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Supplemental Material

Supplemental Table 1. Demographic, clinical, and laboratory characteristics and treatment of the entire study cohort.

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Supplemental Table 4. Daily change in plasma sodium in patients on varying doses of urea.

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Supplemental Table 1. Demographic, clinical, and laboratory characteristics and treatment of the entire study cohort.

Patient No	Age (yr.)	Sex	Admission weight (kg)	Clinical Characteristics of Hyponatremia		Baseline Laboratory Values					Treatment of Hyponatremia			End of Therapy Laboratory Values		
				Etiology	Symptoms	Plasma sodium (mEq/L)	BUN (mg/dL)	Cr (mg/dL)	UOsm (mOsm/kg)	Urine sodium (mEq/L)	Urea dose (grams/day)	Urea duration (days)	Other therapies used	Plasma sodium (mEq/L)	BUN (mg/dL)	Cr (mg/dL)
1	51	M	97	SIADH	Unknown	125	4	0.5	618	277	30	9	FR, ST, LD, HS	136	19	0.6
2	63	M	50	SIADH	Absent	122	21	0.4	901	162	30	16	FR, ST, LD	130	20	0.4
3	32	M	89	AI	Mild to moderate	114	7	0.5	533	175	30	2	FR, GLU	126	24	1
4	55	M	93.6	HF	Mild to moderate	117	24	0.9	809	140	30-90	10	FR, LD, HS	133	56	0.7
5	27	F	59	HF	Absent	129	12	0.5	298	58	15-60	6	FR, LD, HS, KCL	131	18	0.5
6	68	M	76.95	HF	Absent	126	18	0.5	584	38	15	7	FR	131	20	0.7
7	74	F	64	SIADH	Absent	127	11	0.6	605	80	15	1	FR, ST	133	34	0.8
8	61	F	NA	SIADH	Unknown	125	25	0.8	305	77	30	5	FR	137	69	0.6
9	72	F	122	SIADH	Absent	119	8	0.8	351	42	15-30	7	FR	131	26	0.9
10	50	M	122	CIR	Absent	125	14	0.8	289	99	30	6	FR, ST, LD	120	59	1.1
11	59	M	89	SIADH	Absent	127	10	0.8	319	27	30	6	FR	135	26	0.7
12	82	M	76.2	SIADH	Absent	122	18	0.7	727	77	15-60	6	LD, NS	133	46	0.8
13	84	M	66	SIADH	Absent	126	10	0.7	400	140	15	2	FR, ST	126	17	0.7
14	76	M	61	SIADH	Absent	125	10	0.6	561	94	30	3	FR	129	44	1
15	72	M	107.2	SIADH	Absent	128	13	0.7	467	66	15-30	4	FR	133	45	1
16	37	M	131.5	SIADH	Absent	129	15	0.7	590	97	30	3	FR, LD	131	24	0.8
17	78	F	60	SIADH, TZ	Absent	121	16	0.7	550	29	30	3	FR	136	48	0.8
18	55	M	65	SIADH	Absent	123	5	0.4	382	167	30-60	11	FR, NS, KCL	136	52	0.6
19	31	F	64	SIADH	Absent	122	5	0.6	723	156	15	1	FR, ST	133	13	0.6
20	57	M	58	AI	Absent	124	6	0.8	432	165	30	10	FR, ST	127	40	0.9
21	85	M	71	SIADH	Absent	119	17	0.8	431	75	60	8	FR	136	60	0.9
22	55	F	64	HYP, KD	Absent	122	52	1.3	577	10	15	2	FR, NS	125	65	1.7
23	71	F	127	HF	Absent	122	24	0.8	263	92	60	3	LD	127	89	1.1
24	75	F	69.5	KD	Absent	122	50	4.2	249	29	15	4	FR, LD	129	83	3.9
25	67	M	72.9	SIADH	Mild	126	12	0.6	299	45	60	14	FR, ST	132	45	0.7
26	81	F	NA	SIADH	Absent	124	9	0.5	404	130.4	60	4	FR, KCL	131	36	0.5
27	66	M	93	HF	Absent	126	23	0.9	396	15	30	2	FR, LD	127	29	0.8
28	57	M	80.4	SIADH	Absent	121	5	0.6	365	146	15	2	NA	121	20	0.6
29	>89	M	NA	SIADH	Mild	122	13	0.7	462	69	30	4	FR, LD	124	28	0.8

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30	70	M	77.7	SIADH	Absent	126	15	1.1	NA	NA	30	6	FR	129	39	1.2
31	52	M	124.2	SIADH	Absent	125	13	0.6	450	47	45	7	FR, LD	135	28	0.5
32	46	F	71.9	SIADH	Absent	126	7	0.6	361	105	15	6	VRA	126	15	0.5
33	28	F	116.2	SIADH, TZ	Unknown	131	13	0.5	1087	85	15	1	ST	137	12	0.5
34	66	M	68	SIADH, HYP, KD	Absent	121	59	1.6	614	25	15	2	ST, HS	120	78	1.3
35	68	M	NA	SIADH	Absent	122	39	0.6	373	77	30	16	FR, ST, VRA	136	64	0.7
36	58	M	NA	SIADH	Absent	127	24	0.8	635	117	30	9	FR, LD, NS	131	54	0.9
37	79	M	NA	SIADH	Absent	126	17	0.9	573	130	30	3	FR	128	26	0.8
38	75	M	NA	SIADH	Absent	127	16	0.7	361	40	30	3	FR, ST, NS, VRA	129	20	0.6
39	77	F	73.3	SIADH, TZ	Mild	117	11	0.5	343	59	30	3	FR, ST	131	25	0.6
40	53	M	NA	SIADH, TZ	Absent	121	19	0.8	758	30	30	4	FR, ST	126	25	0.9
41	31	F	53.6	SIADH	Absent	129	10	0.3	350	124	15-30	14	ST, NS	136	19	0.3
42	55	M	100	SIADH	Absent	124	10	0.7	363	97	30	7	FR, VRA	133	20	0.8
43	63	M	90	SIADH	Absent	128	13	0.4	675	221	30	6	FR, ST	140	39	0.3
44	86	F	62	SIADH	Mild	124	17	0.5	348	56	45	6	FR, LD, VRA	134	70	0.5
45	65	M	113	SIADH, TZ, HYP	Absent	124	23	1	633	40	30	5	FR, ST, VRA	126	45	1
46	64	M	64	SIADH	Absent	127	8	0.7	309	124	30	2	FR, ST	127	8	0.7
47	79	M	122.9	SIADH	Absent	113	12	0.8	477	68	30	9	FR, LD, NS	130	28	0.9
48	80	F	79	SIADH, HYP	Mild to moderate	109	8	0.4	464	15	60	9	FR, ST	130	35	0.4
49	71	F	NA	SIADH	Absent	122	19	1.2	220	17	30	2	FR	128	45	1.2
50	66	M	95	SIADH	Moderate	125	20	0.9	562	105	30	4	FR	131	35	0.9
51	81	F	48	SIADH	Unknown	124	14	0.3	592	173	30	9	FR, ST, NS	136	18	0.3
52	64	F	40.2	SIADH	Absent	124	15	0.4	325	27	15-45	2	FR, ST, NS	128	34	0.4
53	>89	F	59	SIADH	Absent	124	14	0.8	450	89	30	2	FR, NS	135	61	1
54	88	F	80	SIADH, TZ, HYP, KD	Absent	126	29	0.9	378	13	15	3	FR, LD	130	40	1.1
55	86	F	63.5	SIADH, TZ	Absent	129	29	1.1	316	54	30	4	FR	137	73	1
56	70	F	NA	SIADH, HYP	Absent	128	36	0.8	424	11	15-30	7	FR, LD, NS	132	27	0.7
57	>89	M	51.8	SIADH	Absent	118	15	1	636	80	30	9	FR, ST, LD, NS	126	31	0.8
58	86	M	79	HF	Absent	118	62	2.2	339	18	7.5	1	FR, LD	121	67	1.9

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BUN = blood urea nitrogen, Cr = plasma creatinine, UOsm=urine osmolality, SIADH=Syndrome of inappropriate ADH secretion, TZ=thiazide diuretics, HF=heart failure, HYP=hypovolemia, KD=kidney disease, AI=adrenal insufficiency, CIR=cirrhosis, FR=fluid restriction, ST=salt tablets, LD=loop diuretics, NS=normal saline. VRA=vasopressin antagonists, HS=hypertonic saline, KCL=potassium chloride, GLU=glucocorticoids, NA = not available. Mild symptoms of hyponatremia include fatigue, nausea, and headaches. Moderate symptoms of hyponatremia include confusion, disorientation, and lethargy. Mild to moderate symptoms of hyponatremia is a mixed of mild and moderate symptoms.

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Supplemental Table 2. Demographic, clinical, and laboratory characteristics and treatment in urea-only treated patients.

Patient №	Age (years)	Sex	Etiology of hyponatremia	Baseline laboratory values			Treatment of hyponatremia		Outcomes		
				Plasma sodium (mEq/L)	UOsm (mOsm/kg)	Urine sodium (mEq/L)	Urea dose (grams/day)	Urea duration (days)	Plasma sodium change at 24h (mEq/L)	Plasma sodium change at the end of urea (mEq/L)	LOS (days)
8	61	F	SIADH	125	305	77	30	5	4	12	11
9	72	F	SIADH	119	351	42	15-30	7	4	12	7
11	59	M	SIADH	127	319	27	30	6	1	8	6
14	76	M	SIADH	125	561	94	30	3	0	4	3
15	72	M	SIADH	128	467	66	15-30	4	-1	5	4
21	85	M	SIADH	119	431	75	60	8	3	17	8
28	57	M	SIADH	121	365	146	15	2	0	0	7
30	70	M	SIADH	126	NA	NA	30	6	5	3	6
37	79	M	SIADH	126	573	130	30	3	-1	2	3
49	71	F	SIADH	122	220	17	30	2	6	6	2
50	66	M	SIADH	125	562	105	30	4	2	6	4
55	86	F	SIADH	129	316	54	30	4	5	8	7

UOsm=urine osmolality, LOS=length of hospital stay after initiation of urea, SIADH=Syndrome of inappropriate ADH secretion, TZ=thiazide diuretics, NA = not available

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Supplemental Table 3. Demographic, clinical, and laboratory characteristics and treatment in urea-untreated patients.

Patient №	Age (years)	Sex	Etiology of hyponatremia	Baseline laboratory values			Therapy of hyponatremia		Outcomes		
				Plasma sodium (mEq/L)	UOsm (mOsm/kg)	Urine sodium (mEq/L)	Therapies used	Duration of therapy (days)	Plasma sodium change at 24h (mEq/L)	Plasma sodium change at the end of therapy (mEq/L)	LOS (days)
1	80	F	SIADH	124	409	86	FR, HS, KCL	4	-1	11	4
2	66	F	SIADH	121	415	65	FR, ST, LD, KCL	9	3	3	9
3	60	M	SIADH	128	504	29	FR, NS	6	-3	-2	6
4	89	M	SIADH	123	629	NA	FR, ST, NS	6	-2	7	6
5	40	M	SIADH	126	514	105	FR, ST, HS	6	-2	7	6
6	87	M	SIADH	119	463	138	FR, ST	4	2	7	4
7	62	M	SIADH	121	299	53	FR, NS	7	7	11	7
8	88	M	SIADH	124	730	38	FR, LD, NS, KCL	6	1	3	6
9	87	M	SIADH	123	396	109	FR, ST, VRA	4	-3	1	3
10	48	F	SIADH	121	230	22	FR, NS	5	1	8	4
11	87	M	SIADH	123	583	45	FR, NS	3	0	4	4
12	88	F	SIADH	126	714	151	FR, ST	6	-3	4	6

UOsm=urine osmolality, LOS=length of stay after initiation of therapy for hyponatremia, SIADH=Syndrome of inappropriate ADH secretion, TZ=thiazide diuretics, HF=heart failure, FR=fluid restriction, ST=salt tablets, LD=loop diuretics, NS=normal saline, VRA=vasopressin antagonists, HS=hypertonic saline, KCL=potassium chloride, NA = not available

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Supplemental Table 4. Daily Change in Plasma Sodium in Patients on Varying Doses of Urea.

Patient №	Pre-Urea Therapy	Baseline plasma sodium (mEq/L)	Day 1		Day 2		Day 3		Day 4		Day 5	
			Therapy	Change in plasma sodium (mEq/L)	Therapy	Change in plasma sodium (mEq/L)	Therapy	Change in plasma sodium (mEq/L)	Therapy	Change in plasma sodium (mEq/L)	Therapy	Change in plasma sodium (mEq/L)
4	Furosemide 120 mg IV	117	Urea 30 g	0	Urea 45 g, furosemide 40 mg IV	+4	Urea 45 g, furosemide 60 mg IV	0	Urea 45 g, NaCl 3% 315 mL	+2	Urea 60 g, furosemide 20 mg IV, NaCl 3% 125 mL	+4
5	Furosemide 20 mg IV, KCl 40 mEq IV	129	Urea 15 g	-2	Urea 15 g, furosemide 40 mg IV, NaCl 3% 260 mL	+1	Urea 60 g, furosemide 40 mg IV, KCl 80 mEq, NaCl 3% 960 mL	+1	Urea 60 g, furosemide 40 mg IV, KCl 20 mEq, NaCl 3% 1160 mL	+1	Urea 60 g, furosemide 20 mg IV, KCl 20 mEq, NaCl 3% 280 mL	0
9	None	119	Urea 15 g	+4	Urea 30 g	+3	Urea 30 g	+5	Urea 30 g	0	Urea 15 g	+1
12	None	122	Urea 15 g	+2	Urea 30 g, furosemide 20 mg IV, NaCl 0.9% 1100	+6	Urea 15 g, NaCl 0.9% 225 mL	+1	Urea 60 g	+3	Urea 45 g	-1
15	None	128	Urea 15 g	-1	Urea 15 g	+4	Urea 45 g	+2	Urea 30 g	NA	NA	NA
18	None	123	Urea 30 g	+2	Urea 30 g, NaCl 0.9% 210 mL	-1	Urea 30 g, KCl 40 mEq	+4	Urea 60 g	+2	Urea 60 g	-2
42*	NaCl 1 g PO	129	Urea 15 g	-3	NaCl 1 g PO	+1	NaCl 1 g PO	-1	Urea 15 g	+3	Urea 15 g	0
53 [†]	NaCl 2 g PO	124	Urea 45 g, NaCl 3 g PO	+4	Urea 15 g							
56	NaCl 0.9% 100 mL IV	128	Urea 15 g, NaCl 0.9% 1200 mL IV	+3	NaCl 0.9% 1200 mL	0	Urea 15 g	+3	Urea 15 g	0	Urea 30 g, furosemide 40 mg IV	-1

*Table only shows first 5 days of therapy. Patient's urea dose is eventually titrated up after 14 days of therapy.

[†]Patient received only 2 days of urea therapy and was then discharged.