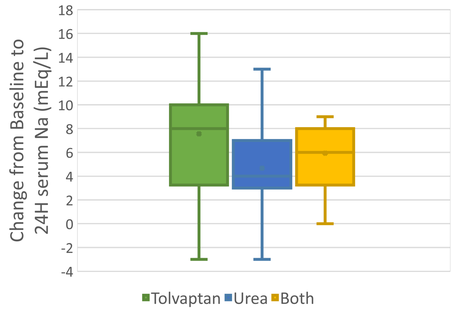

Table 2 – Change in 24-hour serum sodium with corrective measures

	Tolvaptan N=68	Urea N=225	Both N=21	Total N=314
Change in Baseline Serum Sodium Levels (mEq/L)				
Less than 0	6	18	4	28
1 to 5	11	71	3	85
6 to 10	20	38	8	66
11+	11	8	1	20
Unable To Calculate (UTC)	20	90	5	115
Received dextrose 5% in water	13	17	5	35
Received desmopressin	1	1	0	2
Received dextrose 5% in water and desmopressin	4	6	0	10

RESULTS

- Out of the 314 unique encounters, 68 patients received tolvaptan, 225 patients received urea, and 21 received both during their admission.
- Objectively, 178 patients were found to qualify for SIADH diagnosis, but only 123 were subjectively diagnosed via provider notes and diagnosis codes.
- Patients receiving tolvaptan were more likely to have increases in serum sodium by greater than 10 mEq/L in the first 24 hours (16.2%) as compared to urea (3.5%).
- Average duration of therapy varied between treatment groups at 1.7 days and 2.6 days for tolvaptan and urea, respectively.

Table 3 – Average 24-hour change in serum sodium (mEq/L) based on severity

	Tolvaptan	Urea	Both
Mild Hyponatremia	UTC	0.7	-1
Moderate Hyponatremia	7.4	3.7	4.3
Severe Hyponatremia	7.9	7.5	7.25

DISCUSSION & CONCLUSIONS

- Within the first 24 hours following administration, urea and tolvaptan were both satisfactory in improving serum sodium levels.
- A majority of patients were taking medicines that may contribute to hyponatremia; this is something that should always be assessed if a patient is presenting with hyponatremia.
- Only 14.9% patients who received tolvaptan, urea, or both medicines required corrective treatments due to a rapid serum sodium rise.
- Providers should exercise caution when using tolvaptan, as it was associated with a higher risk of rapid serum sodium correction.
- Limitations:
  - Many (36.6%) patients were not assessed, as they did not have follow-up labs drawn within the 24-hour post-initial administration window.
  - Patients may have received varying treatments in addition to those assessed, which may allow for differences in improvement of serum sodium levels.
- Based on rate of improvement in serum sodium levels, it would be appropriate to use either urea, tolvaptan, or both with additional corrective measures and close monitoring for patients with severe hyponatremia.

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Disclosure

The authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:
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