Perlas en Hiponatremia

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05 Septiembre 2025

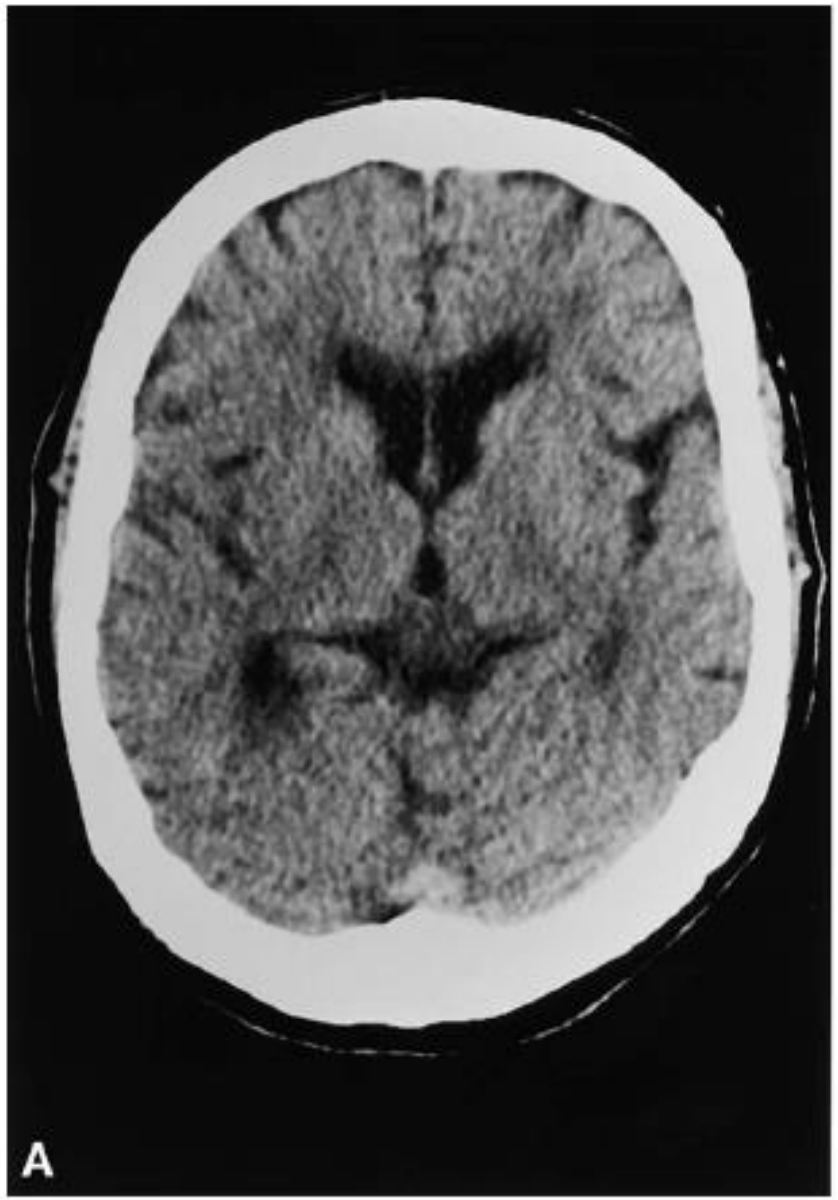
INTRODUCCION

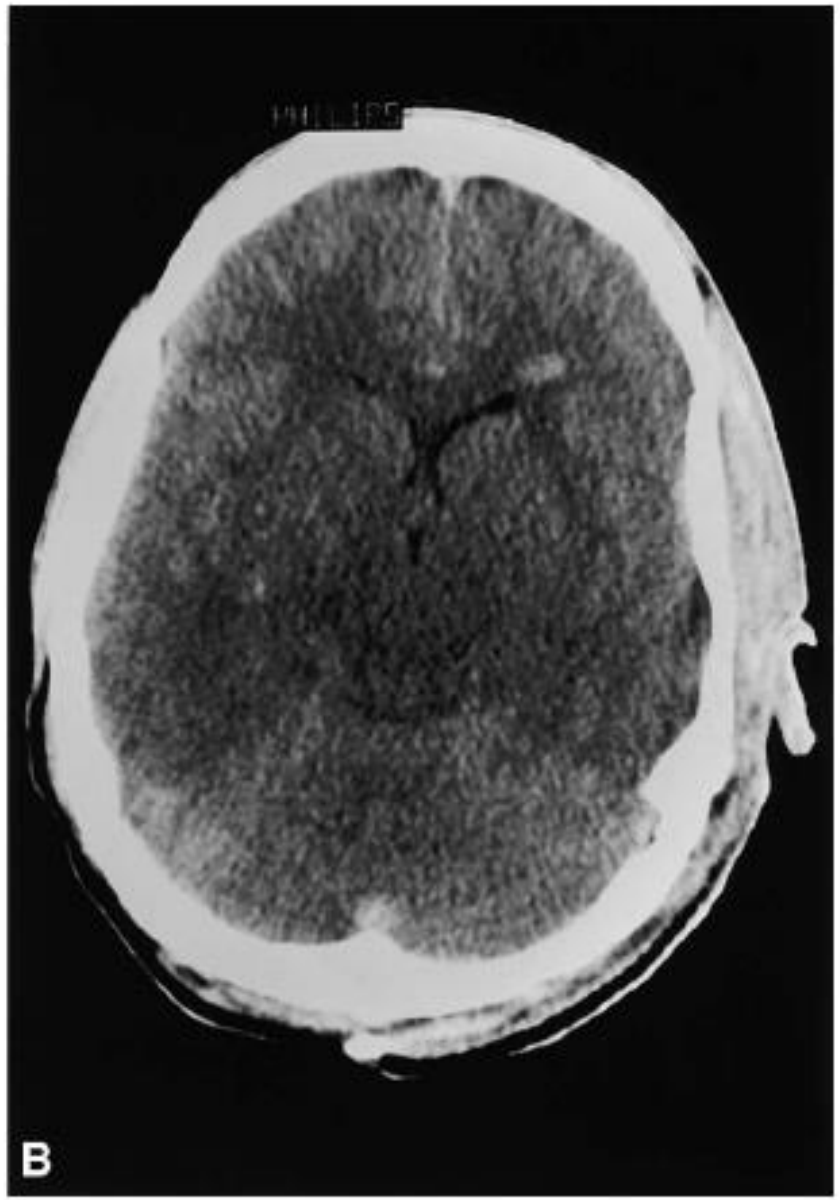
- ✓ La hiponatremia es el trastorno electrolítico más común encontrado en la práctica clínica con tasas de prevalencia de hasta el 30% en pacientes críticos.
- ✓ En pacientes hospitalizados, afecta hasta el 33% de los pacientes con insuficiencia cardíaca (IC) y en cirrosis hepática oscila entre el 20 al 60% siendo más frecuente en la enfermedad avanzada .
- ✓ Se ha asociado con una mayor morbilidad, mortalidad y utilización de la atención sanitaria.
- ✓ En algunos estudios de pacientes con hiponatremia grave (PNa <120 mmol/L) se han observado tasas de mortalidad hospitalaria de hasta el 51%.

Mondellini GM, Verbrugge FH. Evaluation and Management of Hyponatremia in Heart Failure. Curr Heart Fail Rep. 2024 Jun;21(3):252-261. doi: 10.1007/s11897-024-00651-3

Rondon-Berrios H. Diagnostic and Therapeutic Strategies to Severe Hyponatremia in the Intensive Care Unit. Journal of Intensive Care Medicine. 11 Oct. 2023.doi:10.1177/08850666231207334

Rondon-Berrios H, Velez JCQ. Hyponatremia in Cirrhosis. Clin Liver Dis. 2022 May;26(2):149-164. doi: 10.1016/j.cld.2022.01.001



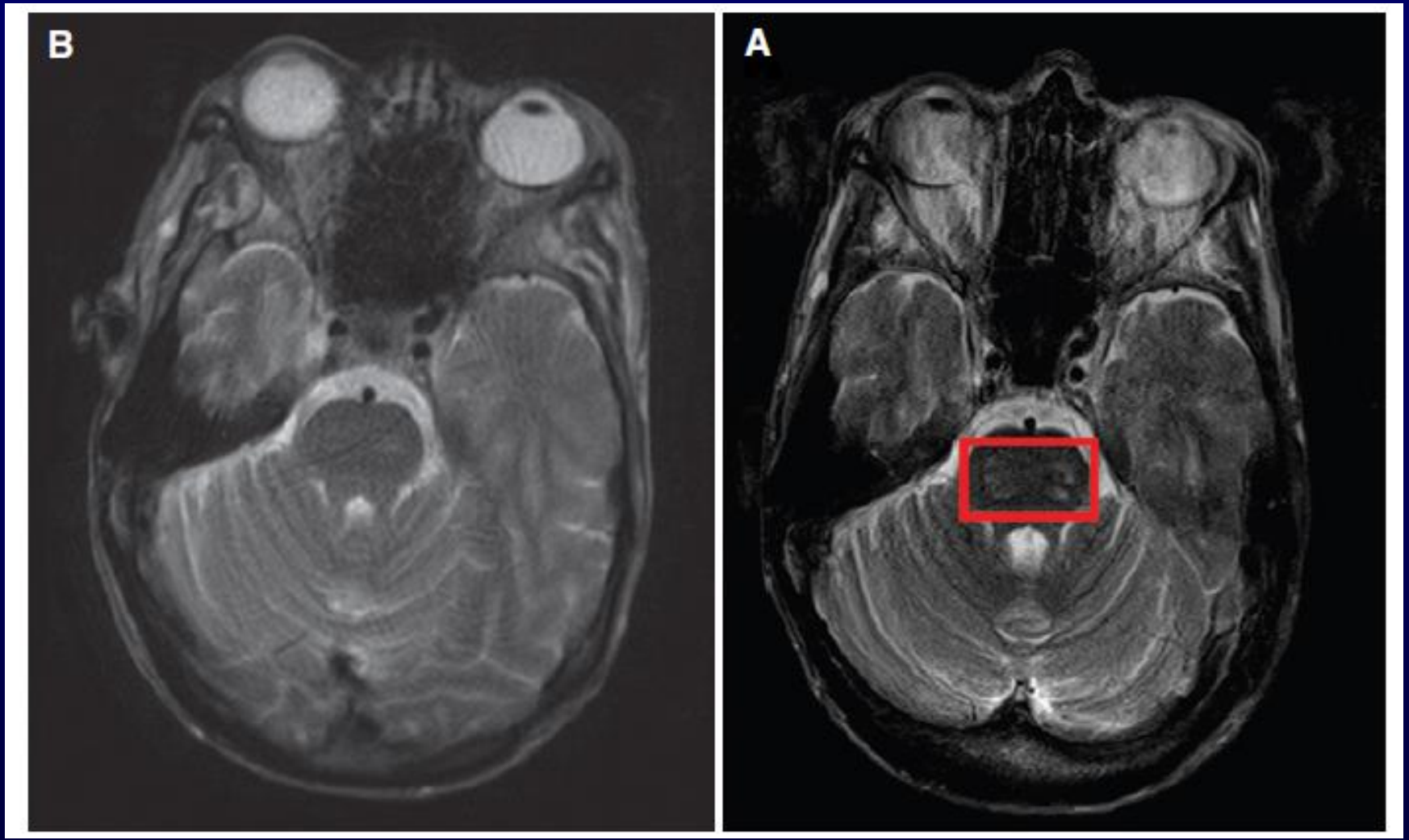


Treatment of severe hyponatremia

Kidney International, Vol. 60 (2001), pp. 2417–2427

Principal discussant: PETER GROSS

Universitätsklinikum Carl Gustav Carus, Dresden, Federal Republic of Germany



DE GRUYTER Diagnosis 2016; 3(2): 81–85

Case Report

Caleb J. Murphy, Peter L. Cathcart and Andrew P.J. Olson*

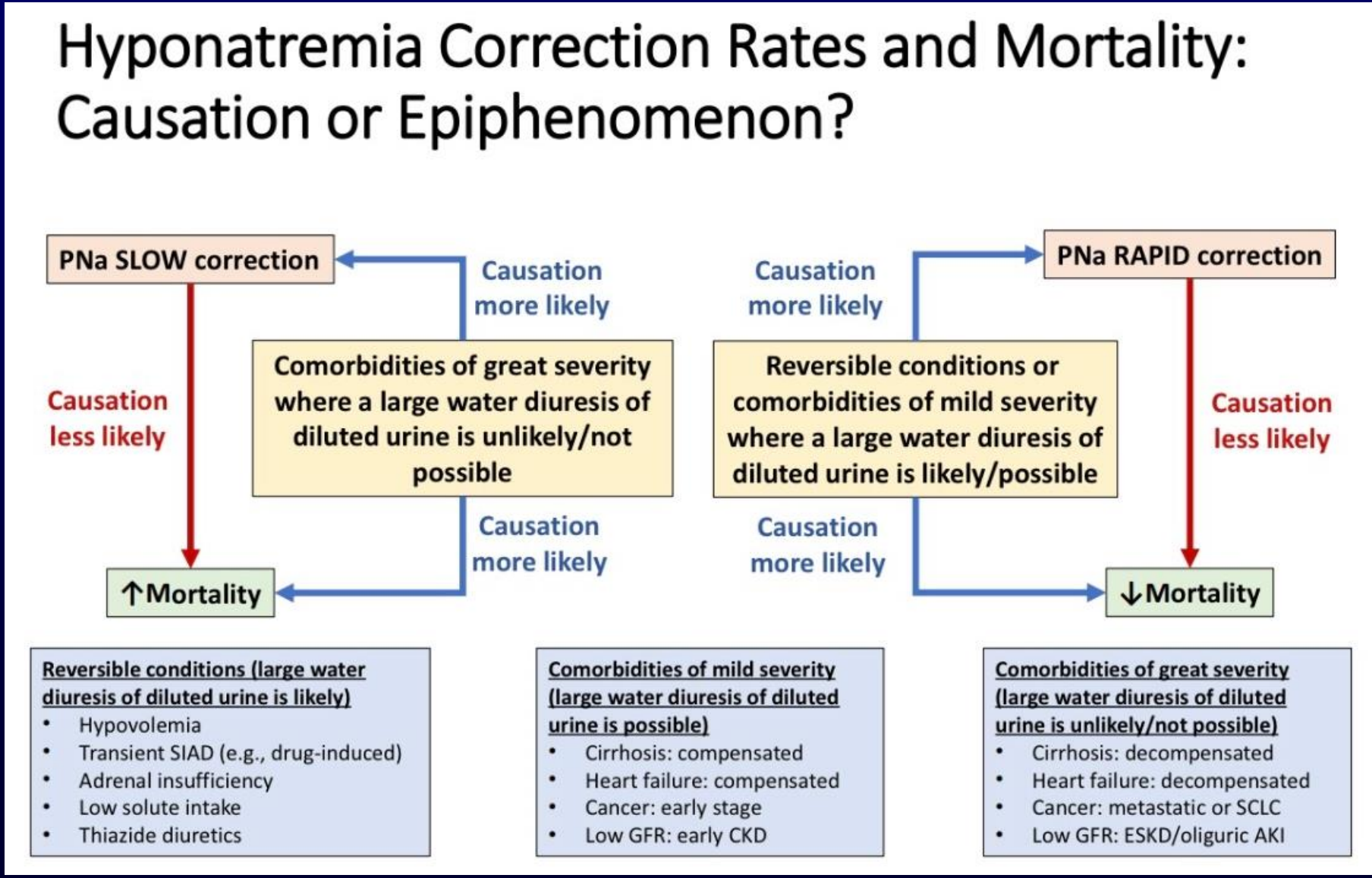
Those eyes don't lie: a case of osmotic demyelination syndrome in a patient with hepatic encephalopathy

DOI 10.1515/dx-2016-0004

Kidney360

Hyponatremia Correction Rates and Mortality: Causality or Epiphenomenon?

Rondon-Berrios, Helbert[1,a]; Sterns, Richard H.[2] March 13, 2024. | *DOI:* 10.34067/KID.0000000000000414

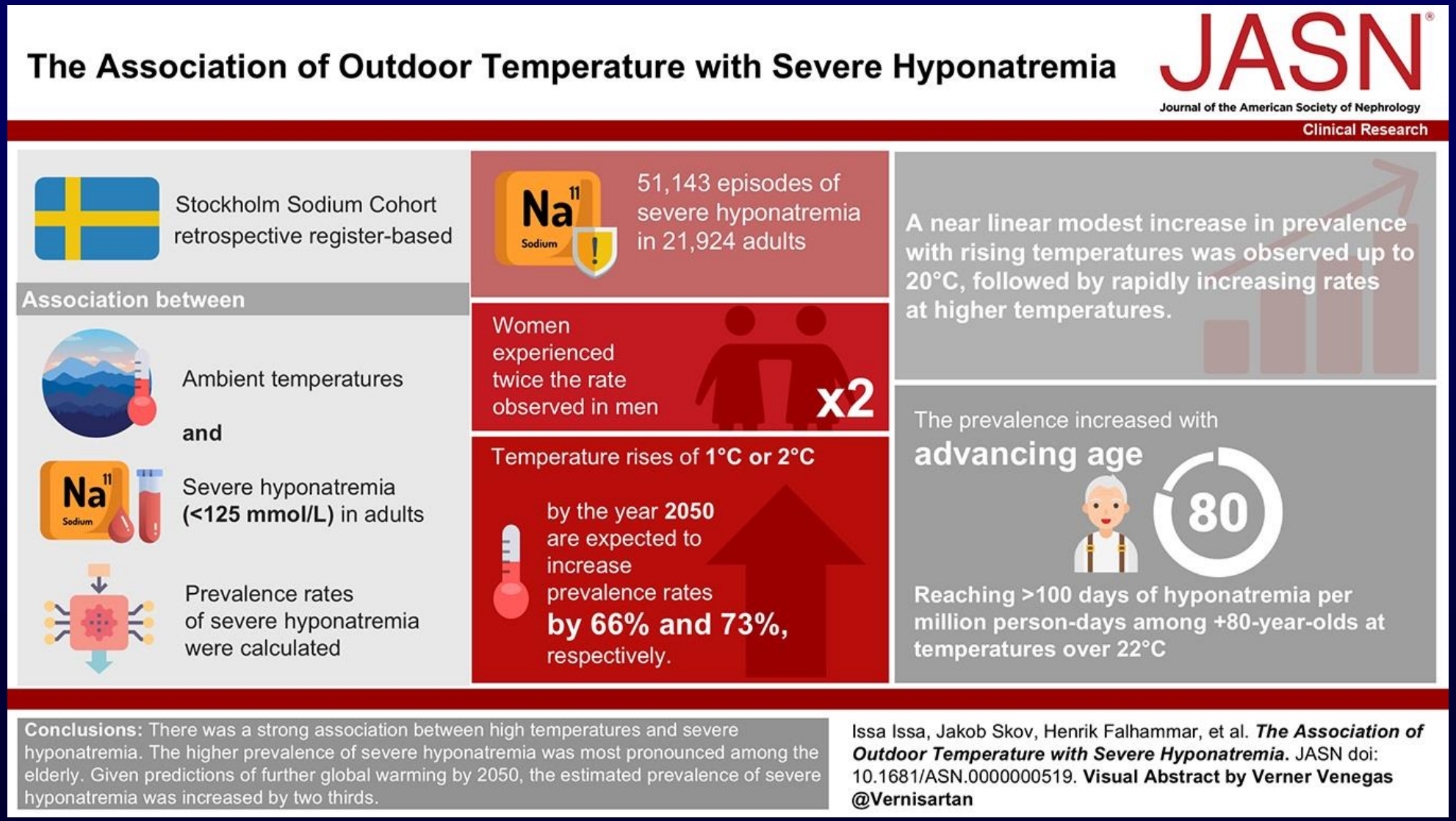


Clinical Research

The Association of Outdoor Temperature with Severe Hyponatremia

Issa Issa,[1] Jakob Skov,[2,3] Henrik Falhammar,

JASN 36: 435–440, March, 2025
doi: https://doi.org/10.1681/ASN.0000000519



CASO CLINICO 1

- ✓ Varón de 55 años de edad con antecedentes de enfermedad renal crónica terminal en hemodiálisis por 6 años se presenta al servicio de emergencias con disnea en reposo de 2 días de duración.
- ✓ No diálisis por 1 semana debido a problemas de movilidad y restricciones por pandemia del COVID.
- ✓ Dificultad respiratoria con Sat 80% al ambiente y FV (TA 200/100 mmHg FC 103 lpm FR 25 rpm T 36.2°C). Anuria. Ingurgitación yugular presente. Crepitantes en ambas bases pulmonares. Ruidos cardiacos regulares, no soplos. Edema de miembros inferiores 1+.
- ✓ Na: 123 mEq/L, K: 6.4 mEq/L, Cl: 91 mEq/L, HCO3 : 18 mEq/L, Urea : 194 mg/dl, Creatinina: 8.7 mg/dl, Glucosa : 104 mg/dl. Osmolalidad: 287 mOsm/Kg.

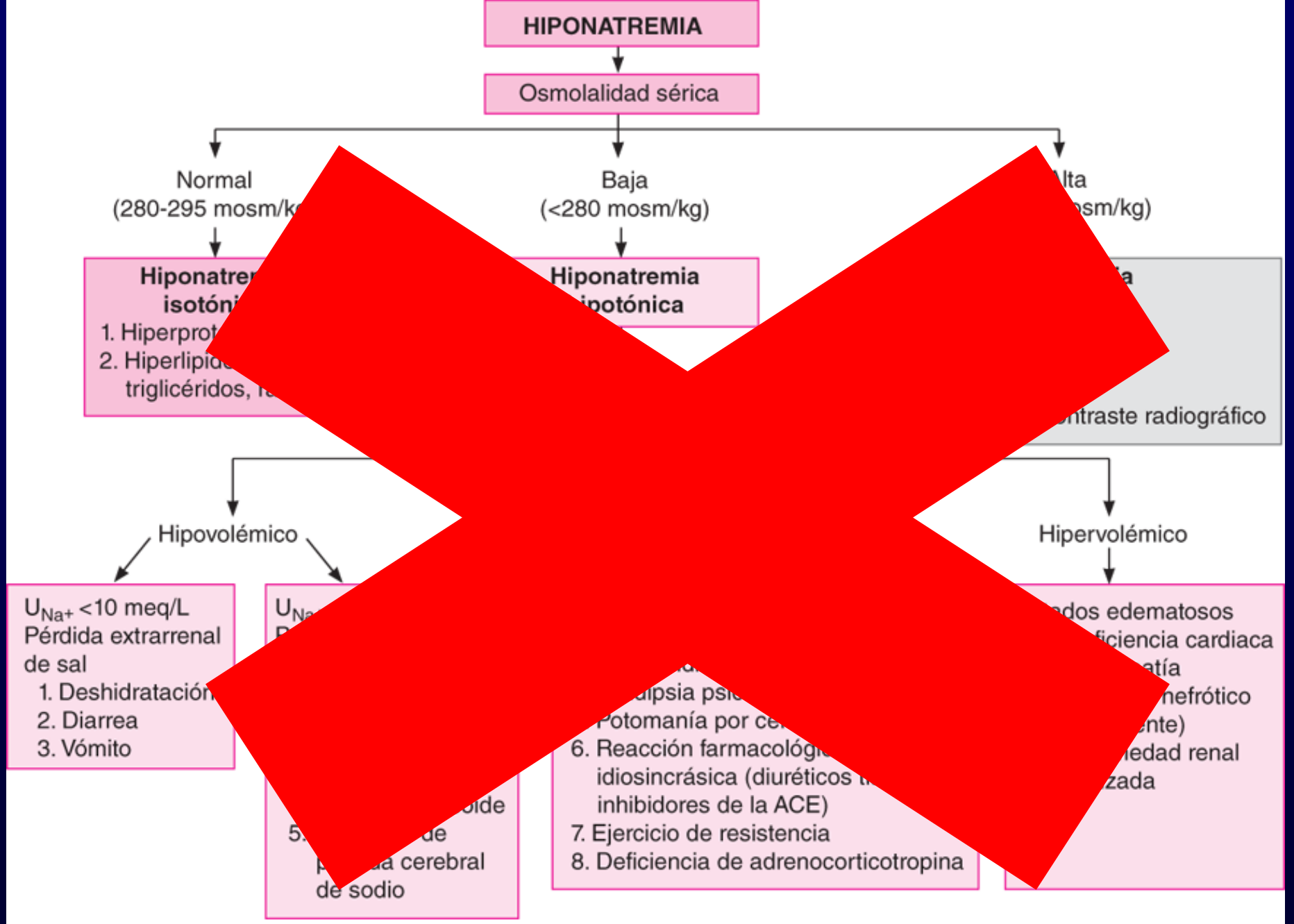
Cuál de los siguientes exámenes auxiliares es el más apropiado para diagnosticar la etiología de la hiponatremia isoosmolar en este paciente?

A) Triglicéridos séricos

B) Electroforesis de proteínas séricas

C) Vasopresina sérica

D) Ningún examen auxiliar adicional es necesario



Fuente: Maxine A. Papadakis, Stephen J. McPhee: Diagnóstico clínico y tratamiento, 2017

Osmolalidad vs. Tonicidad

- POsm = 2 x Na + Glucosa/18 + U[illegible]/6
- PTon = 2 x Na + Glucosa/18
- PTon = Posm – Urea/6
- PTon= 287 – 194/6 = 286-32 = 254 mOsm/Kg

$$\text{PTon (mOsm/kg)} = 2 \times \text{PNa (mmol/L)} + \frac{\text{Glucose (mg/dL)}}{18}$$

Dado que la glucosa plasmática normal es ≈90 mg/dL, la glucosa sólo contribuye con 5 mOsm/kg a la tonicidad plasmática. Por lo tanto, la PNa es el principal determinante de la tonicidad plasmática donde

$$\text{PTon (mOsm/kg)} \approx 2 \times \text{PNa (mmol/L)}$$

Rondon-Berrios H. Diagnostic and Therapeutic Strategies to Severe Hyponatremia in the Intensive Care Unit. Journal of Intensive Care Medicine. 11 Oct. 2023. doi:10.1177/08850666231207334

Evaluación clínica del volumen del LEC en hiponatremia

Evaluación Clinica del LEC	Hiponatremia responde a ClNa 0,9%	Hiponatremia no responde a ClNa 0,9%	Total
LEC contraído	**7**	**22**	**29**
LEC Normal	**8**	**21**	**29**
Total	**15**	**43**	**58**

Sensibilidad = 47%
Especificidad = 49%

VPP = 24%
VPN = 72%

LR+ =0.91
LR- =1.09

Chung HM, Kluge R, Schrier RW, Anderson RJ.: Clinical assessment of extracellular fluid volume in hyponatremia. Am J Med. 1987 Nov;83(5):905-8.

QJM

Diagnostic approach to a patient with hyponatraemia: traditional versus physiology-based options

E.J. HOORN[1], M.L. HALPERIN[2] and R. ZIETSE[1]

Q J Med 2005; **98**:529–540
doi:10.1093/qjmed/hci081

Table 1 Existing algorithms for hyponatraemia and their accuracy in three illustrative test cases

Algorithm	Algorithm hierarchy with included parameters and cut-off values	References	Correct diagnosis in three test cases
1	ECF volume	5, 9	6%
2	ECF volume – U_{Na} (20–40)	6, 14, 20, 21	7%
3	ECF volume U_{Na} (20)	3, 19	8%
4	Acuity of hyponatraemia ECF volume	13	6%
5	ECF volume U_{Na} (20) U_{osm} (500)	4, 16	12%
6	P_{osm} U_{osm} ECF volume	8, 11, 12	9%
7	P_{osm} U_{osm} U_{Na}	17	11%
8	P_{osm} (280–295) ECF volume U_{Na} (10 and 20)	15, 18	7%
9	P_{osm} (280) U_{osm} (100) U_{Na} (20–40) Fluid challenge tests FE_{urea}, FE_{urate}, P_{urate}	10	9%
10	U_{osm} (100) Renal function ECF volume U_{Na} (20)	7	9%

-Una encuesta a 46 médicos con cuatro casos seleccionados de hiponatremia donde usarían los algoritmos clínicos existentes.

-Sólo el 10% de los médicos alcanzaran un diagnóstico correcto.

-Se identificaron varias debilidades en los algoritmos, incluida la falta de *consideración de la hiponatremia aguda*, la creencia de que se puede *detectar* un grado modesto de contracción del *LEC mediante un examen físico* respaldado por laboratorio de rutina y una *tendencia a diagnosticar* el *SIHAD antes de excluir* otras causas de hiponatremia.

Table 3 Analysis of cases with the physiology-based approach

Case	Presentation	Diagnosis	Diagnostic pitfalls	Applied physiological principles	Potential threats to survival
1	Hyponatraemia in the absence of a detectably contracted ECF volume	'Normokalaemic' Addison's disease	Apparent normovolaemia Normokalaemic Addison's disease	ECF contraction may not be detectable[8–34] Calculation of transtubular K gradient[2,70–72]	*Untreated:* haemodynamic collapse *Treatment:* osmotic demyelination
2	Excessive renal excretion of Na	Addison's disease with an additional stimulus for Na excretion	Acute presentation of chronic hyponatraemia Second stimulus for high Na excretion	Calculation of fractional excretion of sodium[2,72] Calculation of tonicity balance[12,43]	*Untreated:* haemodynamic collapse *Treatment:* osmotic demyelination
3	Hyponatraemia with the ability to have a water diuresis	Hyponatraemia due to low delivery of solutes to the collecting duct	Polyuria in the context of hyponatraemia Hyponatraemia with minimal release of ADH	Normal kidneys are able to excrete 12 l of electrolyte-free water[2] Calculation of free water clearance[24]	*Increase in water balance:* cerebral oedema *Treatment:* osmotic demyelination
4	Acute hyponatraemia in a patient who took 'Ecstasy'	Ecstasy-induced hyponatraemia	Acute vs. chronic hyponatraemia Discrepancy between symptoms and P_{Na} Rise in P_{Na} due to seizure	Different pathophysiology acute and chronic hyponatraemia[59] P_{Na} may be confounded after a seizure[55]	*Untreated:* cerebral oedema

Berend et al. BMC Medical Education (2025) 25:751
https://doi.org/10.1186/s12909-025-07235-2

22 May 2025

BMC Medical Education

RESEARCH Open Access

Challenging cases of hyponatremia incorrectly interpreted by ChatGPT

Kenrick Berend[1*], Ashley Duits[2,3] and Reinold O. B. Gans[1,4]

- ✓ **ChatGPT-3.5 falló en todos los casos en 2023 y mostró una leve mejoría en 2024 (sólo un caso correctamente interpretado).**
- ✓ **Su uso en casos complejos de hiponatremia no es seguro ni recomendable actualmente**
- ✓ **Tanto ChatGPT como los médicos tuvieron altos índices de error , la evaluación de hiponatremia sigue siendo un gran reto clínico.**

Table Summary responses ChatGPT and clinicians in 4 patients with complex hyponatremia cases (adapted from Hoorn et al.)

case	Diagnostic and therapeutic aspects of the case	Did ChatGPT recognize the diagnosis and/or recommend dangerous therapy in 2023 and/or 2024?	Did clinicians recognize the diagnosis and/or recommend dangerous therapy?	Comment
1	Normokalaemia Addison's disease with apparent normovolaemia Treatment: saline and steroids.	Diagnosis missed in 2023 and 2024. No therapy recommended in 2023. In 2024 inappropriate treatment with fluid restriction suggested due to diagnostic error (SIADH).	Addison's disease recognized by 11%. Misdiagnosed as SIADH by 48% Inappropriate water restriction recommended by 65%	ChatGPT made no mentioning of the hyponatremia in 2023, but dangerous therapy suggestion because of wrong diagnosis (SIADH) was made in 2024. Diagnosis missed by 48% of clinicians. 65% of the clinicians advised a dangerous treatment with fluid restriction.
2	First and main problem: low osmol intake with a high risk of developing osmotic demyelination syndrome (ODS) with saline infusion. Second and concurrent diagnosis: Addison's disease Treatment: half-isotonic saline and plasma sodium should increase only 4 to 6 mmol/l in the first 24 h.	The main diagnostic aspect of low osmol intake was not recognized in 2023 or 2024. Addison's disease diagnosed in 2023 and 2024. Inappropriate treatment with normal saline recommended in 2023 and 2024.	Main diagnostic aspect of low osmol intake was not recognized. Addison's disease diagnosed by 19% of clinicians. Inappropriate treatment recommended by 57% of clinicians	Diagnosis of chronic hyponatremia with a presumed low osmol intake increases the risk of ODS not recognized by clinicians and ChatGPT in 2023 and 2024. Addison's disease missed by 81% of clinicians but diagnosed by ChatGPT in 2023 and 2024. Dangerous treatment with isotonic saline recommended by ChatGPT and most of the clinicians.
3	Hyponatremia was the result of low protein and salt intake with moderate water intake. If the patient is asymptomatic, fluid restriction should be initiated. Inappropriate treatment with isotonic saline causes overcorrection of sodium.	Diagnosis not recognized in 2023. In 2024 initial appropriate discussion of vegan lifestyle, with low-salt diet and high-water intake. However, in the same discussion diagnosis switched to primary polydipsia or exercise-associated hyponatremia. Dangerous treatment with normal saline recommended in 2023, but proper advice of fluid restriction was made in 2024.	Diagnosis not recognized by any of the clinicians. Wrongly diagnosed as psychogenic polydipsia by (53%) and SIADH by (12%) Appropriate fluid restriction was recommended by 80%. Dangerous treatment with normal saline recommended by 2%	Diagnosis not recognized by clinicians or ChatGPT (2023). In 2024 ChatGPT proposed the correct diagnosis and treatment. High risk treatment with isotonic saline recommended by ChatGPT in 2023 but proper treatment in 2024. Most of the clinicians recommended appropriate fluid restriction for other reasons, because of errors in diagnosis.
4	First and main problem. Temporarily increased plasma natrium due to seizure masking the severity of hyponatremia. Clue: discrepancy between the measured plasma natrium and the severity of the symptoms. Second problem. Severe hyponatremia (masked by seizure) caused by ecstasy and water intake. **Treatment**: because of acute symptomatic hyponatraemia, NaCL 3% is recommended.	The role of seizure on hyponatremia was not recognized in 2023 or 2024, but in both years the role of ecstasy was recognized. Inappropriate fluid restriction was recommended in 2023 and 2024.	No, seizure due to "masked" hyponatremia not recognized. Wrongly diagnosed as SIADH (11%), water ingestion (13%), and natrium loss in sweat (28%). Proper administration with hypertonic saline recommended by 24%.	The point in this case is that seizures can raise the plasma sodium acutely by 10–15 mmol/l was not recognized either by ChatGPT or clinicians [8]. Unsafe management suggestion by CHatGPT in 2023 and 2024 and inadequate management by most clinicians.

- ✓ La IA puede ser útil en el futuro, pero hoy puede inducir errores graves.
- ✓ Los clínicos deben descartar Addison siempre antes de diagnosticar SIADH.
- ✓ Riesgo alto de iatrogenia (ODS, muerte) por malas decisiones terapéuticas.

Problemas con algoritmo clásico de diagnóstico de hiponatremia

1) Tonicidad no es sinónimo de osmolalidad
2) El Examen físico no es sensible ni específico en la evaluación del volumen del líquido extracelular
3) Baja eficacia diagnóstica

Clinical practice guideline on diagnosis and treatment of hyponatraemia

Nephrol Dial Transplant (2014) 29 (Suppl. 2): ii1–ii39
doi: 10.1093/ndt/gfu040
Advance Access publication 25 February 2014

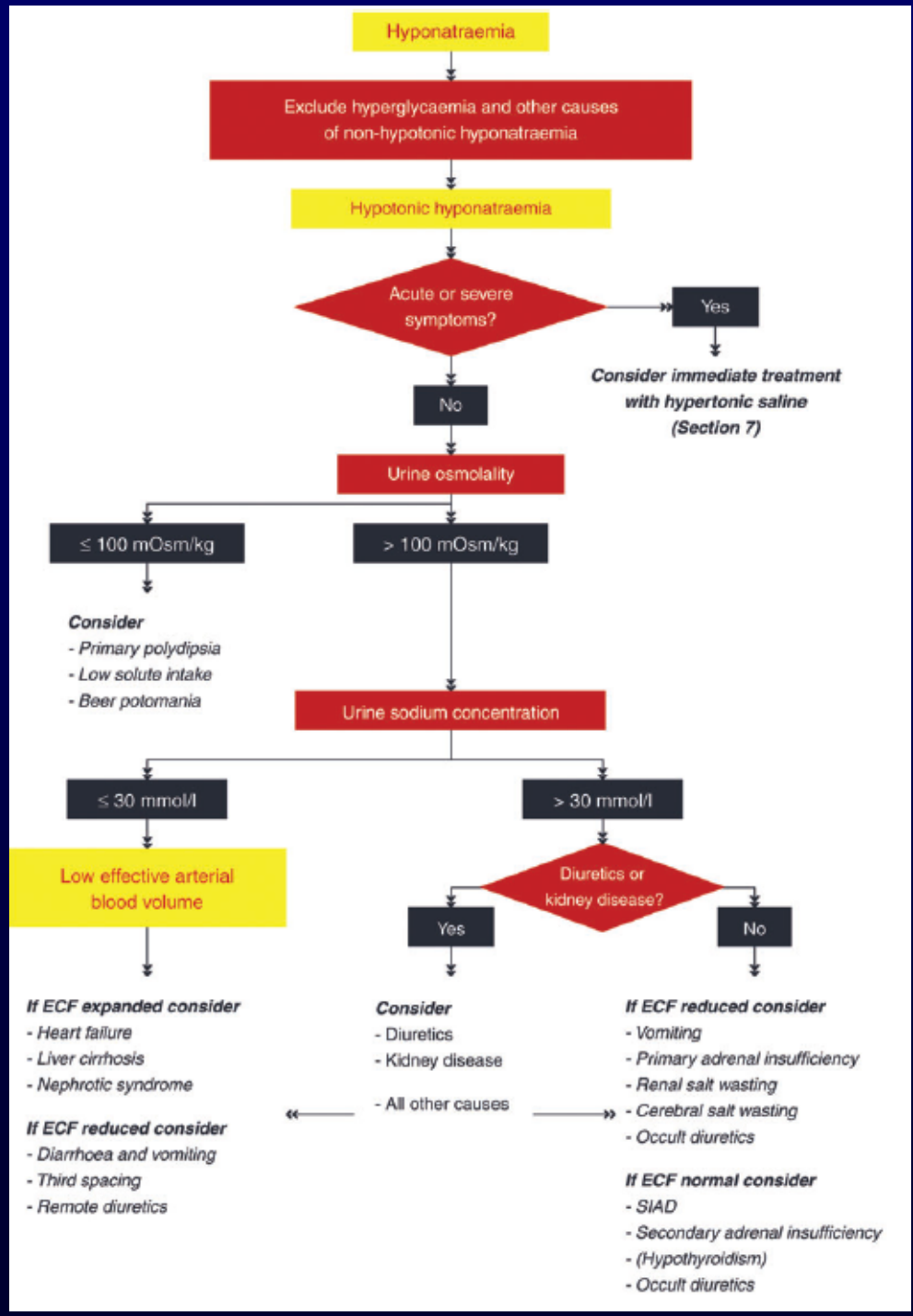
Goce Spasovski[1], Raymond Vanholder[2], Bruno Allolio[3], Djillali Annane[4], Steve Ball[5], Daniel Bichet[6],

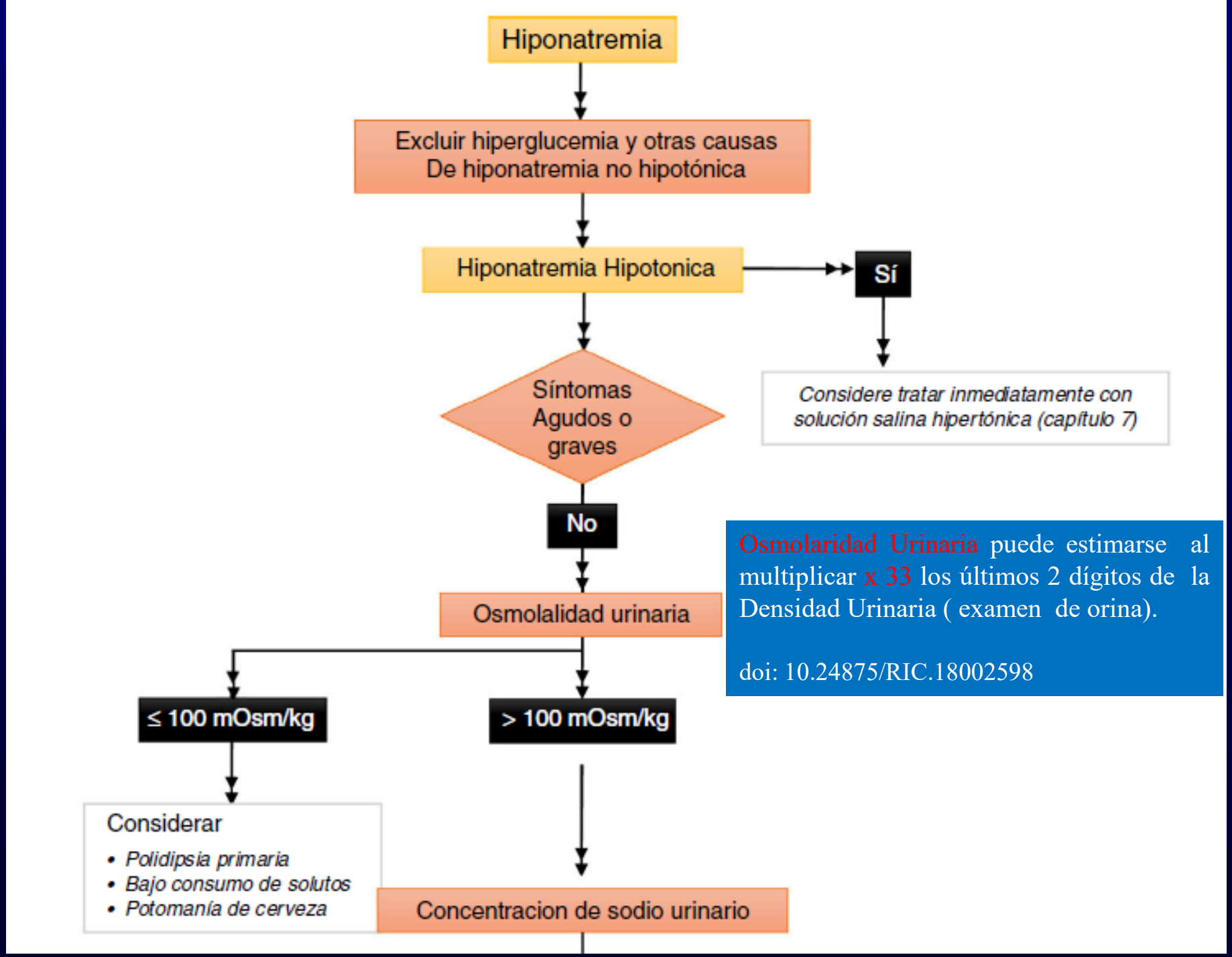
Table 6. Diagnostic criteria for the syndrome of inappropriate antidiuresis. Adapted from Schwartz WB, Bennett W, Curelop S & Bartter

Essential criteria
Effective serum osmolality <275 mOsm/kg
Urine osmolality >100 mOsm/kg at some level of decreased effective osmolality
Clinical euvolaemia
Urine sodium concentration >30 mmol/l with normal dietary salt and water intake
Absence of adrenal, thyroid, pituitary or renal insufficiency
No recent use of diuretic agents
Supplemental criteria
Serum uric acid <0.24 mmol/l (<4 mg/dl)
Serum urea <3.6 mmol/l (<21.6 mg/dl)
Failure to correct hyponatraemia after 0.9% saline infusion
Fractional sodium excretion >0.5%
Fractional urea excretion >55%
Fractional uric acid excretion >12%
Correction of hyponatraemia through fluid restriction

Table 8. Drugs and conditions associated with acute hyponatraemia (<48 h).

Postoperative phase
Post-resection of the prostate, post-resection of endoscopic uterine surgery
Polydipsia
Exercise
Recent thiazides prescription
3,4-Methylenedioxymethamfetamine (MDMA, XTC)
Colonoscopy preparation
Cyclophosphamide (i.v.)
Oxytocin
Recently started desmopressin therapy
Recently started terlipressin, vasopressin





Osmolaridad Urinaria puede estimarse al multiplicar x 33 los últimos 2 dígitos de la Densidad Urinaria (examen de orina).

doi: 10.24875/RIC.18002598

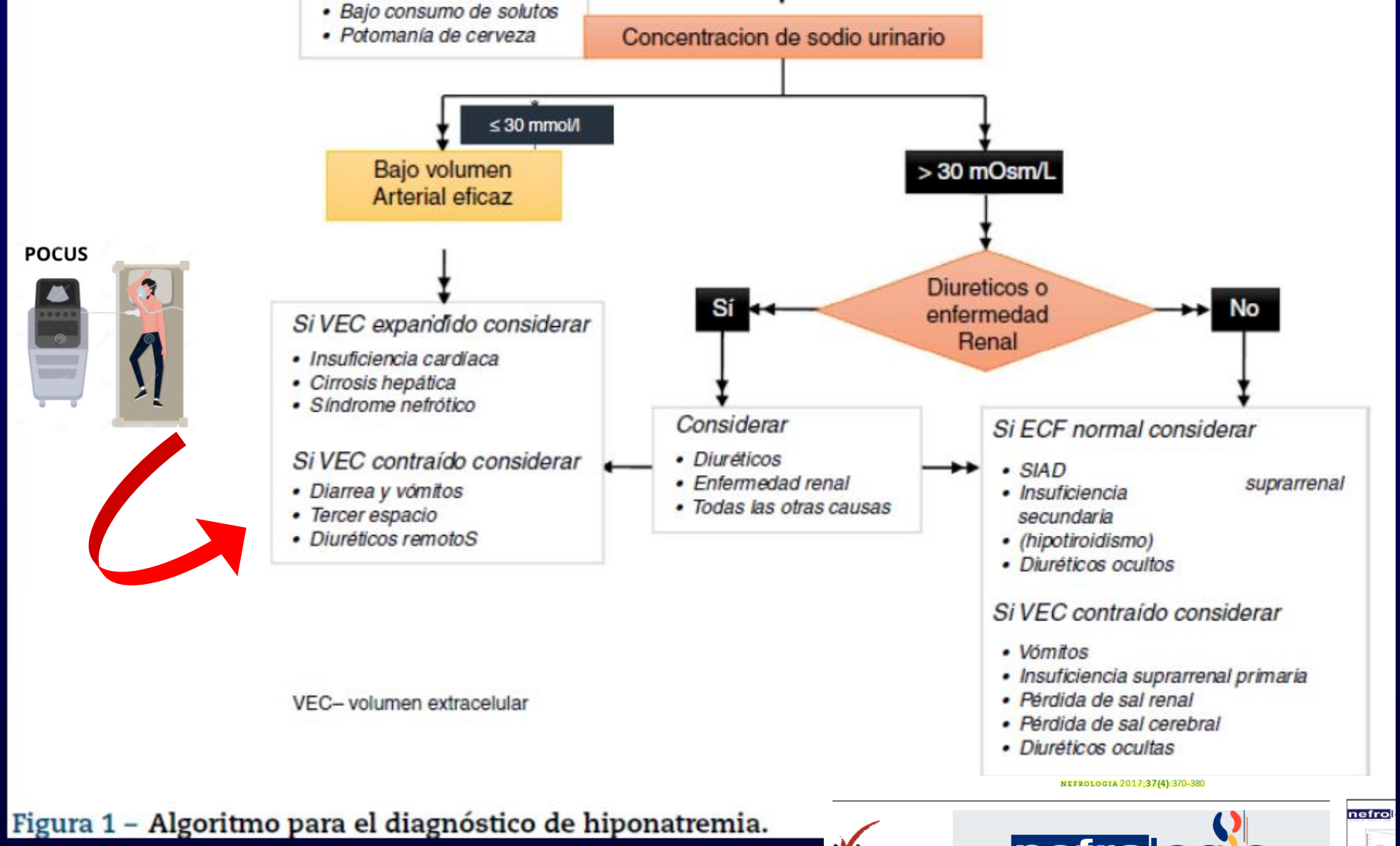


Figura 1 – Algoritmo para el diagnóstico de hiponatremia.

NEFROLOGIA 2017;37(4):370-380

Sociedad Española de Nefrología
nefrología
Revista de la Sociedad Española de Nefrología
www.revistanefrologia.com

Original

Guía de práctica clínica sobre el diagnóstico y tratamiento de la hiponatremia

Goce Spasovski[a], Raymond Vanholder[b], Bruno Allolio[c], Djillali Annane[d], Steve Ball[e],

Sociedad Española de Nefrología

nefrología

Revista de la Sociedad Española de Nefrología

www.revistanefrologia.com

Revisión breve

Medicina de precisión: «Point of Care Ultrasound» (PoCUS) en el abordaje diagnóstico del paciente con hiponatremia

DOI: 10.1016/j.nefro.2023.02.011 6 de Abril de 2023

Jaime Mazón Ruiz[a,*], *Eduardo Josue Banegas*[a], *Jose Luis Pérez Canga*[b],

PRINCIPALES LIMITACIONES DEL PROTOCOLO VExUS

VENA CAVA INFERIOR (VCI)

- **Determinar el diámetro de la VCI en la confluencia con las venas hepáticas** (sobrestima el diámetro). Se debe medir unos 2 cm por debajo de la unión con AD.
- **Efecto cilindro:** El haz de ultrasonido corta el vaso por su periferia. (infraestimación del diámetro máximo).
- Los **pacientes atletas y/o bajo IMC** pueden presentar una VCI dilatada (> 2 cm) sin aumento de presión en AD.
- **Aumentos de presión abdominal** pueden colapsar la VCI pese a una presión en AD elevada.
- **Ventilación mecánica** invasiva / no invasiva.

VENAS HEPÁTICAS

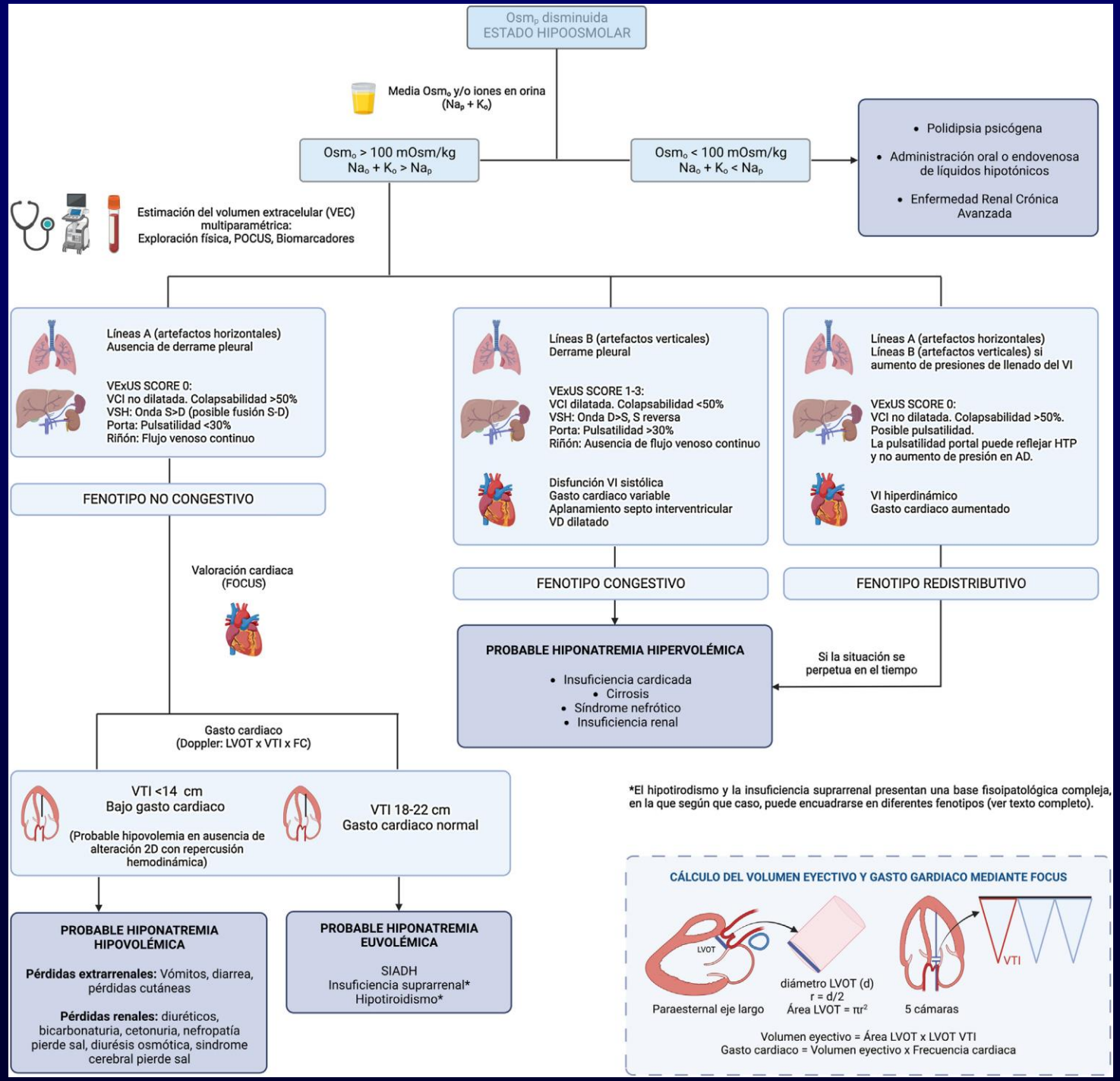
- **Insuficiencia tricuspidea significativa**: Posible S<D o D reversa sin congestión venosa significativa.
- **Disfunción del VD** sin desplazamiento del anillo valvular tricuspideo.
- Aplanamiento - embotamiento ("blunted waveform") en presencia de **cirrosis, hígado graso, linfoma hepático, estenosis VCI, maniobra de Valsava, aumento de presión abdominal.**
- **Fibrilación auricular:** pérdida de onda A y posible S<D en ausencia de aumento de presión en AD.

VENA PORTA

- Los **pacientes delgados** pueden presentar pulsatibilidad sin presentar aumento de presión en AD.
- Posible ausencia de pulsatilidad pese a una presión en AD elevada o viceversa con ausencia de pulsatilidad y presión en AD normal en pacientes con **cirrosis / hipertensión portal o hígado graso.**

VENAS RENALES INTERLOBARES

- **Dificultad técnica** para localizar el vaso, derivada de su **pequeño tamaño.** Aguantar la respiración unos segundos puede ser de ayuda.
- La **evaluación de los vasos hiliares** puede mostrar pulsatilidad en ausencia de congestión.
- **Alteraciones estructurales** como las derivadas de la enfermedad renal crónica o de la anastomosis del injerto renal pueden alterar la morfología de la onda.



Review
July 19, 2022

Diagnosis and Management of Hyponatremia
A Review

Horacio J. Adrogué, MD[1,2]; Bryan M. Tucker, DO, MS[1,2]; Nicolaos E. Madias, MD[3,4]
JAMA. 2022;328(3):280-291. doi:10.1001/jama.2022.11176

Figure 2. Clinical Approach to Hypotonic Hyponatremia

Patient with hyponatremia

- Perform clinical history, physical examination, and assessment of extracellular fluid volume to determine hyponatremia classification (hypovolemia, euvolemia, or hypervolemia)
- Exclude hyperglycemia and other causes of nonhypotonic hyponatremia to confirm **hypotonic hyponatremia**

Hypovolemia

- Measure urine sodium concentration

>30 mEq/L	<30 mEq/L
Kidney losses such as Diuretics Glucosuria in uncontrolled diabetes	Non-kidney losses such as Diarrhea Hemorrhage

Euvolemia

- Measure urine sodium concentration
- Measure urine specific gravity
- Measure urine osmolality

>30 mEq/L >1.003 >100 mOsm/kg	<30 mEq/L <1.003 <100 mOsm/kg
Syndrome of inappropriate antidiuresis Glucocorticoid deficiency Severe hypothyroidism	Excessive water intake Low solute intake

Hypervolemia

- Measure urine sodium concentration

>30 mEq/L	<30 mEq/L
Acute kidney injury Chronic kidney disease	Heart failure Cirrhosis Nephrotic syndrome

AKDH Volume 30, Issue 2, March 2023, Pages 85-101
https://doi.org/10.1053/j.akdh.2022.11.004

Hyponatremia Demystified: Integrating Physiology to Shape Clinical Practice

Biruh T. Workeneh, Priti Meena, Mirjam Christ-Crain, and Helbert Rondon-Berrios

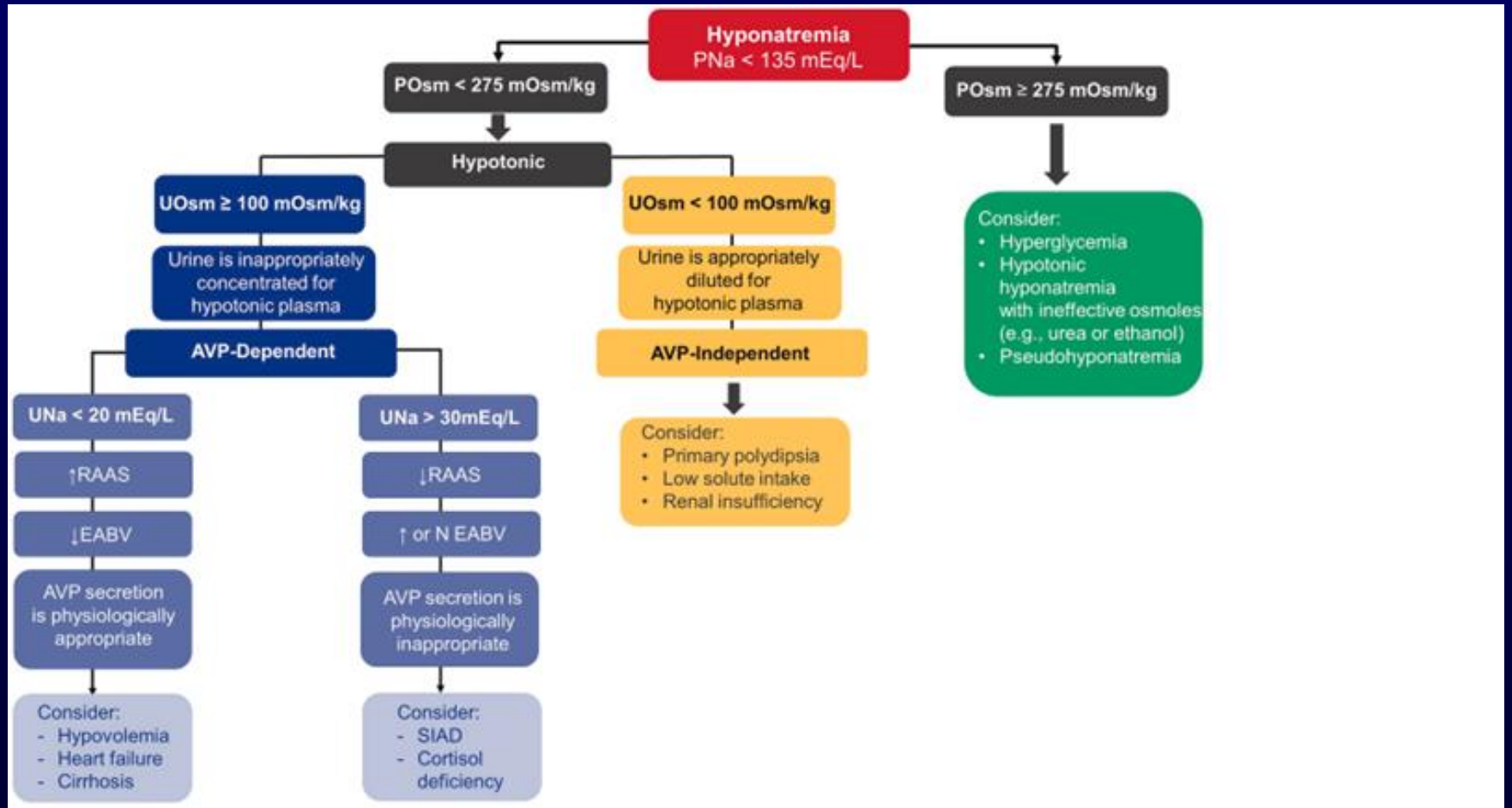


Figure 4. Diagnostic approach to hyponatremia. Abbreviations: AVP, arginine vasopressin; EABV, effective arterial blood volume; PNa, plasma sodium concentration; POsm, plasma osmolality; RAAS, renin-angiotensin-aldosterone system; SIAD, syndrome of inappropriate antidiuretic hormone; UNa, urine sodium concentration; UOsm, urine osmolality.

Analytic Review

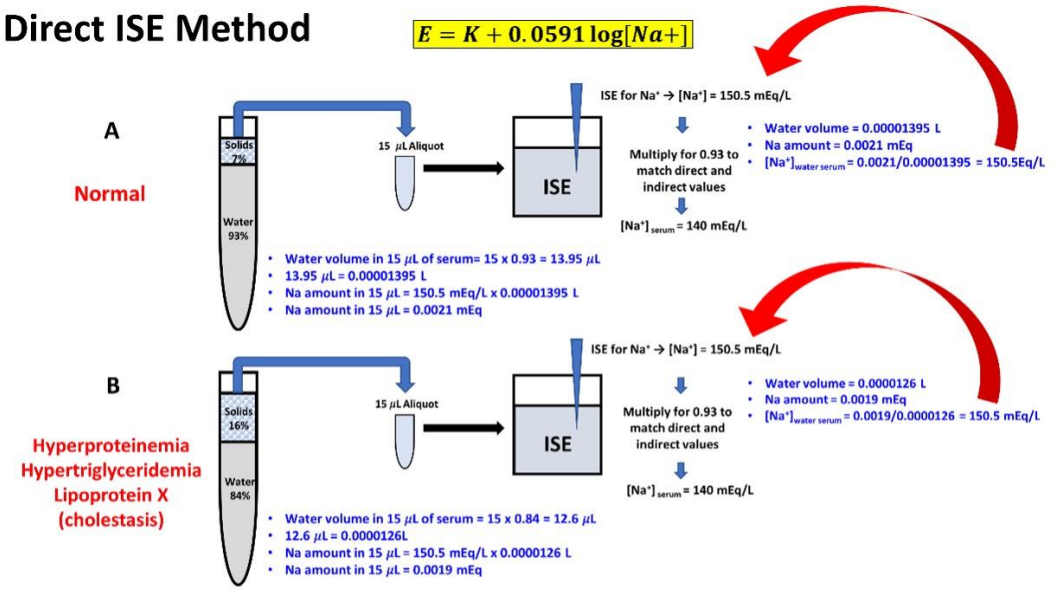
Diagnostic and Therapeutic Strategies to Severe Hyponatremia in the Intensive Care Unit

Helbert Rondon-Berrios, MD, MS[1]

DOI: 10.1177/08850666231207334
journals.sagepub.com/home/jic
Sage
October 11, 2023

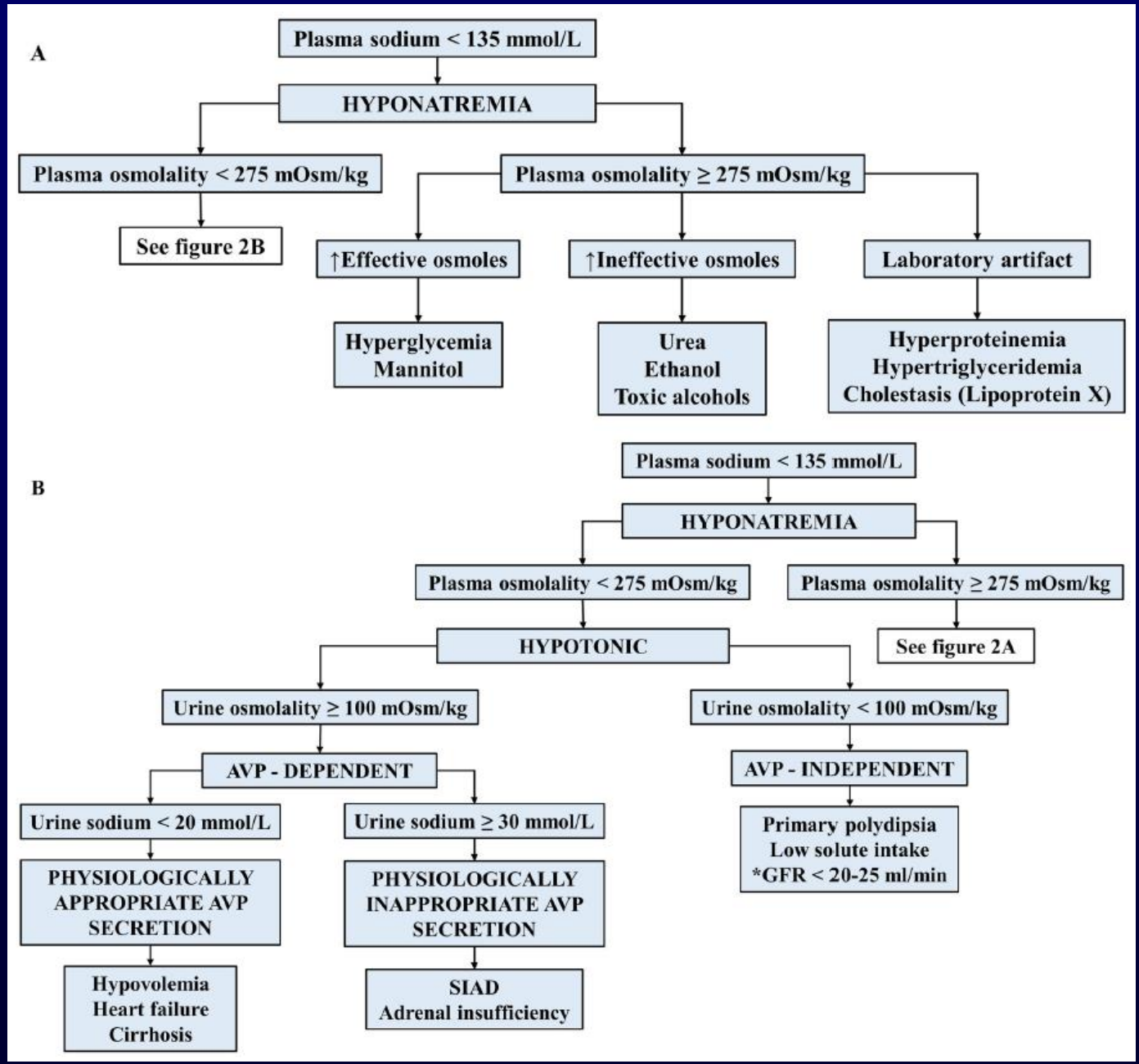
Direct ISE Method

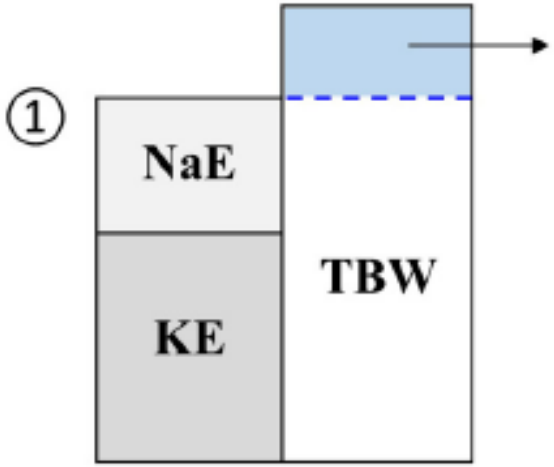
$$E = K + 0.0591 \log[Na+]$$



La mayoría de laboratorios miden Na sérico utilizando el método ISE indirecto.

El Na tiende a ser 2 mmol/L menor que la obtenida con métodos ISE indirectos.

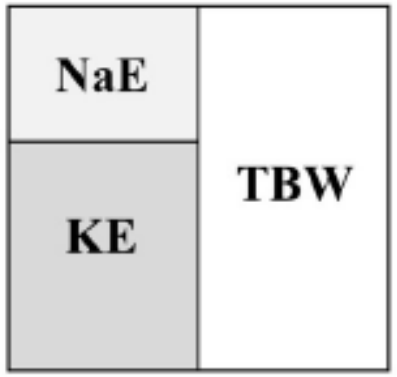


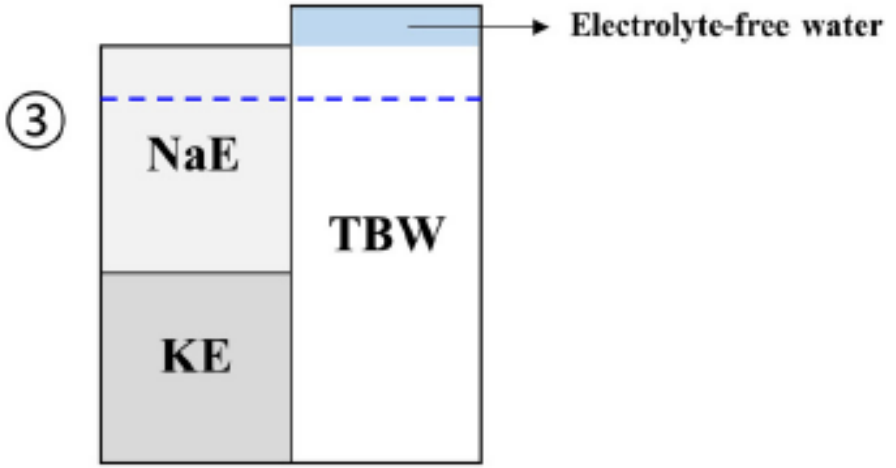


Polidipsia Primaria

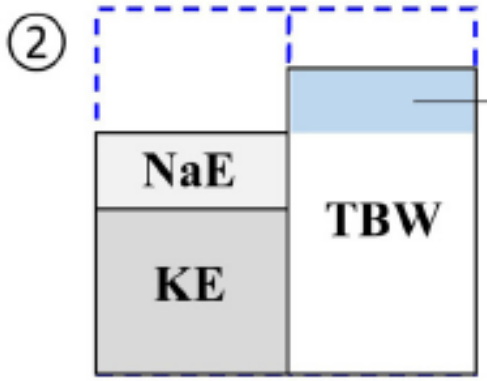
EDELMAN EQUATION (Simplified)

$$PNa = \frac{NaE + KE}{TBW}$$

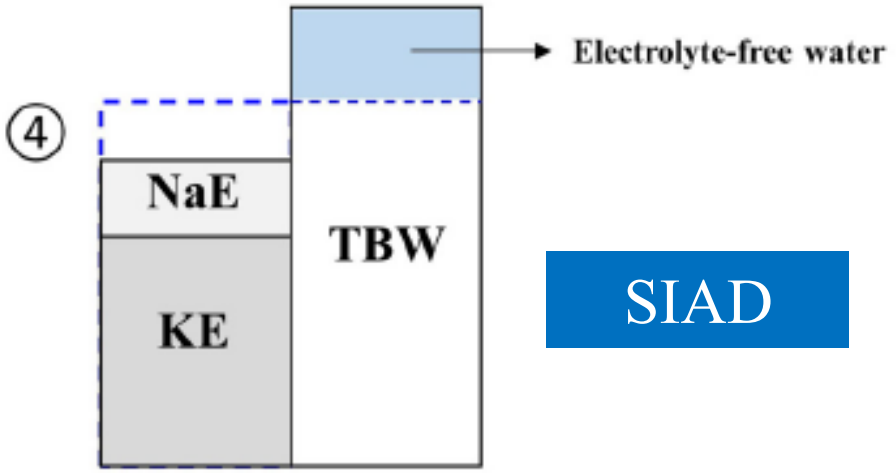




Cirrosis, ICC



Hipovolemia



SIAD

Edelman Gamblegrams: a tool to teach and learn disorders of water/plasma tonicity homeostasis

Helbert Rondon-Berrios 06 MAR 2024 // https://doi.org/10.1152/advan.00253.2023

Ecuación Edelman y cuatro escenarios diferentes que conducen a una hiponatremia hipotónica

European Journal of Internal Medicine 137 (2025) 11–20

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Review Article

Drug-induced hyponatremia in clinical care

Buster Mannheimer [a,b,*], Jonatan D. Lindh [c,d], Cecilia Bergh Fahlén [a,b],

10.1016/j.ejim.2025.04.034 July 2025

Principales fármacos causantes de hiponatremia

- ✓ Diuréticos tiazídicos → principal causa (hasta 25% de hospitalizaciones) Riesgo máximo en primeras 2–4 semanas, luego se estabiliza.
- ✓ Antidepresivos (ISRS, venlafaxina, tricíclicos, mirtazapina) → fuerte asociación, sobre todo con inicio reciente de tratamiento.

Fig. 1. Mechanisms of drug induced hyponatremia

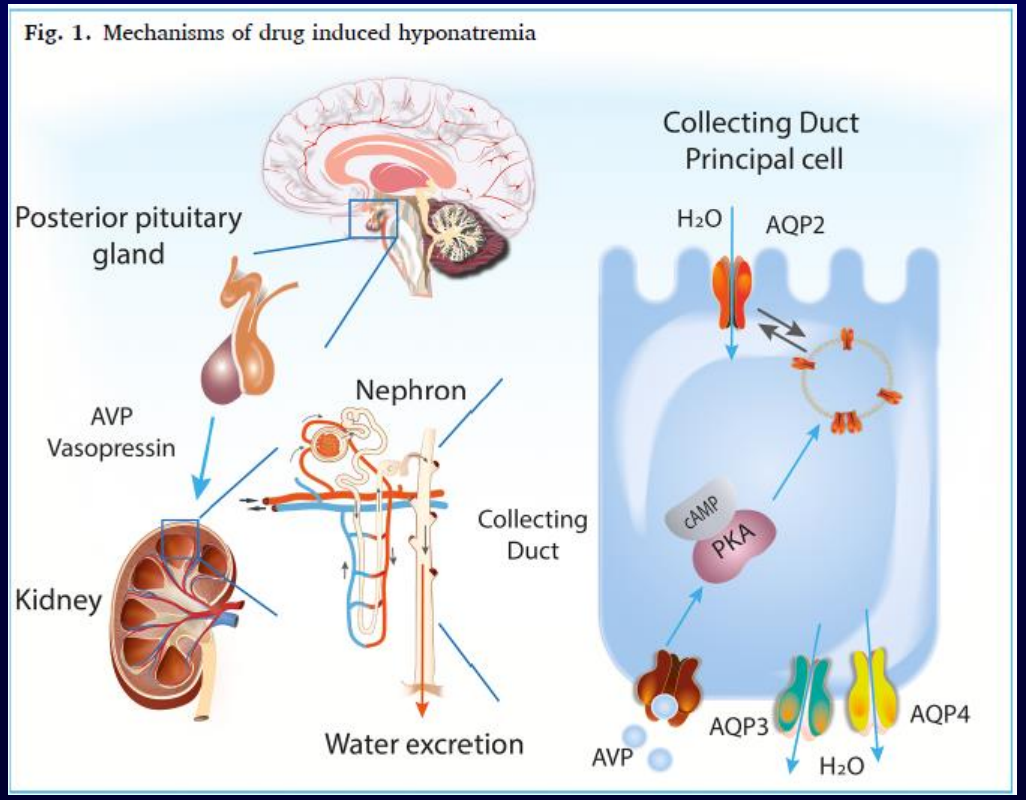


Table 1
Strength mechanism and brief characterization of associations between drugs and potential hyponatremia. Mild, moderate and marked effect defined by a relative risk increase of a magnitude of up to two, between two and five and over five times, is illustrated by +,++ and +++. An inverse association is illustrated by -.

Drugs	Risk of hyponatremia	Proposed mechanism by which sodium levels are affected	Characterization of association between drug and hyponatremia
Analgesics			
Non-steroidal anti-inflammatory drugs	+	Nephrogenic SIAD* through reduction of renal prostaglandin synthesis [147]	Weak association [93]
Opioids	+	SIAD [88,148]	Moderate association, uncertain temporal association [32, 89,90]
Antibiotics			
Aminoglycosides	+	Unknown	Weak association [115]
Linezolid	+++	SIAD[112, 149].	Marked association [110–114]
Quinolones	+	SIAD[150, 151]	Weak association [116]
Trimethoprim-sulfamethoxazole	+++	Renal salt wasting[152]	Marked dose-dependent association[108]
Antidepressants			
Noradrenergic and specific serotonergic antidepressants	++	SIAD[153]	Moderate association substantially lower than that of SSRIs[50,52, 53]
Selective serotonin reuptake inhibitors	+++	Nephrogenic SIAD[8,9]	Marked association primarily associated with newly initiated treatment[49,50, 52–56]
Serotonin–norepinephrine reuptake inhibitors	+++	SIAD[154]	Marked association primarily associated with newly initiated treatment[53]
Tricyclic antidepressants	+	SIAD[155]	Mild effect substantially lower than that of SSRIs[49,53]
Antihypertensives			
Angiotensin-converting enzyme inhibitors	+	SIAD[41]	Mild effect with uncertain causal association[38, 40–42]
Angiotensin II receptor blockers	+	Unknown	Mild effect with uncertain causal association[38, 43]
Beta blockers	+	Unknown	Mild effect with uncertain causal association[38]
Calcium channel blockers	+	SIAD[156, 157]	Mild effect with uncertain causal association [37–39]
Loop diuretics	-	Inhibits electrolyte free water reabsorption [126]	Data indicate an inverse effect regarding the development of hyponatremia [33]
Potassium sparing diuretics	+	Unknown	Mild effect with uncertain causal association [33–36]
Thiazides	+++	Multiple mechanisms leading to water retention and weight gain similar to that in SIAD[158]	Marked immediate effect that to some extent persists over time[4,12, 26,30]
Antipsychotics			
First generation	+	Nephrogenic SIAD[7,9]	Mildely elevated risk[51,80–83, 85,86]
Second generation	+	Nephrogenic SIAD[7]	Association about half that of first-generation antipsychotics [51,83,85,86]
Antiepileptic drugs			
Carbamazepine	+++	Nephrogenic SIAD[9,159]	Strong association[58, 59,61,63,68,69]
Gabapentin	+	Unknown	Weak association [69]
Lamotrigine	+	SIAD[160, 161]	Weak association [69]
Levetiracetam	(+)	SIAD[162]	Conflicting results[69, 163–167]
Oxcarbazepine	+++	Nephrogenic SIAD[168]	Marked association [59–63,69]
Phenytoin	++	Unknown	Moderate association[68, 69]
Valproate	++	SIAD[169, 170]	Moderate association[68, 69]
Desmopressin	+++	AVP-analog [22]	Marked association[22]
Lithium		Blunted response to AVP. Exact mechanism unknown . [135]	Data indicate an inverse effect regarding the development of hyponatremia [136]
Lipid lowering agents			
Ezetimib	-	Unknown	Data indicate an inverse effect regarding the development of hyponatremia [138,140]
Statins	-	Unknown	Data indicate an inverse effect regarding the development of hyponatremia [138–140,171]
Proton pump inhibitors	++	SIAD[74–76]	Moderate association with newly initiated. use. Causuality of

CASO CLINICO 2

- ✓ Mujer de 65 años con antecedentes de cáncer de mama con mastectomía radical y radioterapia 5 años atrás se presenta al servicio de emergencias por dolor de columna lumbar de 2 días de duración .
- ✓ Disconfort moderado por dolor. TA 140/80 mmHg, FC 93 lpm FR 21 rpm, T 37.1°C. Volumen urinario en 24 h: 1 L.
- ✓ No ingurgitación yugular. Examen de Tórax , Cardio y Abdomen sin alteraciones. Dolor a la palpación de apófisis espinosas de vertebras L3 y L4.
- ✓ Paciente despierta, orientada, sin signos neurológicos focales .

CASO CLINICO 2

- ✓ Sangre: Na 125 mEq/L, K 3.9 mEq/L, Cl 90 mEq/L, HCO3 24 mEq/L, Urea 11mg/dl, Creatinina 0,5mg/dl, Glucosa 102 mg/dl, Osmolalidad : 257mOsm/Kg

- ✓ Orina: UNa 200 mEq/L, UK 28 mEq/L, Osmolalidad : 678 mOsm/Kg

- ✓ RMN de columna lumbar demuestra la presencia de metástasis óseas nuevas en cuerpos vertebrales de L3,L4 y L5 sin invasión al espacio epidural

A parte de la restricción de fluidos, cuál de los siguientes es la mejor terapia inicial para el tratamiento de la hiponatremia en este paciente?

A) Ninguna terapia adicional es necesaria

B) Cloruro de Sodio 0,9%

C) Cloruro de Sodio 0,9% y furosemida

D) Cloruro de Sodio 3%

Depuración de agua libre de electrolitos (C_eH_2O)

$$C_eH_2O = \mathrm{V} \times \left\{1 - \left[\frac{U_{Na}+U_K}{P_{Na}}\right]\right\}$$

Cociente urinario plasmático de electrolitos	CeH2O	P_{Na}
$(U_{Na}+U_k)/P_{Na} > 1$	NEGATIVO	DISMINUYE
$(U_{Na}+U_k)/P_{Na} = 1$	0	IGUAL
$(U_{Na}+U_k)/P_{Na} < 1$	POSITIVO	AUMENTA

Balance de agua libre en nuestro paciente cuando la restricción de fluidos es CERO

- $C_eH_2O = V \times \{1 - (U_{Na} + U_k) / P_{Na} \}$
- $C_eH_2O = 1 \times \{1 - 228/120\}$
- $C_eH_2O = 1 \times \{1 - 1.9\} = -0.9$

INGRESOS	
Ingesta	0
C_eH_2O	900
Total	900

EGRESOS	
Perdidas Insensibles	800
Orina	0
Total	800

Balance de Agua Libre = + 100 ml

Cociente urinario plasmático de electrolitos guía la restricción de fluidos en SIAD

Cociente Urinario Plasmático de Electrolitos	Restricción de Fluidos	Terapia Adicional
> 1	≤ 1000 mL/día	Si
0,5 - 1	≤ 800 mL/día	No
< 0,5	≤ 1200 mL/día	No

SIAD: $U_{Na} + U_K = 228$ mEq/L (Uosm es "fija")

SIAD

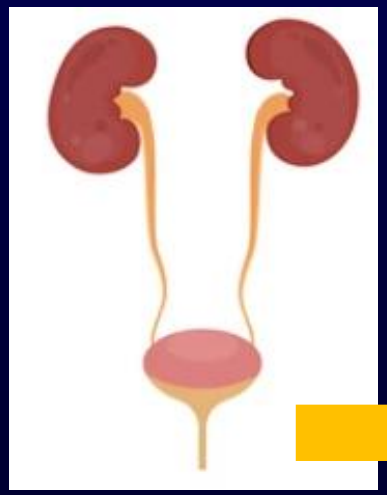
MANEJO DE AGUA ES ANORMAL PERO MANEJO DE SODIO ES NORMAL

228 mEq/L = 154 mEq / V

V=0.6L

1 L de Cl Na 0.9%

Na+ = 154 mEq



Paciente retiene 400 ml por cada Litro de ClNa 0.9% administrado "DESALINIZACION"

$U_{Na} + U_K = 228$ mEq/L

SIAD: $U_{Na} + U_K = 228$ mEq/L (Uosm es "fija")

SIAD

MANEJO DE AGUA ES ANORMAL PERO MANEJO DE SODIO ES NORMAL

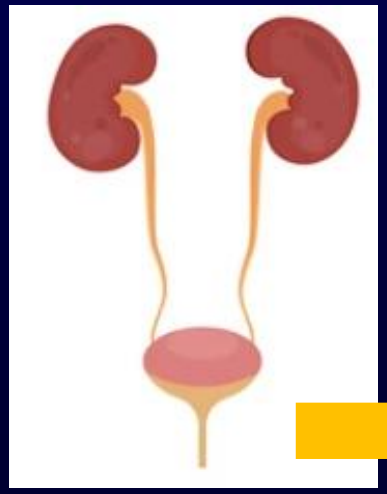
228 mEq/L = 513mEq / V

V=2.2L

Paciente retiene 1200 ml por cada Litro de ClNa 3% administrado

1 L de Cl Na 3%

Na+ = 513 mEq



$U_{Na} + U_K = 228$ mEq/L

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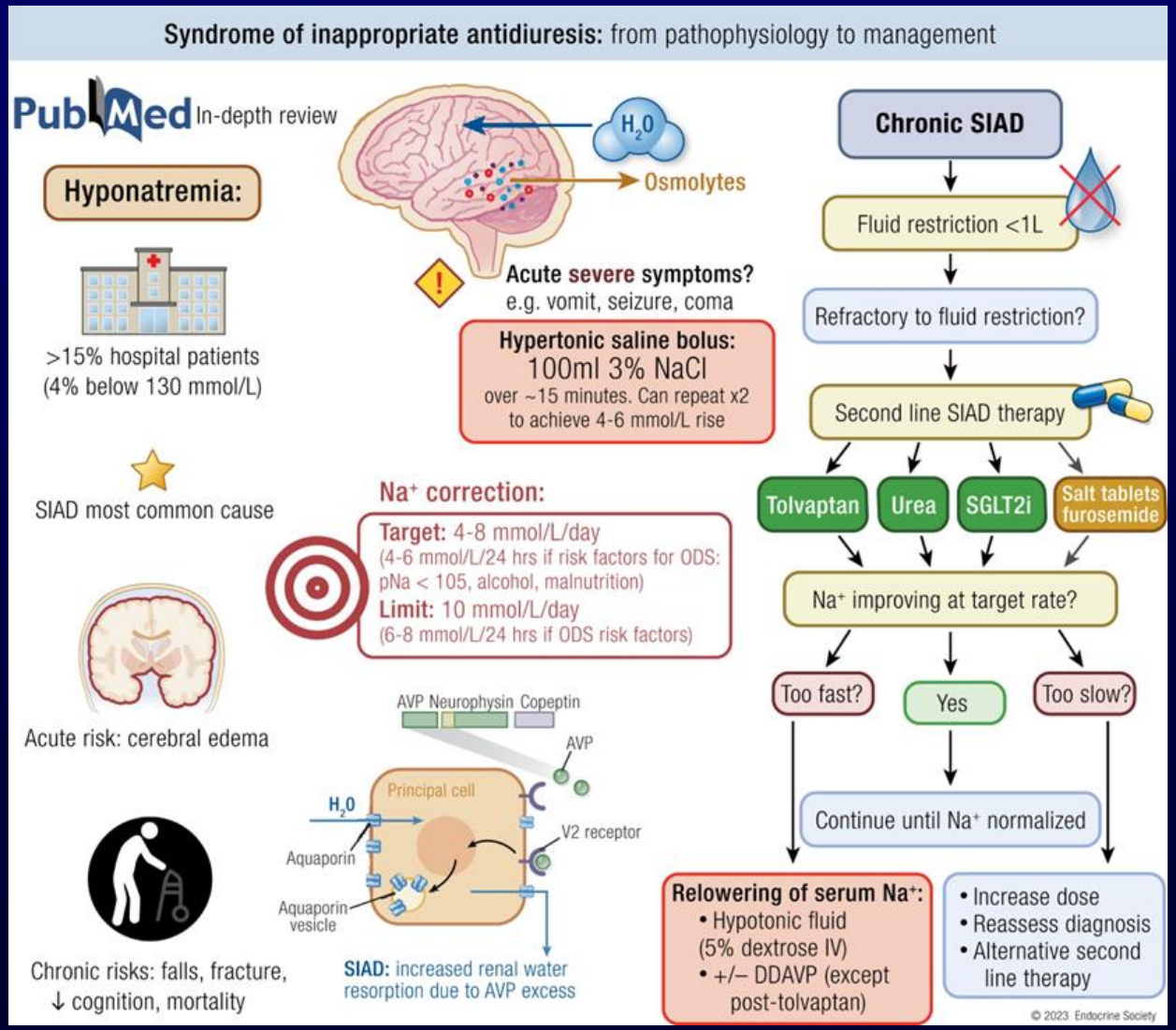
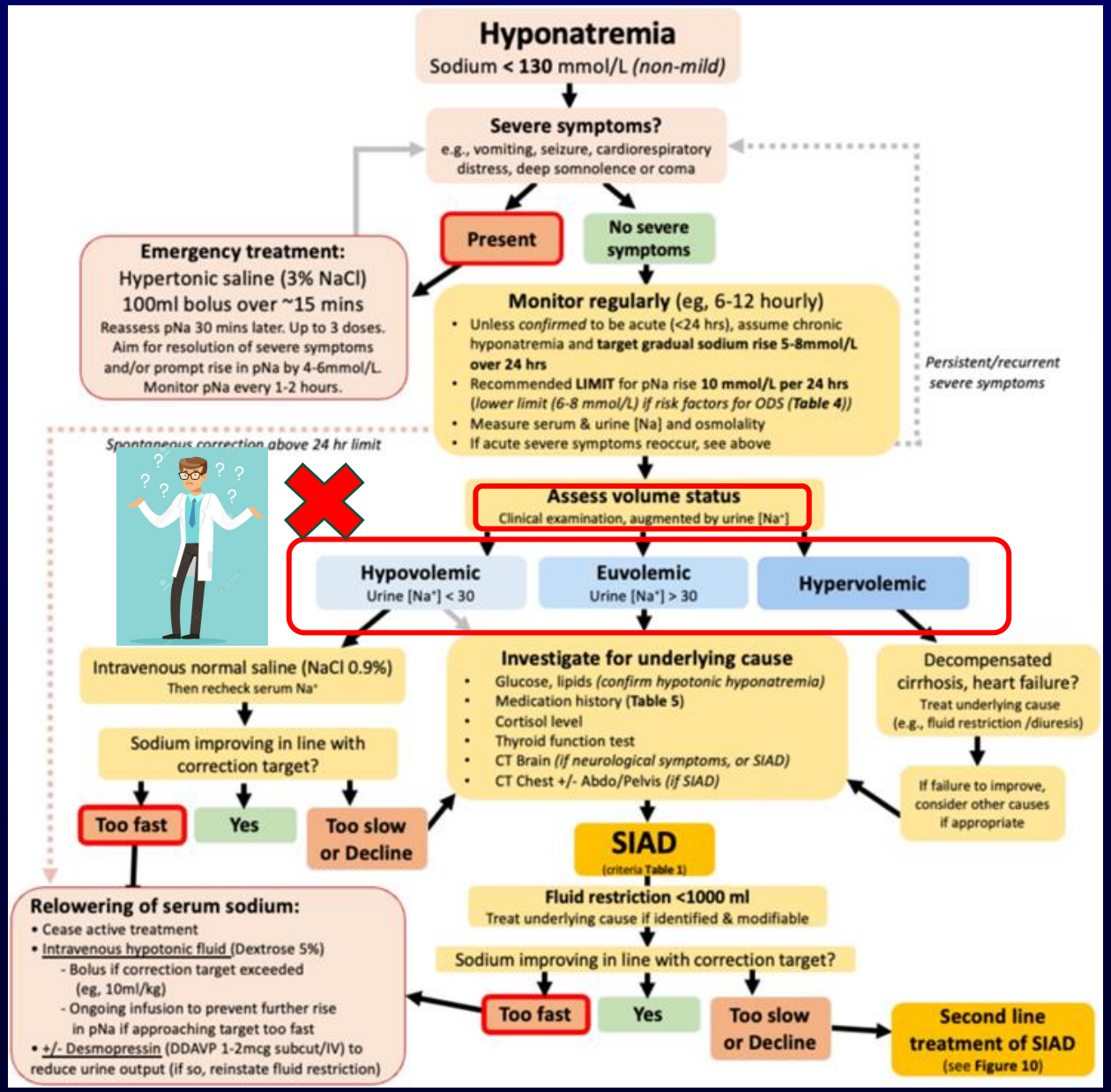
Review

Syndrome of Inappropriate Antidiuresis: From Pathophysiology to Management

Annabelle M Warren,[1,2] Mathis Grossmann,[1,2] Mirjam Christ-Crain,[3,4] and Nicholas Russell[1,2]





The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

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DOI: 10.1056/NEJMcp2210411
OCTOBER 19, 2023

Caren G. Solomon, M.D., M.P.H., *Editor*

The Syndrome of Inappropriate Antidiuresis

Horacio J. Adrogué, M.D., and Nicolaos E. Madias, M.D.

Table 1. Causes of the Syndrome of Inappropriate Antidiuresis (SIAD).*

Categories	Causes	Comments
Cancer	Pulmonary and mediastinal, nasopharyngeal, gastrointestinal, genitourinary	Most commonly observed in small-cell lung cancer (approximately 25% of the cases of SIAD that are caused by cancer), followed by head and neck cancer and olfactory neuroblastoma; ectopic production of AVP by some cancers has been documented (e.g., small-cell lung cancer and its metastases and olfactory neuroblastoma); tumor regression can reverse SIAD
Pulmonary conditions	Infections, asthma, acute respiratory failure	Most commonly seen in pneumonia of all causes; observed with positive-pressure ventilation
Central nervous system disorders	Mass lesions, infections, cerebrovascular accident, head trauma, pituitary surgery, acute psychosis	Develops in up to 56% of patients with subarachnoid hemorrhage and up to 35% of those with transsphenoidal pituitary surgery; a rare but treatable cause of rapidly progressive dementia, anti-LGI1 limbic encephalitis, leads to SIAD in 60 to 90% of patients
Drug-related	Stimulants of AVP release (e.g., opiates, ifosfamide, MDMA [also known as "ecstasy"], vincristine, and platinum compounds), enhancers of AVP effects (e.g., NSAIDs), AVP analogues (e.g., desmopressin and oxytocin), and stimulants of V2R (e.g., SSRIs, haloperidol, carbamazepine, cyclophosphamide, and chlorpropamide)	MDMA intoxication can result in severe hyponatremia because AVP stimulation is coupled with excessive ingestion of fluids on the users' belief that they can avoid the characteristic hyperthermia; desmopressin, prescribed for enuresis (nocturnal polyuria), can cause severe hyponatremia and occasionally osmotic demyelination syndrome; antidepressants are among the most common causes, especially in underweight older women (risk is highest with SSRIs and lowest with mirtazapine); high-dose intravenous cyclophosphamide can result in severe hyponatremia if large amounts of fluid are prescribed for prevention of hemorrhagic cystitis
Other	Exercise-associated, pain, stress, severe nausea, general anesthesia, postoperative state, gain-of-function variants in V2R gene (nephrogenic SIAD)	Prevention of exercise-associated hyponatremia requires that athletes drink only in response to thirst and avoid weight gain during exercise; in postoperative state, hyponatremia reflects combined effects of pain, stress, nausea, anesthesia, opiates, and hypotonic fluids; most cases of hereditary SIAD feature persistent activation of V2R (gene located on the X chromosome) that is unresponsive to vaptans
Idiopathic		Widely variable prevalence (17 to 60% of cases), most commonly reported in older patients; occasionally, an apparent idiopathic case has later been found to have been caused by occult tumor

* AVP denotes arginine vasopressin, LGI1 leucine-rich, glioma-inactivated 1 antibodies, MDMA 3,4-methylene-dioxymethamphetamine, NSAIDs nonsteroidal antiinflammatory drugs, SSRIs selective serotonin-reuptake inhibitors, and V2R vasopressin 2 receptor.

El SIAD, que anteriormente se denominaba síndrome de secreción inadecuada de hormona antidiurética (SIADH), sufrió un cambio de nombre debido a la identificación de un trastorno genético poco común conocido como SIAD nefrógeno (NSIAD).

Rondon-Berrios H. Diagnostic and Therapeutic Strategies to Severe Hyponatremia in the Intensive Care Unit. Journal of Intensive Care Medicine. 11 Oct. 2023.doi:10.1177/08850666231207334

Hyponatremia

Obtain clinical history and perform physical examination
Confirm hypotonic hyponatremia by excluding hyperglycemia and other causes of nonhypotonic hyponatremia

Hypotonic Hyponatremia

Clinically assess patient's volume status as euvolemic by excluding hypovolemia and hypervolemia

Euvolemic Hypotonic Hyponatremia

Establish presence of natriuresis (urine sodium, >30 mmol per liter) and inappropriate urine concentration (urine osmolality, >100 mOsm per kg of water; urine specific gravity, >1.003)
Rule out secondary adrenal insufficiency (normal early-morning serum cortisol and if equivocal, normal corticotropin stimulation test) and severe hypothyroidism (normal thyrotropin)

SIAD Diagnosed

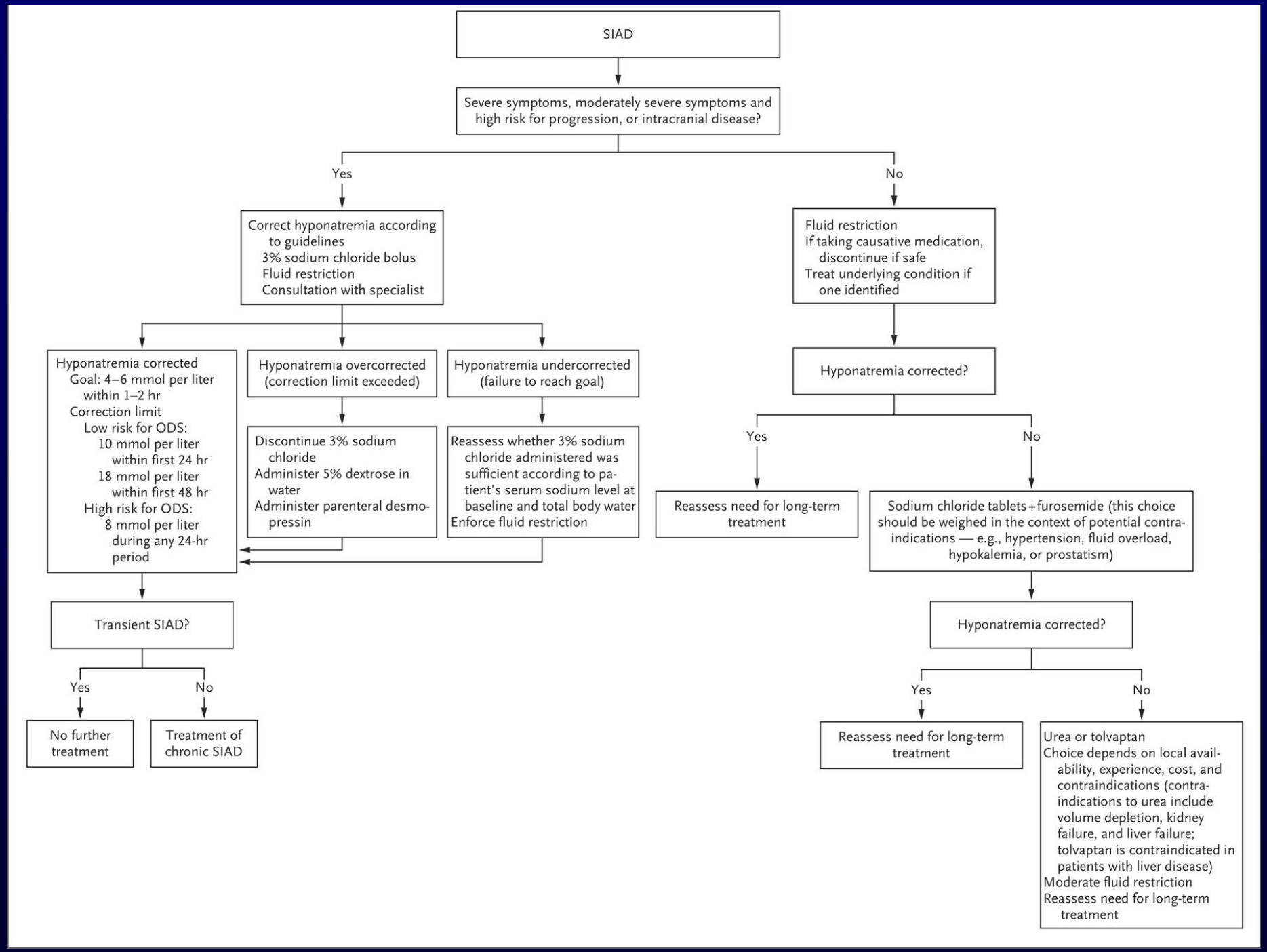
Review clinical history for potentially causative drugs and clues for underlying cause or causes; imaging dependent on clinical cues
Absent clinical clues, CT imaging of the head and chest; if negative, consider CT imaging of the abdomen and pelvis

If uncertainty about volume status persists, infusion of 1–2 liters of isotonic saline and assessing urine output and serum sodium can help resolve the question
Urine sodium reflects dietary salt intake; if patient has a very low salt intake, urine sodium would be <30 mmol per liter
Verify presence of normal kidney function and no recent use of diuretic agents
SIAD is a diagnosis of exclusion and requires ruling out secondary adrenal insufficiency and severe hypothyroidism
Measurement of serum AVP or copeptin, its surrogate, is not required for diagnosing SIAD

There are no formal guidelines regarding diagnostic body imaging; recommendations reflect expert opinion
If no cause is identified, SIAD is considered idiopathic

Table 2. Treatment Approaches.

Treatment	Mechanism	Amount or Dose	Efficacy	Adverse Effects	Comments
Fluid restriction	Reduces electrolyte-free water intake and total body water; should include all fluids, not just water	Moderate, <1.5 liters per day; severe, <1 liter per day	First-line treatment; difficult to adhere to and thus often ineffective	Increases thirst; may result in low caloric intake	Inexpensive and safe; predictors of failure at baseline include urine output of <1.5 liters per day, urine osmolality >500 mOsm per kg of water, and the sum of urine sodium and urine potassium levels exceeding the serum sodium level; contraindicated in subarachnoid hemorrhage and other intracranial processes
Sodium chloride supplement	Increases body sodium content, reduces electrolyte-free water intake, and increases water excretion	2–5 g per day (500 mg per tablet); frequently combined with furosemide 20 mg twice daily or equivalent loop diuretic to increase aquaresis	Limited long-term efficacy	Increases body sodium content, risking sodium and fluid excess; combining with furosemide can cause potassium depletion	Inexpensive; addition of sodium chloride plus furosemide to severe fluid restriction has no persistent benefit with respect to correction of serum sodium levels; contraindicated in hypertension, heart failure, and other sodium-retentive states
Urea	Increases electrolyte-free water excretion (by means of osmotic diuresis); decreases sodium excretion	15–60 g per day orally or enterally combined with moderate fluid restriction; 30 g of urea (500 mOsm) increases water excretion by 1 liter (for urine osmolality of 500 mOsm per kg of water)	Short- and long-term efficacy reported in observational studies	Nausea, diarrhea, and bitter taste; rare overly rapid correction of serum sodium, but osmotic demyelination not reported	Palatability is improved by dissolving in fruit juice or syrup (European guideline provides a recipe); citrus-flavored U.S. formulation (ure-Na) is available; initially used in Europe but more recently prescribed worldwide; contraindicated in volume depletion, kidney failure, and liver failure
Tolvaptan	Sole therapy that addresses underlying pathophysiology; competitive vasopressin receptor 2 blocker	15–60 mg per day orally combined with moderate fluid restriction; initiated in hospital to allow close monitoring of serum sodium (every 6–8 hr or more frequently depending on risk of osmotic demyelination syndrome) and dose adjustment; fluid restriction should not be used during the initial dose-finding phase to decrease risk of overly rapid correction of serum sodium; 7.5 mg per day appears as effective as 15 mg per day as a starting dose	Highly effective both in short- and long-term use; aquaretic response and increase in serum sodium correlate directly with severity of hyponatremia	Polyuria and increased thirst; overly rapid correction of serum sodium occurs in 13 to 25% of patients in real-life experience (appears to be exclusive to baseline serum sodium of <125 mmol per liter); sporadic cases of osmotic demyelination syndrome; 7.5-mg dose not associated with overly rapid correction in chronic SIAD	Food and Drug Administration warns against use for >30 days (on the basis of duration of pivotal trials) and in patients with liver disease; not recommended by the European guideline owing to risks of overly rapid correction of serum sodium level and hepatotoxicity; hepatotoxicity not observed in tolvaptan trials for hyponatremia, but reversible hepatotoxicity was reported in trials that used high doses of tolvaptan to alter course of polycystic kidney disease; cost is a barrier to use in some countries


SIAD
Severe symptoms, moderately severe symptoms and high risk for progression, or intracranial disease?
Yes
No
Correct hyponatremia according to guidelines
3% sodium chloride bolus
Fluid restriction
Consultation with specialist
Fluid restriction
If taking causative medication, discontinue if safe
Treat underlying condition if one identified
Hyponatremia corrected
Goal: 4–6 mmol per liter within 1–2 hr
Correction limit
Low risk for ODS:
10 mmol per liter within first 24 hr
18 mmol per liter within first 48 hr
High risk for ODS:
8 mmol per liter during any 24-hr period
Hyponatremia overcorrected (correction limit exceeded)
Hyponatremia undercorrected (failure to reach goal)
Discontinue 3% sodium chloride
Administer 5% dextrose in water
Administer parenteral desmopressin
Reassess whether 3% sodium chloride administered was sufficient according to patient's serum sodium level at baseline and total body water
Enforce fluid restriction
Hyponatremia corrected?
Yes
No
Reassess need for long-term treatment
Sodium chloride tablets+furosemide (this choice should be weighed in the context of potential contraindications — e.g., hypertension, fluid overload, hypokalemia, or prostatism)
Transient SIAD?
Hyponatremia corrected?
Yes
No
Yes
No
No further treatment
Treatment of chronic SIAD
Reassess need for long-term treatment
Urea or tolvaptan
Choice depends on local availability, experience, cost, and contraindications (contraindications to urea include volume depletion, kidney failure, and liver failure; tolvaptan is contraindicated in patients with liver disease)
Moderate fluid restriction
Reassess need for long-term treatment

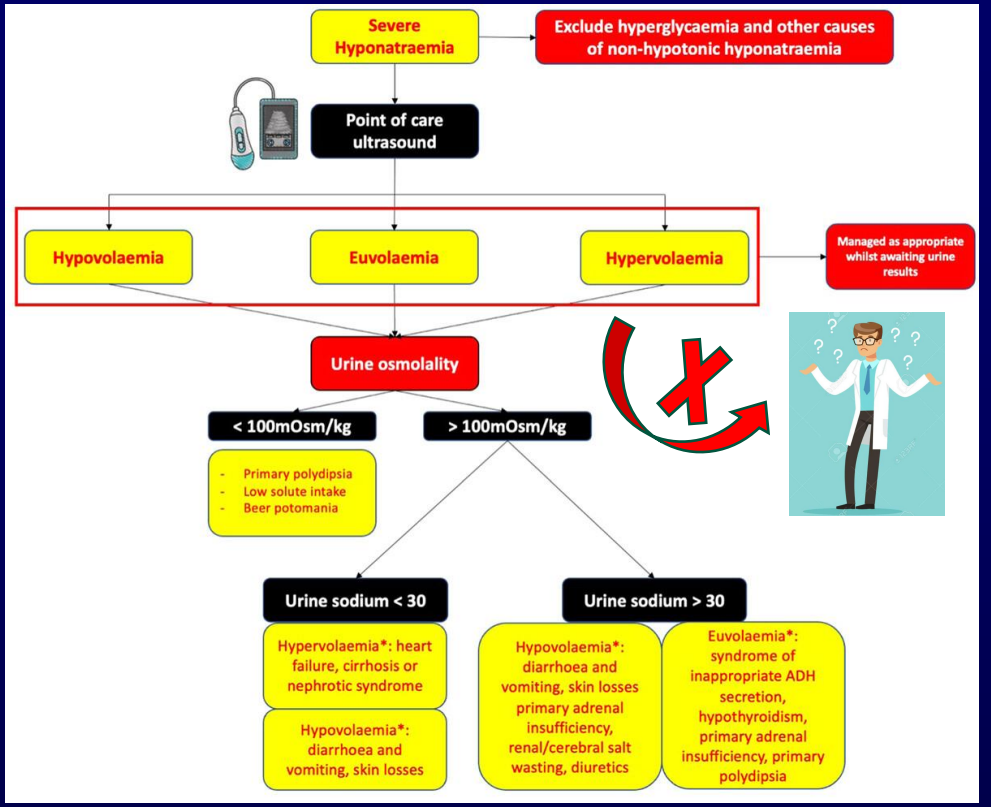
ORIGINAL ARTICLE | Open Access | CLINICAL ENDOCRINOLOGY | WILEY

Point-of-care ultrasound is a useful adjunct tool to a clinician's assessment in the evaluation of severe hyponatraemia

Latif R. Rahman, Eka Melson, Salam Al Alousi, Muhammad Sardar, Miles I. Levy, Shahriar Shafiq,
First published: 16 January 2024 | https://doi.org/10.1111/cen.15024

TABLE 1 Fluid assessments of patients admitted to Emergency Department and Acute Medical Unit.

No	Age (yrs)	Clinician assessment of fluid status	Point of care ultrasound (POCUS)	Initial fluid management	Final diagnosis	Modality in agreement with the final diagnosis
1	36	Hypo	Euvol	Appropriate	Polydipsia (Euvol)	POCUS
2	67[a]	Hypo	Hypo	Appropriate	Dehydration (Hypo)	Clinician + POCUS
3	75[a]	Euvol	Hypo	Appropriate	Polydipsia (Euvol)	Clinician
4	89[a]	Hypo	Hypo	Appropriate	Diuretics induced (Hypo)	Clinician + POCUS
5	71	Hypo	Hypo	Appropriate	Dehydration (Hypo)	Clinician + POCUS
6	85[a]	Hypo	Hypo	Not appropriate	Pneumonia (Hypo)	Clinician + POCUS
7	70	Hyper	Euvol	Appropriate	Heart failure (Hyper)	Clinician
8	82[a]	Hypo	Hyper	Not appropriate	Heart failure (Hyper)	POCUS
9	71	Hypo	Hyper	Appropriate	Heart failure (Hyper)	POCUS
10	52	Euvol	Euvol	Not appropriate	SIAD (Euvol)	Clinician + POCUS
11	68[a]	Hypo	Hypo	Appropriate	Dehydration (Hypo)	Clinician + POCUS
12	93[a]	Euvol	Euvol	Appropriate	Hypothyroid (Euvol)	Clinician + POCUS
13	85	Hypo	Euvol	Not appropriate	SIAD (Euvol)	POCUS
14	80[a]	Hypo	Euvol	Not appropriate	SIAD (Euvol)	POCUS
15	39	Hypo	Euvol	Not appropriate	Decompensated cirrhosis (Hyper)	POCUS
16	84[a]	Euvol	Hyper	Appropriate	SIAD (Euvol)	Clinician + POCUS
17	87[a]	Hypo	Euvol	Appropriate	Diuretics induced (Hypo)	Clinician
18	70[a]	Hypo	Hypo	Appropriate	Diuretics induced (Hypo)	Clinician + POCUS
19	59	Hypo	Euvol	Appropriate	SIAD (Euvol)	POCUS



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https://doi.org/10.1007/s10157-025-02624-9
Published online: 23 January 2025

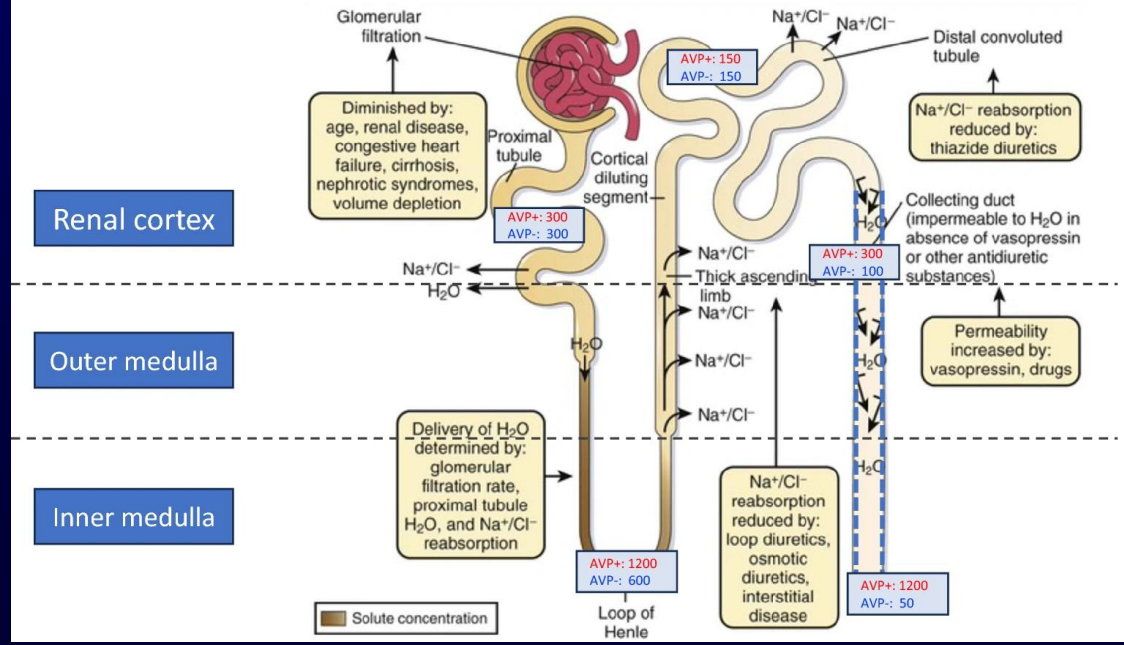
INVITED REVIEW ARTICLE

Pathophysiology, symptoms, outcomes, and evaluation of hyponatremia: comprehension and best clinical practice

Hirofumi Sumi[1,2] · Naoto Tominaga[1,2] · Yoshiro Fujita[3] · Joseph G. Verbalis[4] · and the Electrolyte Winter Seminar, Collaborative Group

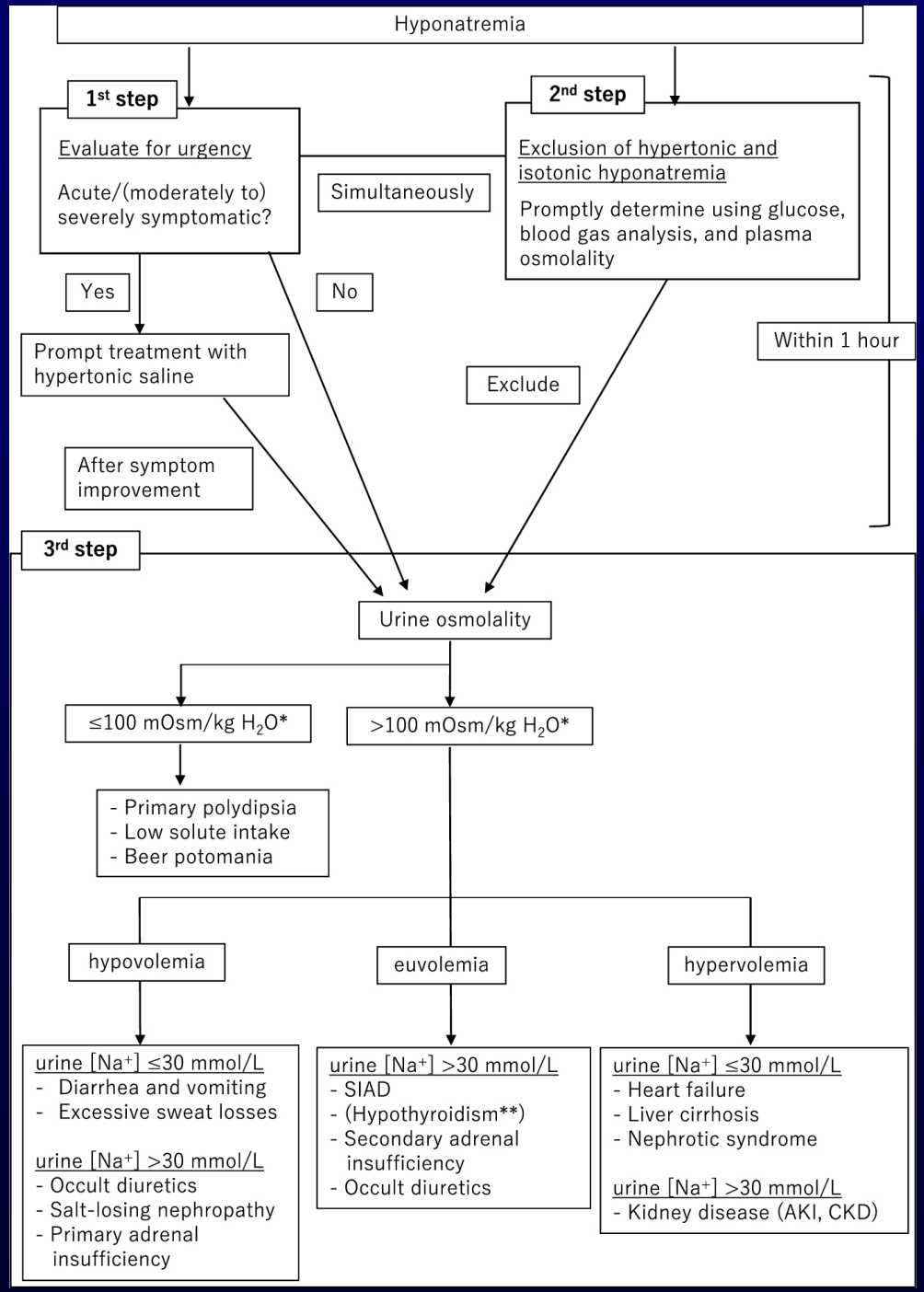
Elements of urinary dilution

1. **Sufficient urinary flow to distal nephron**
2. **Dilution in the thick ascending limb of loop of Henle**
3. **No AVP action in the renal collecting duct**



Interstitial osmolality	
Water diuresis (AVP-)	**Volume depletion (AVP+)**
300	300
300	300
300 ↓ ↓	300 ↓ 600
400 ↓ ↓ 600	800 ↓ ↓ 1200

(mOsm/kg H_2O)



CASO CLINICO 3

- ✓ Varón de 48 años con antecedentes de alcoholismo se presenta a la emergencia con hinchazón, enrojecimiento y dolor de la pierna derecha de 6 días de duración.
- ✓ Disconfort moderado por dolor. TA 100/70 mmHg, FC 88lpm, FR 15 rpm, T 38.9°C
- ✓ No ingurgitación yugular. La pierna derecha esta edematosa con eritema difuso y dolor a la palpación. Presencia de tinea pedis interdigital en ambos pies. La pierna izquierda no presenta edema. El examen cardiopulmonar y abdominal no presenta alteraciones significativas.
- ✓ Paciente despierto, orientado y sin signos neurológicos focales .

CASO CLINICO 3

- ✓ Sangre: Na 96 mEq/L, K 2 mEq/L, Cl 90 mEq/L, HCO3 24 mEq/L, Urea 7mg/dl, Creatinina 0,3mg/dl, Glucosa 96 mg/dl, Osmolalidad= 200mOsm/Kg

- ✓ Orina: UNa 23 mEq/L, UK 30 mEq/L, Osmolalidad =95 mOsm/Kg

- ✓ ECG : Ritmo sinusal. No ondas U

- ✓ El paciente se hospitaliza y se administra Oxacilina EV para celulitis, se le da una dieta regular con restricción de fluidos 800 mL/día y se administra un total de 400 mEq de cloruro de potasio.

Evolución clínica

Parámetro	Día # 1 (7am)	Día # 1 (7pm)	Día # 2 (7am)	Día # 2 (7pm)
Na sérico	96 mEq/L	115 mEq/L	122 mEq/L	135 mEq/L
Flujo Urinario	25 mL/h	100 mL/h	75 mL/h	60 mL/h
Osmolaridad urinaria	95 mOsm/Kg	45 mOsm/Kg	-	-

- ✓ Evolución es aparentemente normal con mejoría clínica
- ✓ Paciente es dado de alta con antibióticos vía oral el 4to día
- ✓ Paciente retorna por emergencia 4 días después del alta refieriendo disfagia. TAC de cráneo no muestra patología intracraneal aguda
- ✓ Paciente es hospitalizado y cuadro neurológico empeora desarrollando hiperreflexia , bradicinesia marcada y cuadriparesia. Se le realiza RMN cerebral que presenta una lesión en forma triangular en una zona central de la protuberancia con señal hiperintensa en T2 y Flair.

Cuál de las siguientes hubiese sido el manejo más apropiado cuando el Na+ sérico incrementó a 115 mEq/L durante el primer día de hospitalización?

A) Reponer pérdida horaria de orina con Dextrosa al 5% una vez que el Na+ sérico alcance la meta de corrección de 6 mEq/L

B) Reponer pérdida horaria de orina con Dextrosa al 5% una vez que el Na+ sérico alcance la meta de corrección de 8 mEq/L

C) Reinducir la hiponatremia con despromesina y Dextrosa al 5% hasta que el Na+ sérico alcance la meta de corrección de 6 mEq/L

D) Reinducir la hiponatremia con despromesina y Dextrosa al 5% hasta que el Na+ sérico alcance la meta de corrección de 8 mEq/L

ACID-BASE AND ELECTROLYTE TEACHING CASE AJKD

A Patient With Severe Hyponatremia and Hypokalemia: Osmotic Demyelination Following Potassium Repletion

Tomas Berl, MD,[1] and Asghar Rastegar, MD[2]

2010 Apr;55(4):742-8. doi: 10.1053/j.ajkd.2009.12.024.

Ecuación de Isidoro Edelman

$$\uparrow [Na^+]p = \frac{\uparrow Na^+ \text{ CorpTot} + \uparrow K^+ \text{ CorpTot}}{H_2O \text{ Corp.Total} \downarrow}$$

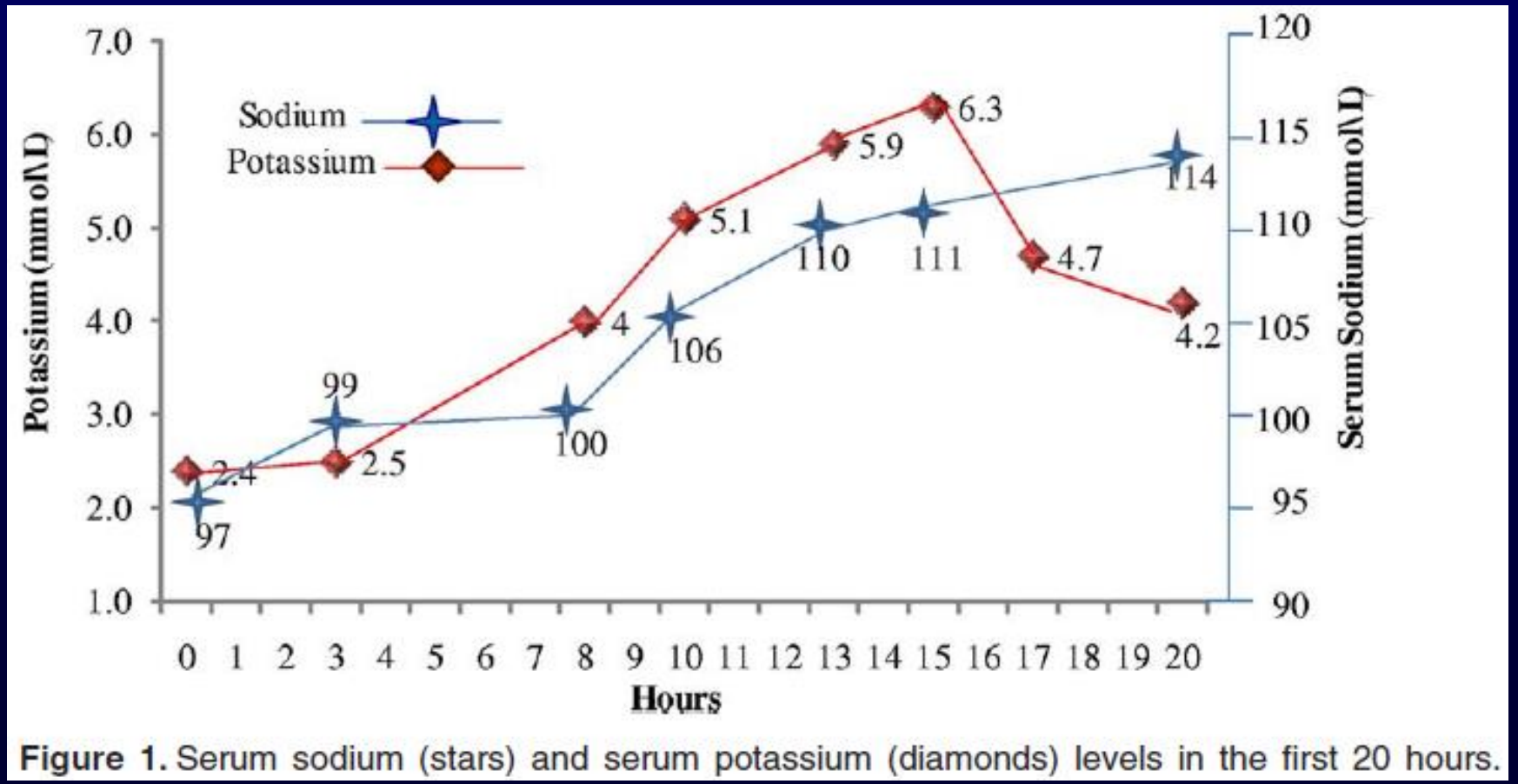


Figure 1. Serum sodium (stars) and serum potassium (diamonds) levels in the first 20 hours.

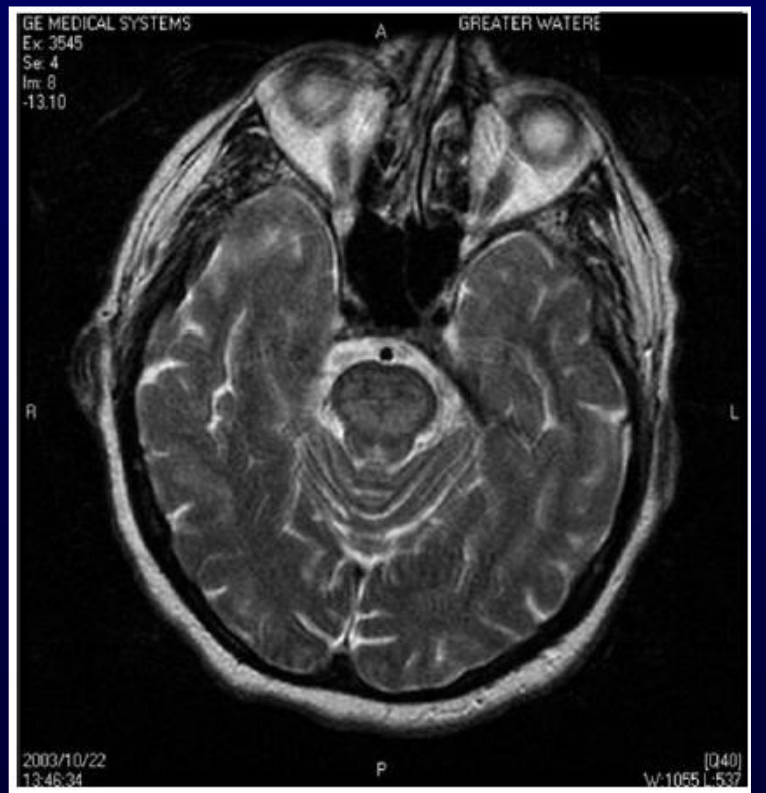


Figure 2. Magnetic resonance image of the brain on day 12 shows pontine myelolysis.

Factores de riesgo para el Síndrome de desmielinización osmótica (SDO)

- ✓ Na sérico menor a 105 mEq/L
- ✓ Alcoholismo
- ✓ Cirrosis hepática
- ✓ Desnutrición
- ✓ Hipokalemia
- ✓ Uso ambulatorio de diuréticos tiazídicos
- ✓ Sobrecorrección de hiponatremia crónica

Table 2. Risk Factors for Overcorrection of Hyponatremia.

Risk factor	Mechanism of water diuresis
Volume expansion in hypovolemia	Inhibition of AVP secretion
Glucocorticoid replacement in adrenal insufficiency	Inhibition of AVP secretion
Resolution of transient SIAD	Inhibition of AVP secretion
Discontinuation of desmopressin	Decreased V2 receptor stimulation
Initiation of vasopressin antagonists	Decreased kidney responsiveness to AVP
Discontinuation of thiazide diuretics	Restoring DCT diluting capacity
Administration of solutes in low solute intake	Increasing osmolar excretion rate

Rondon-Berrios H. Diagnostic and Therapeutic Strategies to Severe Hyponatremia in the Intensive Care Unit. Journal of Intensive Care Medicine. 11 Oct. 2023.doi:10.1177/08850666231207334

George JC, Zafar W, Bucaloiu ID, Chang AR. Risk factors and outcomes of rapid correction of severe hyponatremia. Clin J Am. Soc Nephrol. 2018;13(7):984-992.

Annals of Internal Medicine®
Original Research | 19 December 2023 https://doi.org/10.7326/M23-1989

Cumulative Incidence of Thiazide-Induced Hyponatremia:

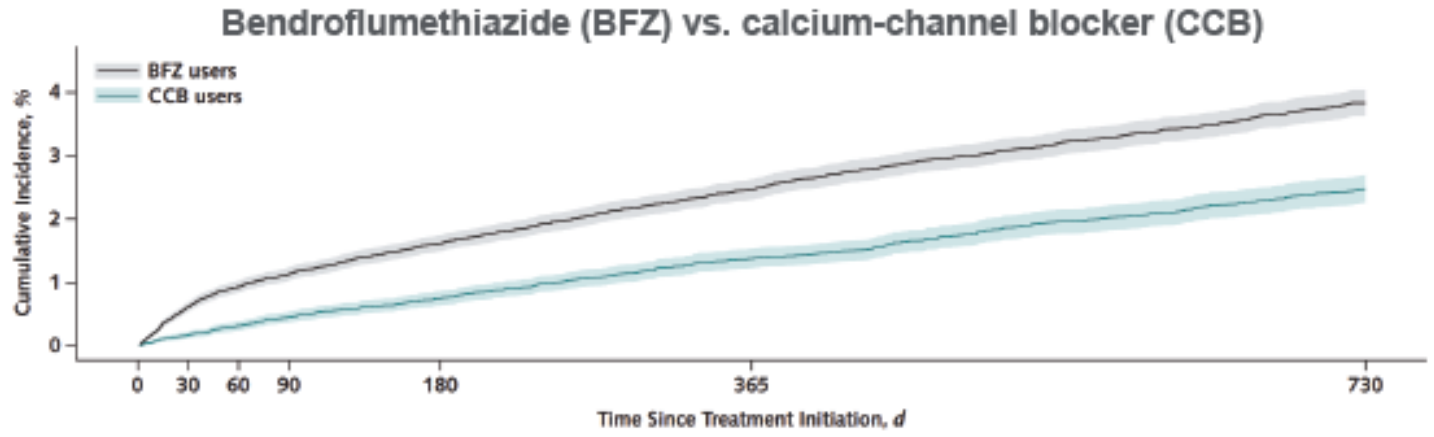
A Population-Based Cohort Study

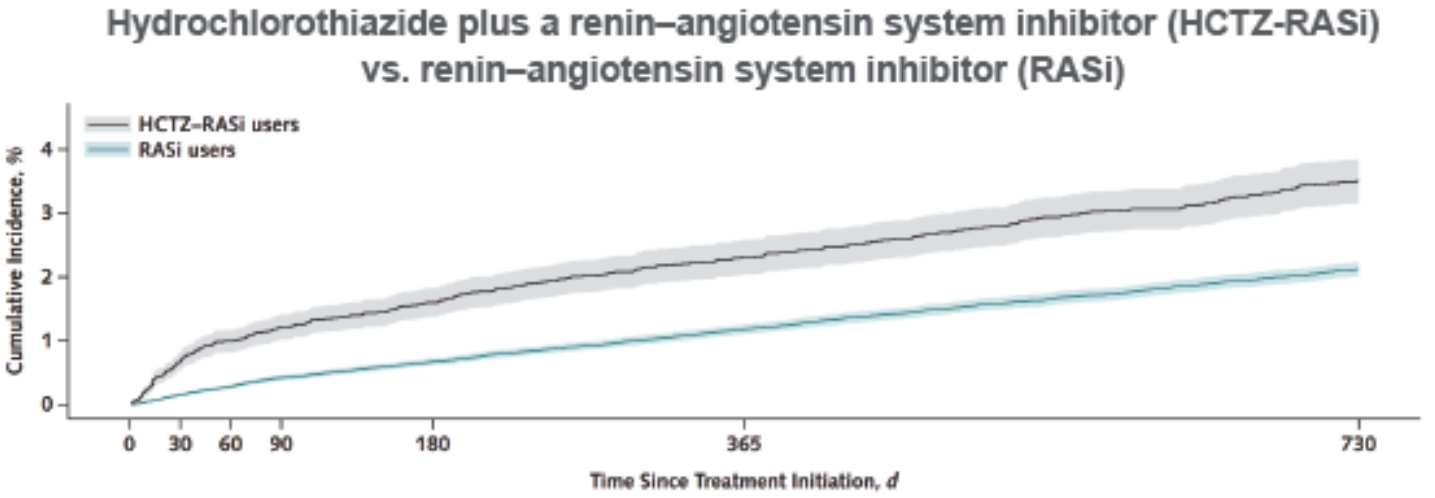
Authors: Niklas Worm Andersson, MD, Jan Wohlfahrt, DMSc, Bjarke Feenstra, PhD, Anders Hviid, DMSc

Denmark, January 2014–October 2018

- Patients aged ≥ 40 years
- New users of antihypertensive drugs
- No prior hyponatremia

How does the incidence of hyponatremia compare in patients receiving antihypertensive therapy with thiazide versus nonthiazide antihypertensive drugs?





- ✓ El nuevo uso de diuréticos tiazídicos sugiere un riesgo excesivo sustancial de hiponatremia que es mayor que el indicado en la etiqueta del medicamento.
- ✓ El riesgo es particularmente pronunciado durante los primeros meses de tratamiento y en personas mayores o con comorbilidades.
- ✓ Estos hallazgos sugieren que la hiponatremia es una reacción adversa común al tratamiento con tiazidas y resaltan la necesidad continua de concientización clínica, así como de monitoreo de esta reacción adversa al medicamento.

THE AMERICAN JOURNAL of MEDICINE®

Diagnosis, Evaluation, and Treatment of Hyponatremia: Expert Panel Recommendations

http://dx.doi.org/10.1016/j.amjmed.2013.07.006

Joseph G. Verbalis, MD,[a] Steven R. Goldsmith, MD,[b] Arthur Greenberg, MD,[c] Cynthia Korzelius, MD,[d]

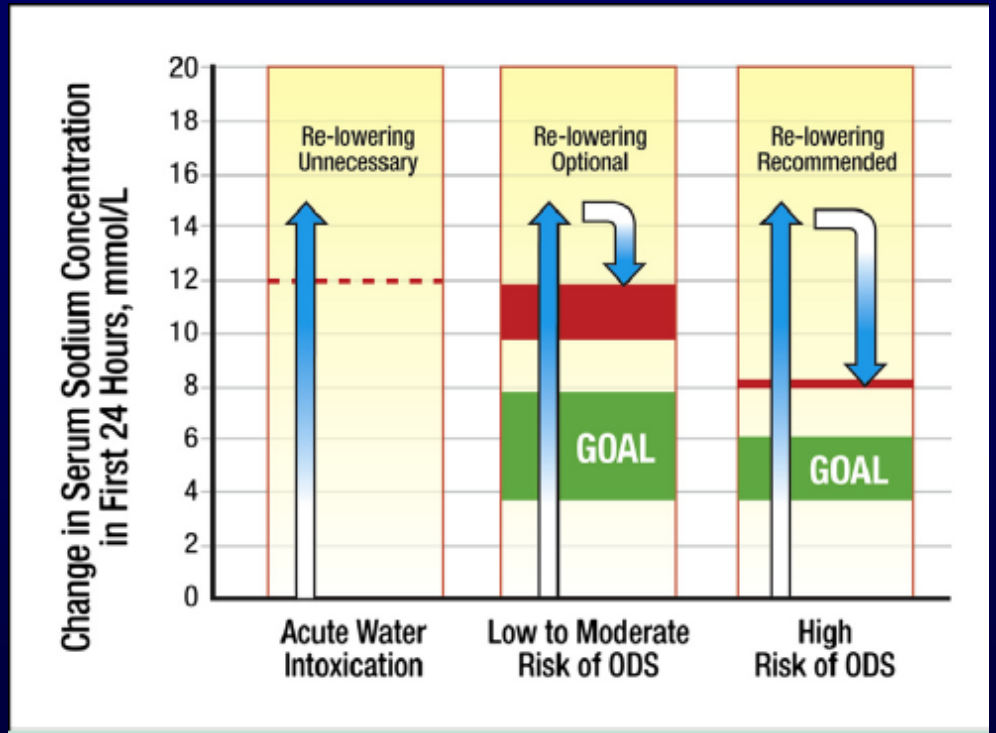


Figure 3 Recommendations for relowering of serum sodium concentration ($[Na^+]$) to goals (green) for patients presenting with serum $[Na^+]$ <120 mmol/L who exceed the recommended limits of correction (red) in the first 24 hours. Abbreviations: L = liter; mmol = millimole; ODS = osmotic demyelination syndrome.

Objetivos de corrección del Na Sérico

-Riesgo promedio de SDO

✓ Δ Na ≤10 mEq/L en 24 horas

-Alto riesgo de SDO

✓ Δ Na ≤8 mEq/L en 24 horas

✓ **4-6 mEq/L** en 24 horas para hiponatremia aguda o crónica

Original Investigation

Kidney360

Osmotic Demyelination Syndrome following Correction of Hyponatremia by ≤10 mEq/L per Day

Srijan Tandukar,[1] *Richard H. Sterns*,[2] *and Helbert Rondon-Berrios*[3]

KIDNEY360 2: 1415–1423, 2021. doi: https://doi.org/10.34067/KID.0004402021

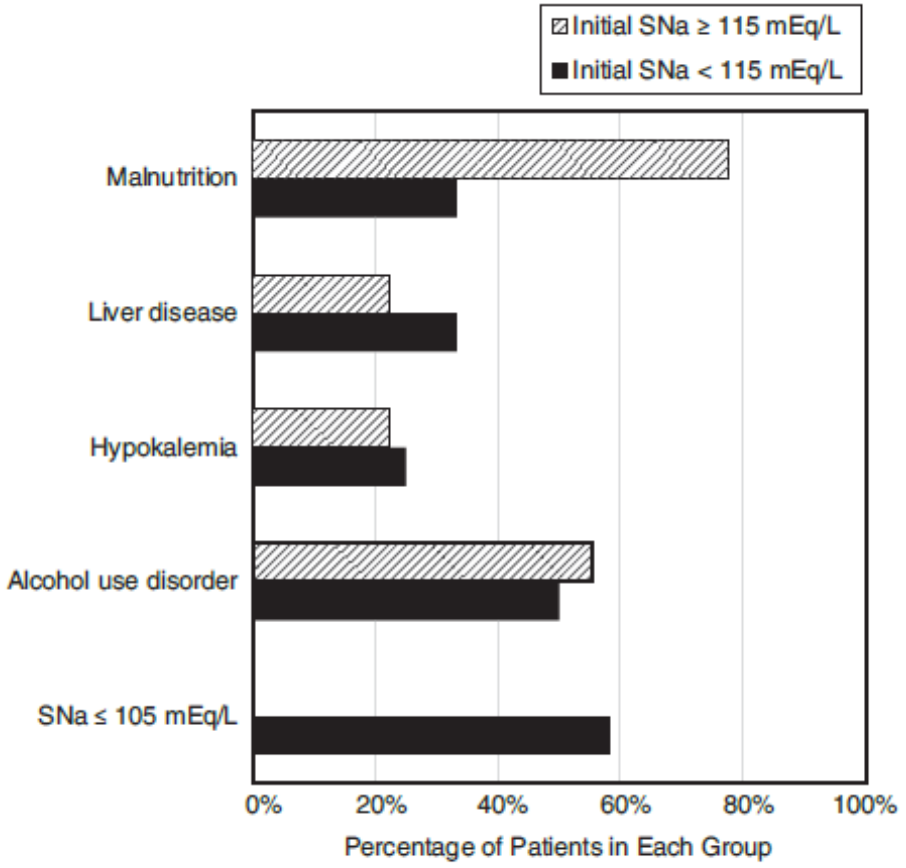


Figure 2. | Risk factors for osmotic demyelination syndrome in reported cases based on initial serum sodium.

- ✓ El SDO puede ocurrir a pesar del cumplimiento de las pautas de corrección de hiponatremia actuales, especialmente en pacientes con **Na <115** mEq / L.
- ✓ Límite de corrección de Na <8 mEq / L en 24 h en para minimizar el riesgo de SDO.
- ✓ Se debe considerar la suplementación con Tiamina para cualquier paciente hiponatrémico cuya ingesta dietética haya sido deficiente.

Kidney Med Vol 7 | Iss 3 | March 2025 | 100953
https://doi.org/10.1016/j.xkme.2024.100953
Original Research
Kidney Medicine

Hyponatremia Correction and Osmotic Demyelination Syndrome Risk: A Systematic Review and Meta-Analysis

Supawadee Suppadungsuk, Pajaree Krisanapan, Sara Kazeminia, Nasrin Nikravangolsefid,

- ✓ La corrección rápida >8 mmol/L/24 h tuvo una correlación estadística con un mayor riesgo de SDO.
- ✓ La corrección rápida de sodio ocurrió en el 21.5% de los pacientes con hiponatremia.
- ✓ La incidencia general de SDO fue del 0.23% y del 0.73% entre aquellos con corrección rápida de sodio

Study or Subgroup	Rapid rate Events	Rapid rate Total	Non-rapid rate Events	Non-rapid rate Total	Weight	Risk Ratio IV, Random, 95% CI	Year
Sterns 1986	8	41	0	19	5.6%	8.10 [0.49, 133.39]	1986
Stern 1987	3	34	0	26	5.2%	5.40 [0.29, 100.16]	1987
Sterns 1994	3	43	0	13	5.3%	2.23 [0.12, 40.54]	1994
Heng 2007	3	10	4	12	17.4%	0.90 [0.26, 3.11]	2007
Vu 2009	4	37	0	218	5.3%	51.87 [2.85, 943.96]	2009
Geohegan 2015	1	114	0	298	4.4%	7.80 [0.32, 190.09]	2015
Gorge 2018	7	606	1	884	8.9%	10.21 [1.26, 82.78]	2018
Park 2019	4	43	0	82	5.3%	16.98 [0.94, 308.17]	2019
Mustajoki 2023	2	104	3	280	11.3%	1.79 [0.30, 10.59]	2023
MacMillan 2023	5	3632	7	16940	18.8%	3.33 [1.06, 10.49]	2023
Seethapathy 2023	2	1067	5	2207	12.6%	0.83 [0.16, 4.26]	2023
Total (95% CI)		**5731**		**20979**	**100.0%**	**3.16 [1.54, 6.49]**	
Total events	42		20				

Heterogeneity: $Tau^2 = 0.37$; $Chi^2 = 13.68$, df = 10 (P = 0.19); $I^2 = 27\%$
Test for overall effect: Z = 3.14 (P = 0.002)

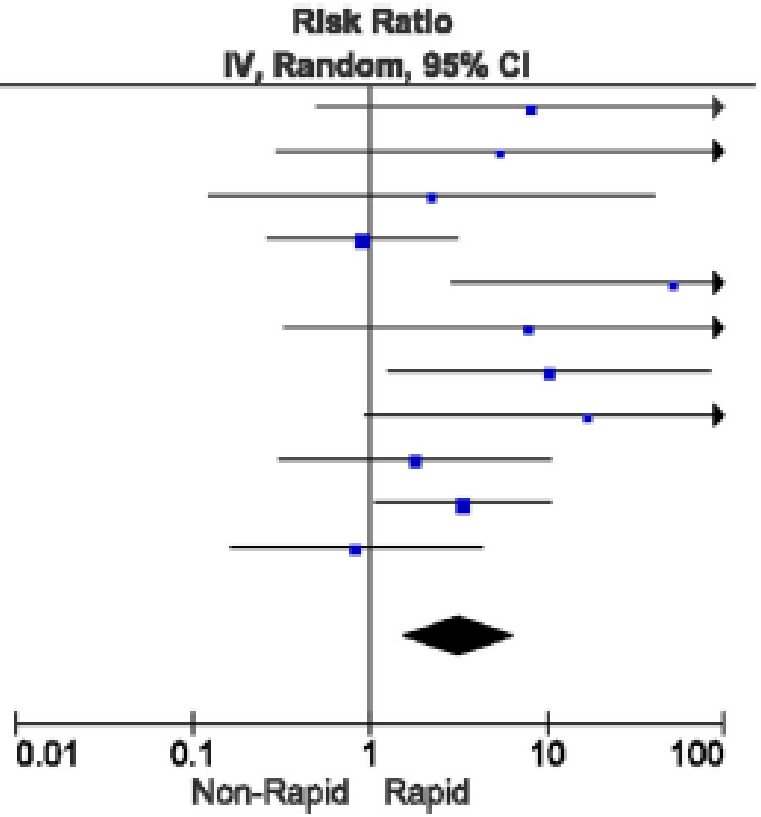


Figure 2. Forest plots of all included studies assessing the ODS outcome and rate of serum sodium correction among hospitalized hyponatremia patients.

Review

Hyponatremia in the Neurologically Ill Patient: A Review

SAGE 2020

David P. Lerner, MD[1], Starane A. Shepherd, MD[2], and Ayush Batra, MD[3]

DOI: 10.1177/1941874419895124

Table 4. Recommendations on Treatment of Hyponatremia.

		US Recommendations	European Recommendations
Severe symptoms	Self-induced acute water intoxication, known duration <24-48, intracranial pathology or increased intracranial pressure, seizures, or coma Vomiting, cardiorespiratory distress, abnormal or deep somnolence, seizure, and coma	100 mL 3% NaCl bolus over 10 minutes up to 3 doses to manage symptoms	150 mL 3% NaCl bolus over 20 minutes. Recheck Na and repeat 150 mL 3% NaCl bolus Goal Na rise 10 mmol/L/d, then 8 mmol/L/d, and thereafter to 130 mmol/L/d • If no increase can repeat • If no improvement 3% NaCl with goal 1 mEq/L/h to <10 total increase
Mild to moderate symptoms	At-risk Na <120 mEq/L of >48 hours duration. Nausea without emesis, confusion, and headache	3% NaCl infusion at 0.5-2 mL/kg/h	250 mL 3% NaCl bolus over 20 minutes. Goal 5 mEq/L increase over 24 hours
Chronic hyponatremia		Minimum correction of Na 4-8 mEq/L, and if high risk, then 4-6 mEq/L	Avoid increase >10 mEq/L in the first 24 hours, then >8 mEq/L daily
Acute hyponatremia without symptoms			Stop fluids or the factors contributing to hyponatremia If Na decrease >10 mEq/L, treatment with 150 mL 3% NaCl over 20 minutes.

Table 3. Differentiating Cerebral Salt Wasting and Syndrome of Inappropriate Antidiuretic Hormone.

	Cerebral Salt Wasting	Syndrome of Inappropriate Antidiuretic Hormone
Extracellular volume status	Decreased	Unchanged
Heart rate	Unchanged to increased	Unchanged
Body weight	Decreased	Unchanged
Urine output	Unchanged to increased	Unchanged to decreased
Hematocrit	Increased (relative to baseline)	Unchanged
Blood urea nitrogen	Increased	Unchanged
Serum bicarbonate	Increased	Unchanged
Serum urate	Unchanged to decreased	Unchanged
Urine osmolality	>100 mOsm/kg	>100 mOsm/kg
Urine Na excretion	>40 mmol/L	>40 mmol/L

Table 2. Medications Associated With Syndrome of Inappropriate Antidiuretic Hormone.

Antiepileptic Medications
- Carbamazepine
- Lamotrigine
- Oxcarbazepine
- Sodium valproate

Oncologic Medications
- Alkylating agents (cyclophosphamide)
- Ifosfamide
- Imatinib
- Methotrexate
- Platinum (cisplatin)
- Vinca alkaloids (vincristine)

Pain Medications
- Non-steroidal anti-inflammatory
- Opiates

Psychiatric Medications
- Butyrophenones (haloperidol)
- Monoamine oxidase inhibitors
- Phenothiazine (fluphenazine, chlorpromazine)
- Risperidone
- Selective Serotonin Reuptake Inhibitors
- Tricyclic antidepressants
- Venlafaxine

Miscellaneous
- Amiodarone
- Bromocriptine
- Ciprofloxacin
- Desmopressin or Vasopressin
- Ecstasy (methylenedioxy methamphetamine)
- Interferon-alpha

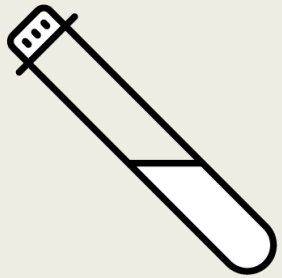
JAMA Internal Medicine

Estudio SALSA

RCT: Risk of Overcorrection in Rapid Intermittent Bolus vs Slow Continuous Infusion for Symptomatic Hyponatremia

POPULATION

80 Men, 98 Women

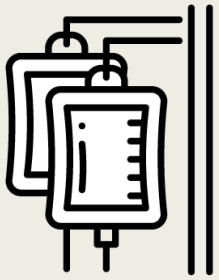


Adults aged >18 y with symptoms of hyponatremia and glucose-corrected serum sodium ≤125 mmol/L

Mean (SD) age: 73.1 (12.2) y

INTERVENTION

178 Patients randomized

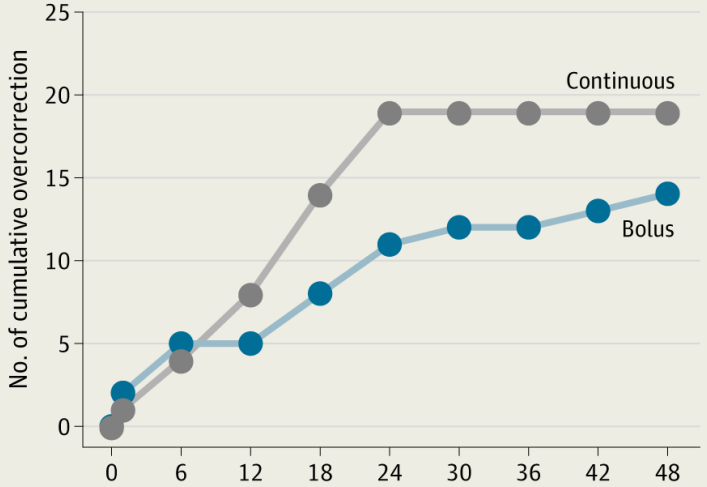


87 Rapid intermittent bolus
Hypertonic saline, 3%, infusion of 2 mL/kg over 20 min every 6 h

91 Slow continuous infusion
Hypertonic saline, 3%, continuous infusion at a rate of 0.5-1 mL/kg/h

FINDINGS

Both rapid intermittent bolus and slow continuous infusion for treating symptomatic hyponatremia are effective and safe with no difference in overcorrection risk (17.2% vs 24.2%, respectively; absolute risk difference, −6.9% (95% CI, −18.8% to 4.9%); *P* = .26)



SETTINGS / LOCATIONS

3 General hospitals in the Republic of Korea

PRIMARY OUTCOME

Overcorrection at any given period, defined as increase in serum sodium level by >12 mmol/L within 24 h or >18 mmol/L within 48 h

Hubo más pacientes en el grupo de bolo que alcanzaron el objetivo de PNa en 1 hora y tuvieron una menor incidencia de reducción terapéutica de PNa.

Baek SH, Jo YH, Ahn S, et al. Risk of overcorrection in rapid intermittent bolus vs slow continuous infusion therapies of hypertonic saline for patients with symptomatic hyponatremia: the SALSA randomized clinical trial. *JAMA Intern Med.* Published online October 26, 2020. doi:10.1001/jamainternmed.2020.5519

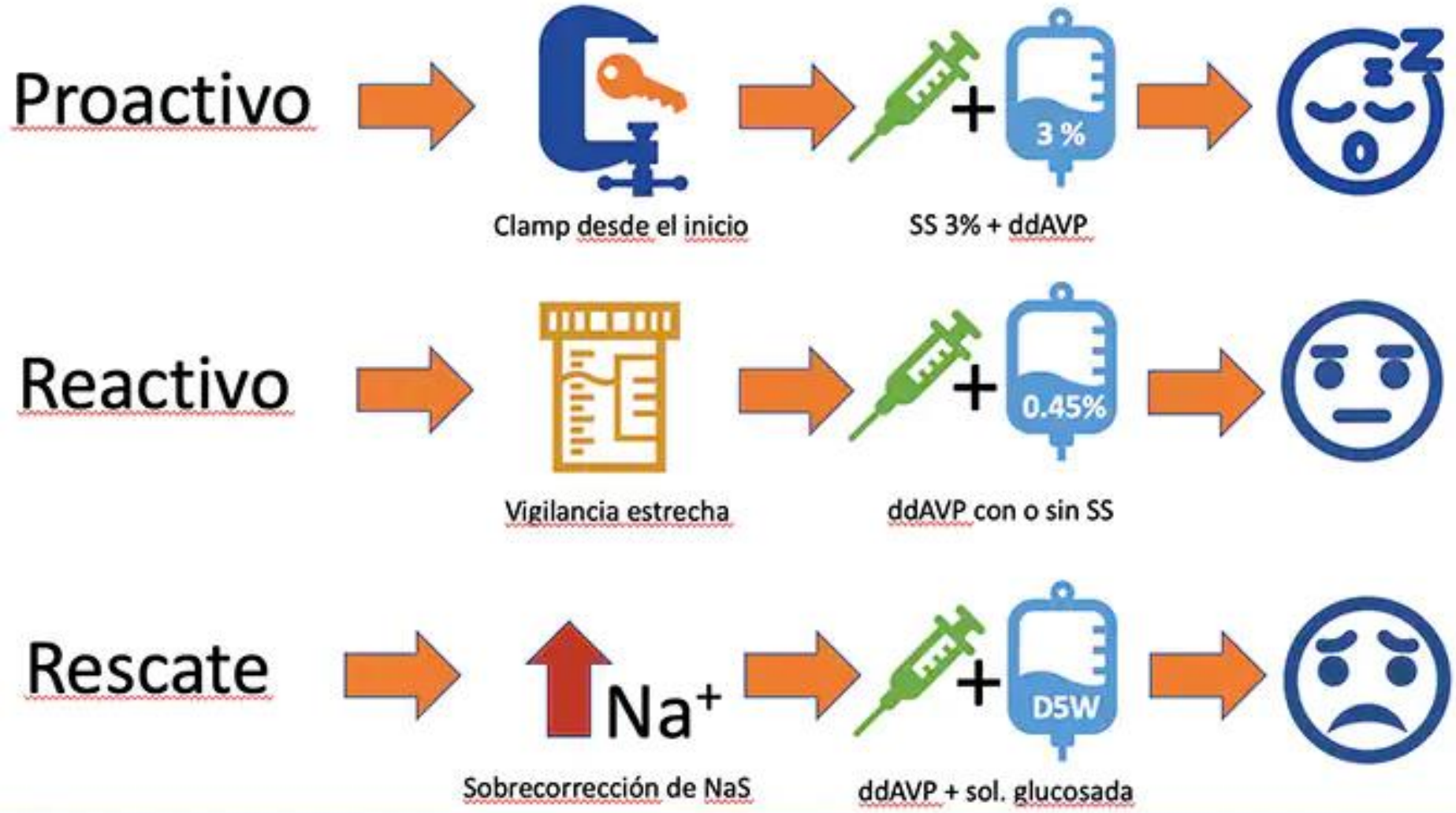
Table 2. Strategies to Prevent and Treat Overly Rapid Correction of Hyponatremia Using Desmopressin

Strategy	Indications	Description
Proactive ("DDAVP clamp")	Start immediately when PNa <120 mEq/L AND: • High risk for rapid correction*, AND/OR • High risk for ODS†	• Desmopressin 2 – 4 mcg IV/SC every 6 – 8 h, AND • NaCl 3% 100 mL bolus for seizures, coma, or rapidly falling PNa‡, OR • NaCl 3% 1 – 1.5 mL/kg IV over 6 h (to increase PNa by ≈ 1 mEq/L every 6 h)
Reactive	Worrisome PNa trajectory: • PNa goal of 6 mEq/L in a 24-h period has been achieved, AND/OR • UOP > 1 mL/kg/h	• Desmopressin 2 – 4 mcg IV/SC every 6 – 8 h
Rescue	Overly rapid correction of hyponatremia has already occurred: • Increase in PNa ≥ 8 mEq/L in any 24-h period	• Desmopressin 2 – 4 mcg IV/SC every 6 – 8 h, AND • Dextrose 5% in water 3 mL/kg IV (to decrease PNa by ≈ 1 mEq/L) until PNa is just below the correction limit

Abbreviations: IV, intravenously; ODS, osmotic demyelination syndrome; PNa, plasma sodium; SC, subcutaneously; SIAD, syndrome of inappropriate antidiuresis; UOP, urine output.

Workeneh, Biruh T et al. "Hyponatremia Demystified: Integrating Physiology to Shape Clinical Practice." Advances in kidney disease and health vol. 30,2 (2023): 85-101. doi:10.1053/j.akdh.2022.11.004

Estrategias para el uso de ddAVP:



Cortesía: Dr. Alejandro Yared Meraz Muñoz

Journal of
Clinical Medicine

Review

Adaptation of the Brain to Hyponatremia and Its Clinical Implications

Fabrice Gankam Kengne https://doi.org/10.3390/jcm12051714 Published: 21 February 2023

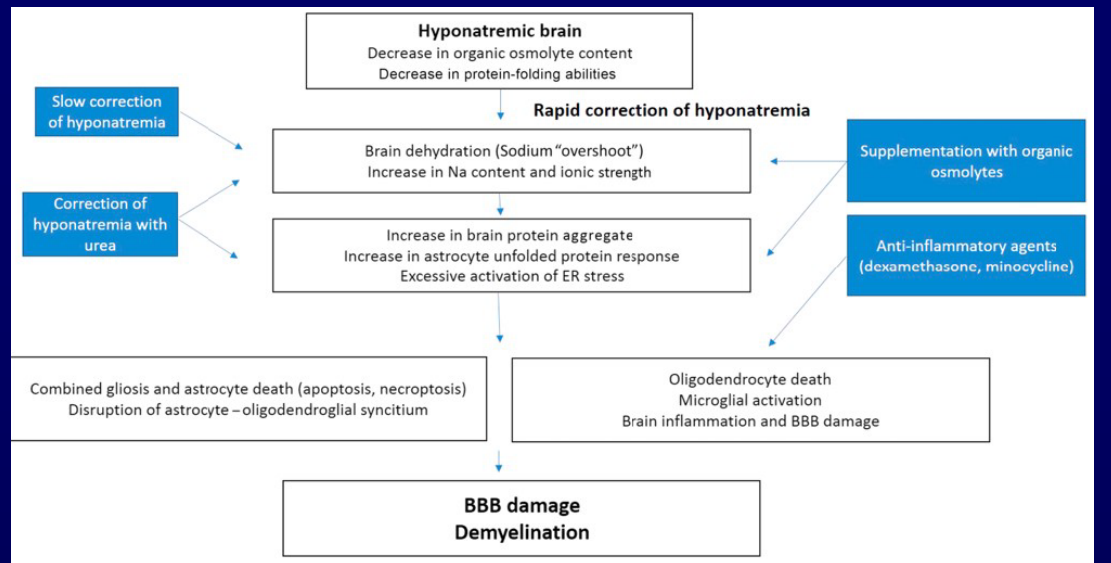
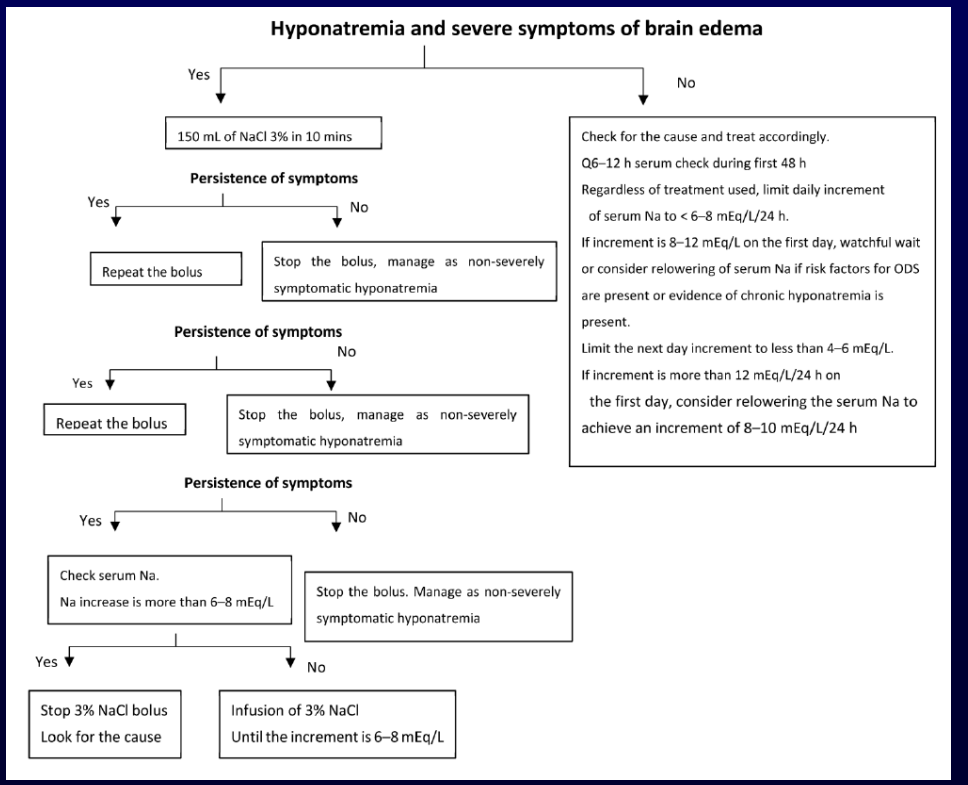


Figure 2. Proposed model for the physiopathology of osmotic demyelination syndrome.

Table 2. Proposed approach for the treatment of severe hyponatremia.

Treatment of Severe Hyponatremia	
Signs or symptoms of Brain Edema	**No signs or symptoms of brain edema**
ICU admission	Etiological evaluation
Hypertonic saline boluses (100 mL NaCl 3%)	Determine chronicity (>48 h)
Repeat if symptoms persist	Assess for risk factors for ODS (chronic hyponatremia, hypokalemia, liver disease, alcoholism)
Measure serum Na q1–2 h	Treatment of the cause and avoid hypertonic saline
Stop when symptoms abate	If risk factors for ODS are present
Stop when sodium increment is 6 mEq/L	q6–12 h serum Na check
Keep checking serum Na q3–4 h	Limit increment of Na to < 6 mEq/L/24 h *
	If no risk factors for ODS
	Limit increment of Na to < 8 mEq/L/24 h *
	Additional measures:
	If SIADH, use of urea is better
	Relower the serum Na if increment of > 12 mEq/L/day
	Desmopressin + D5W



Current Heart Failure Reports
https://doi.org/10.1007/s11897-024-00651-3 Published online: 27 February 2024

REVIEW

Evaluation and Management of Hyponatremia in Heart Failure

Giulio M. Mondellini[1,2] · Frederik H. Verbrugge[2,3]

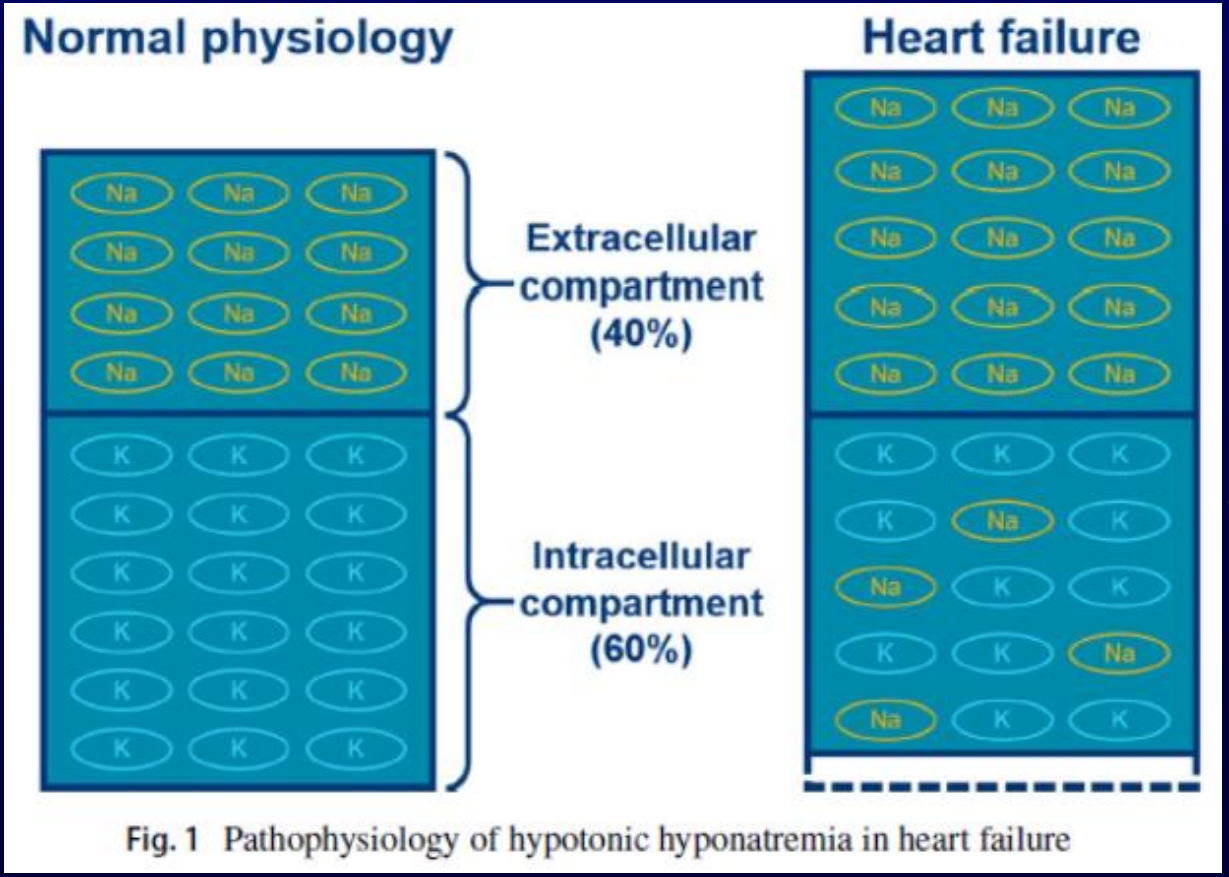
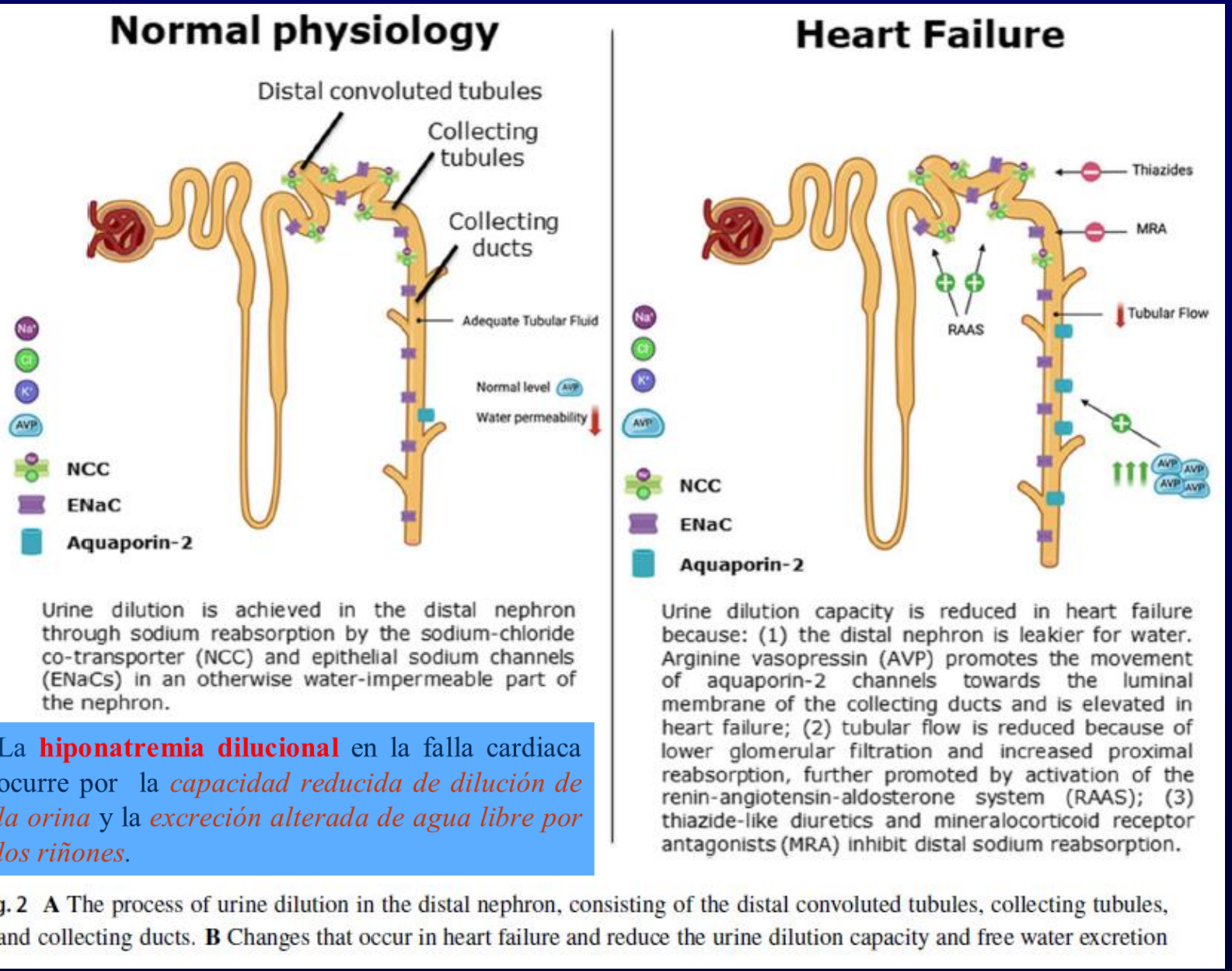


Fig. 1 Pathophysiology of hypotonic hyponatremia in heart failure

Causes of Hyponatremia in Patients with Heart Failure

1. Continued release AVP despite a reduction in osmolality due to the following reasons:
   - Low cardiac output
   - Decreased renal blood flow
   - Reduced baroreceptor stimulation mediated by low blood pressure
2. Low cardiac output leads to activation of RAAS and increase in angiotensin II levels, potent stimuli to thirst, resulting in enhanced water intake
3. Medications used to treat heart failure, hypertension, or cardiac-related conditions
   - Diuretics (especially thiazides, less commonly aldosterone antagonists, amiloride, loop diuretics)
4. Hyponatremia in the setting of advanced CKD/ESRD due to Cardiorenal syndromes
   - Hypotonic hyponatremia due to increased free water intake in the setting of low GFR

- ✓ Alteración de la excreción de agua
- ✓ Expansión del volumen extracelular
- ✓ Depleción del volumen intracelular
- ✓ Desplazamiento del sodio intracelular
- ✓ Depleción de potasio (y magnesio)
- ✓ Raro: verdadera depleción de sodio con diuresis exagerada



La **hiponatremia dilucional** en la falla cardiaca ocurre por la *capacidad reducida de dilución de la orina* y la *excreción alterada de agua libre por los riñones*.

Fig. 2 **A** The process of urine dilution in the distal nephron, consisting of the distal convoluted tubules, collecting tubules, and collecting ducts. **B** Changes that occur in heart failure and reduce the urine dilution capacity and free water excretion

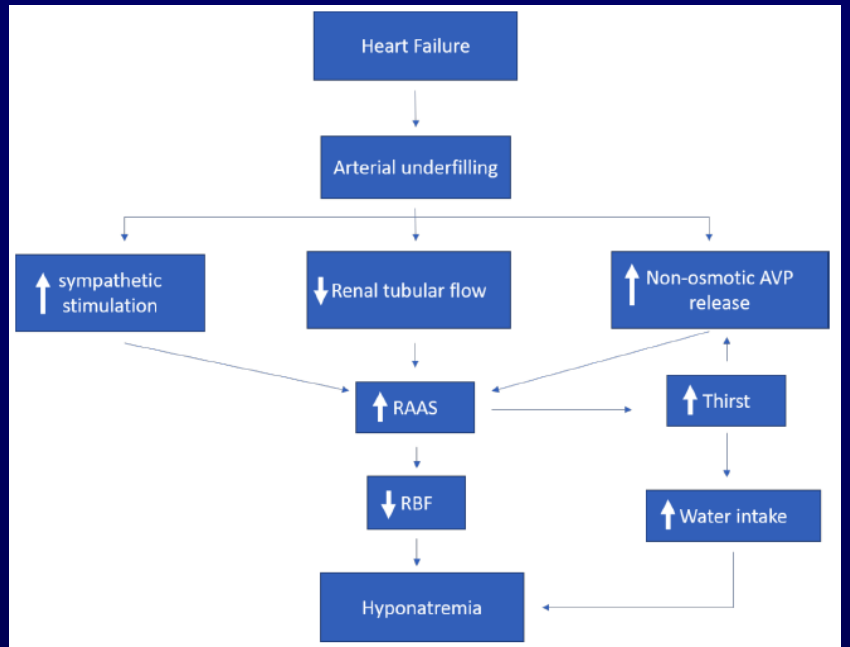


Fig. (1). Pathophysiology of dilutional hyponatremia in heart failure.

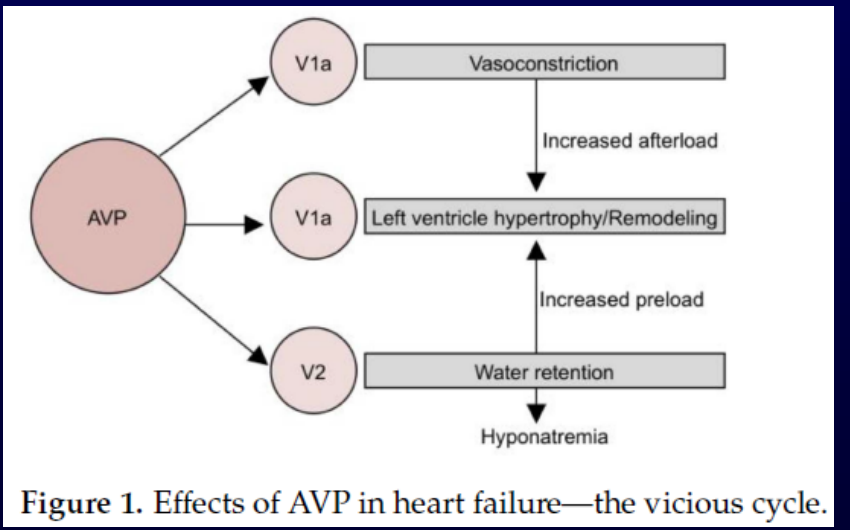


Figure 1. Effects of AVP in heart failure—the vicious cycle.

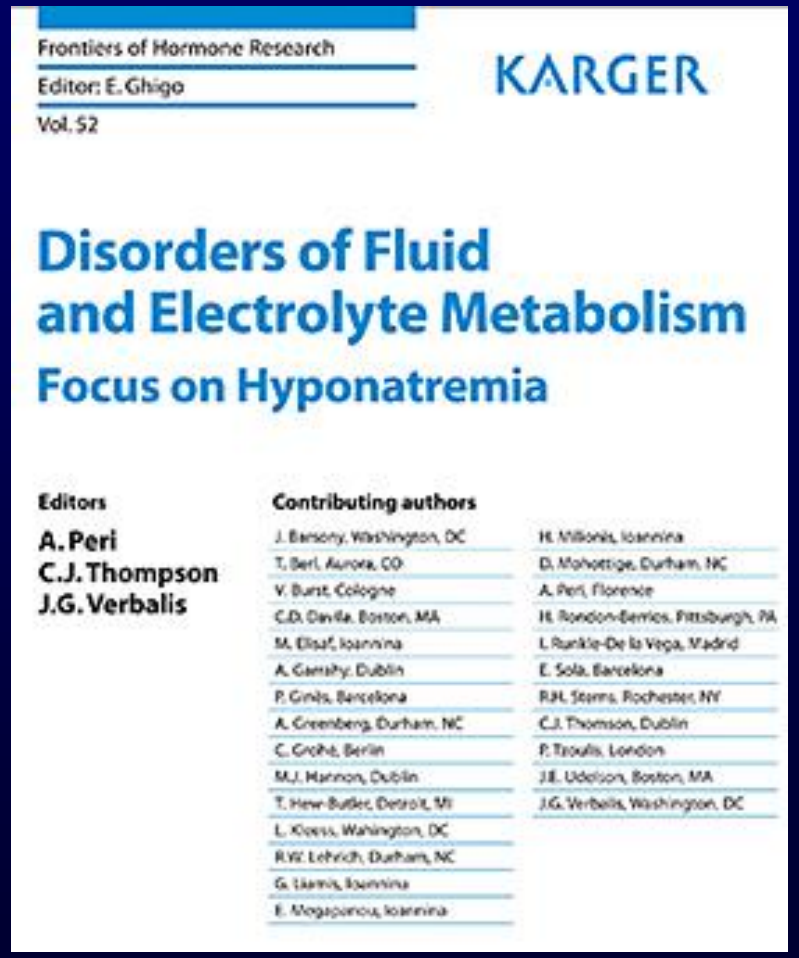
Mondellini GM, Verbrugge FH. Evaluation and Management of Hyponatremia in Heart Failure. Curr Heart Fail Rep. 2024 Jun;21(3): 252-261. doi: 10.1007/s11897-024-00651-3

Peri A, Thompson CJ, Verbalis JG (eds): Disorders of Fluid and Electrolyte Metabolism. Focus on Hyponatremia. Front Horm Res. Basel, Karger, 2019, vol 52, pp 113–129 (DOI: 10.1159/000493242)

Hypervolemic Hyponatremia in Heart Failure

Carlos D. Davila · James E. Udelson

Division of Cardiology and the CardioVascular Center, Tufts Medical Center, Boston, MA, USA



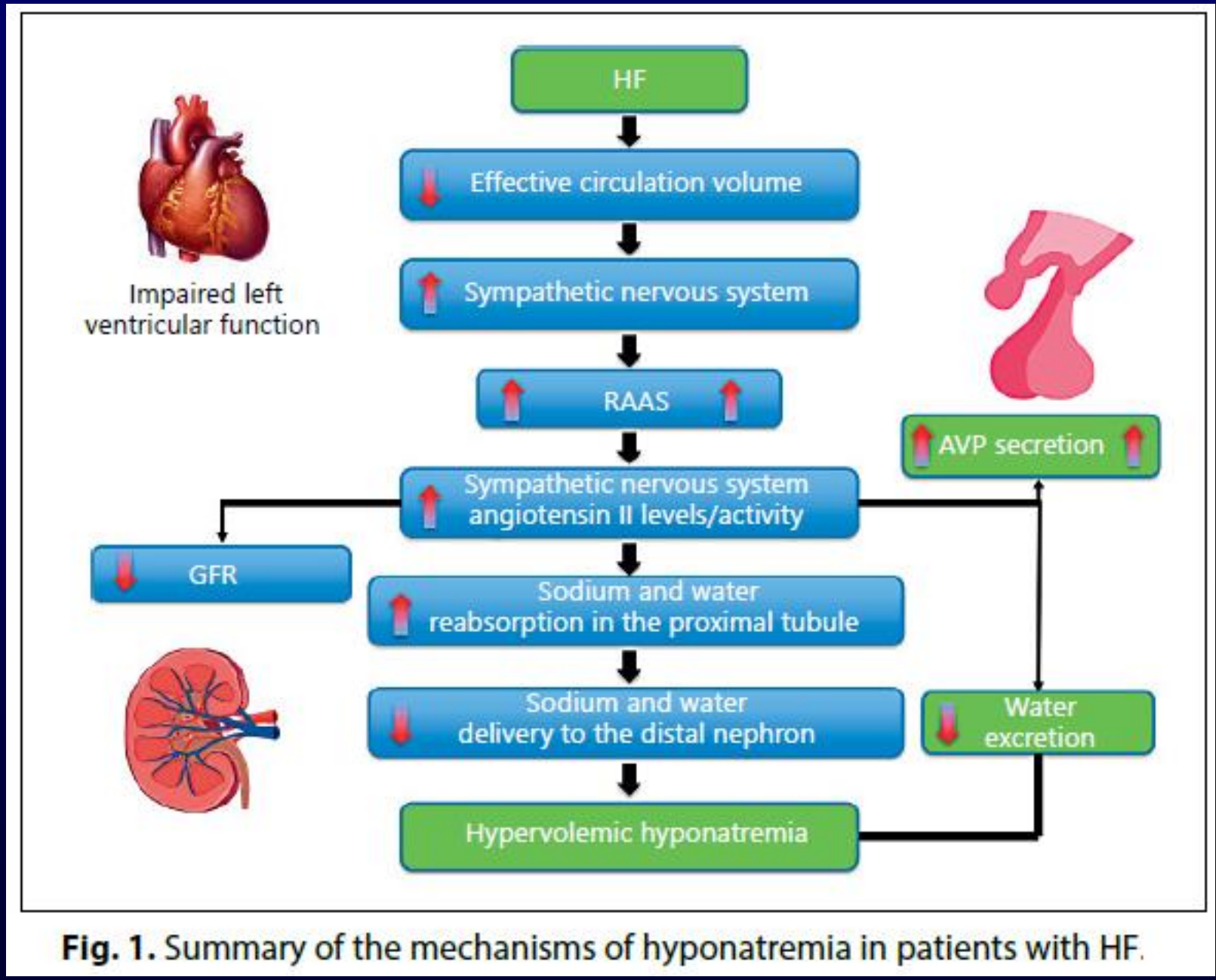


Fig. 1. Summary of the mechanisms of hyponatremia in patients with HF.

Gong et al. BMC Cardiovascular Disorders (2023) 23:520 26 October 2023 BMC Cardiovascular Disorders
https://doi.org/10.1186/s12872-023-03557-5

RESEARCH Open Access

Construction of risk prediction model for hyponatremia in patients with acute decompensated heart failure

Huanhuan Gong[1†], Ying Zhou[1†], Yating Huang[1], Shengen Liao[1*] and Qin Wang[1*]

Table 2 Univariate and multivariate analysis of the factors associated with hyponatremia

Variables	Univariate analysis		Multivariate analysis	
	OR(95%CI)	*P* value	OR(95%CI)	*P* value
Age	1.008(0.991, 1.025)	0.358		
Male	0.679(0.400, 1.154)	0.152		
Diabetes mellitus	1.309(0.737, 2.327)	0.359		
Hypertension	0.692(0.410, 1.167)	0.167		
Ischemic heart failure	1.08(0.80, 1.46)	0.614		
NYHA class				
II	**1.00**		**1.00**	
III	**14.17(1.92, 104.65)**	**0.009**	**12.31(1.66, 91.44)**	**0.014**
IV	**16.73(2.23, 125.70)**	**0.006**	**11.55(1.51, 88.14)**	**0.018**
Heart rate	1.004(0.992, 1.016)	0.551		
Systolic blood pressure	**0.981(0.968, 0.994)**	**0.005**	**0.978(0.965, 0.992)**	**0.002**
Diastolic blood pressure	**0.979(0.960, 0.999)**	**0.035**		
Potassium	**2.102(1.260, 3.507)**	**0.004**		
Albumin	**1.003(1.002, 1.005)**	**<0.001**		
Creatinine	**1.085(1.041, 1.132)**	**<0.001**	**1.006(1.001, 1.011)**	**0.024**
Uric acid	**1.006(1.002, 1.010)**	**<0.001**		
Urea nitrogen	0.951(0.902, 1.002)	0.060	**1.046(1.004, 1.090)**	**0.034**
Alanine aminotransferase	1.001(1.000, 1.002)	0.104		
Aspartate aminotransferase	**1.001(1.000, 1.002)**	**0.016**		
pro B-type natriuretic protein	**2.654(1.418, 4.965)**	**0.002**		
Left ventricular ejection fraction	0.994(0.976, 1.012)	0.522		
Body mass index	**0.948(0.906, 0.991)**	**0.019**		
antisterone	0.873(0.394, 1.934)	0.739		
ACEI/ARB	1.495(0.755, 2.959)	0.249		
β blocker	0.930(0.494, 1.752)	0.823		
Aspirin, n(%)	1.401(0.833, 2.357)	0.204		

pro B-type natriuretic protein was log10 transformed

Los hallazgos del estudio sugieren que existe **riesgo de hiponatremia** en pacientes con ICC que presentan :

- ✓ Cr ↑ ↑
- ✓ BUN ↑ ↑
- ✓ TAS ↓↓
- ✓ NYHA Clase III y IV.

Velat et al. BMC Pharmacology and Toxicology (2020) 21:57
https://doi.org/10.1186/s40360-020-00431-4 03 August 2020
BMC Pharmacology and Toxicology
RESEARCH ARTICLE Open Access

Furosemide and spironolactone doses and hyponatremia in patients with heart failure

Ivan Velat[1], Željko Bušić[1], Marina Jurić Paić[2] and Viktor Čulić[2,3*]

Table 3 Multivariate analysis of the predicting association of clinical factors with occurrence of hyponatremia

	OR (95% *CI*)	*p*
Age (per 10-year increase)	1.115 (1.023–1.159)	0.03*
Alcohol consumption	1.112 (1.002–1.273)	0.04*
Male sex	0.947 (0.861–1.047)	0.29
Kidney failure	1.043 (0.945–1.154)	0.39
LVEF ≤45%	0.943 (0.994–1.001)	0.25
Arterial hypertension	0.947 (0.854–1.049)	0.29
Diabetes mellitus	1.114 (1.012–1.224)	0.02*
Previous AMI	1.053 (0.946–1.191)	0.31
Current smoking	1.069 (0.953–1.258)	0.19
Hydrochlorothiazide	0.976 (0.863–1.093)	0.63
250 to 500 mg furosemide	1.138 (1.043–1.344)	0.009*
50 to 100 mg spironolactone	1.197 (1.126–1.484)	0.0003*
β-blocker	0.959 (0.878–1.053)	0.39
Calcium antagonist	0.935 (0.827–1.036)	0.18
ARB	1.049 (0.929–1.249)	0.32
ACEI	1.074 (0.973–1.178)	0.16
Aspirin	0.977 (0.886–1.076)	0.63
Digoxin	0.943 (0.837–1.045)	0.24

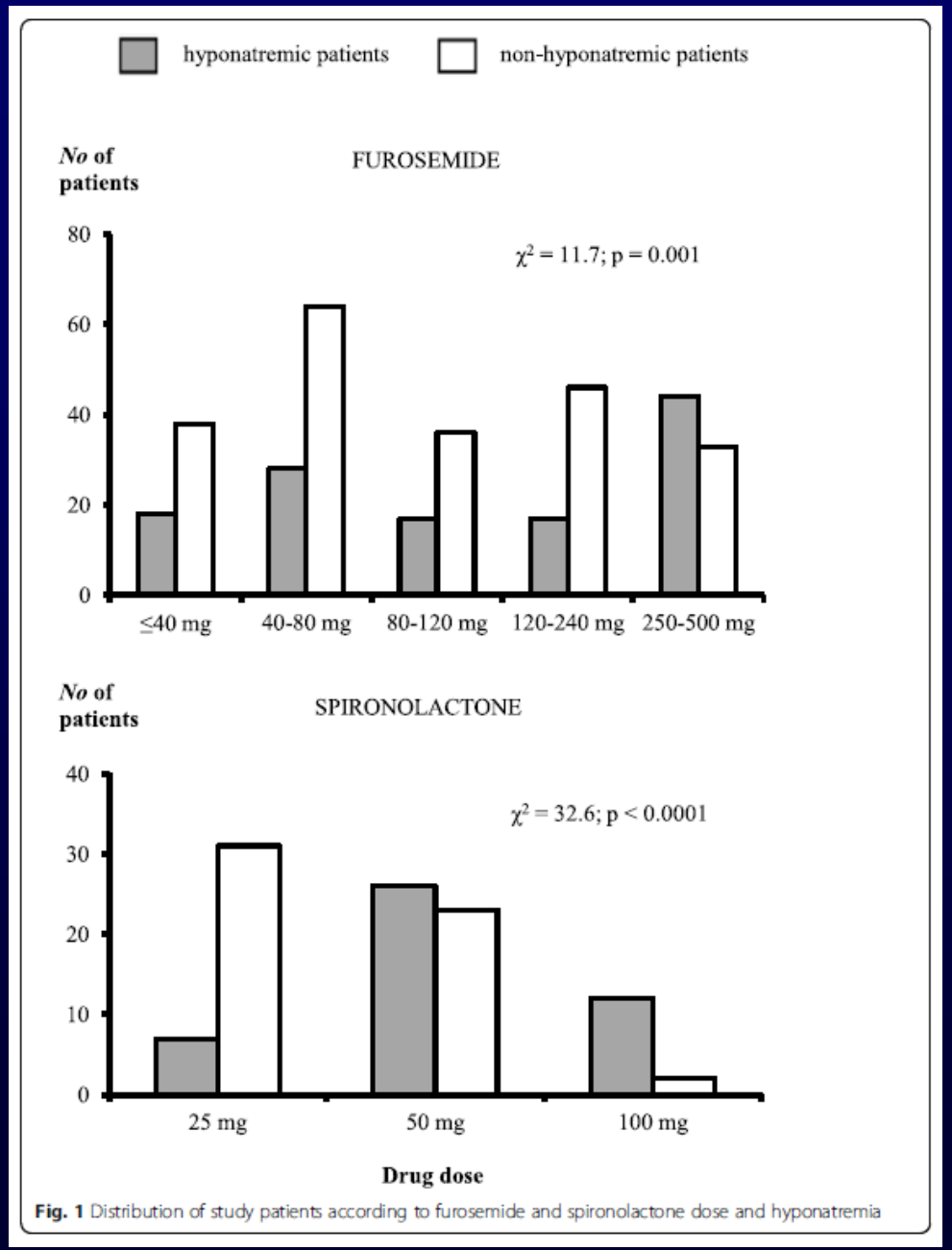


Fig. 1 Distribution of study patients according to furosemide and spironolactone dose and hyponatremia

Journal of *Personalized Medicine*

MDPI

Review

Management of Hyponatremia in Heart Failure: Practical Considerations

https://doi.org/10.3390/jpm13010140 10 January 2023

Victoriţa Şorodoc [1,†], Andreea Asaftei [2,*], Gabriela Puha [1,†], Alexandr Ceasovschih [1,*],

Figure 4. 2021 European Society of Cardiology Guidelines for the diagnosis and treatment of acute and chronic failure.

- Fluid restriction
- Consider increasing dose of loop diuretic
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- i.v. inotropic support
- Consider ultrafiltration

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Table 2. Studies on hypertonic saline in patients with acute decompensated heart failure.

First Author (Ref. #)	Year	Type of Study	Treatment	Effects of Hypertonic Saline Association to Loop Diuretics
Tuttolomondo et al. [53]	2021	Randomized Controlled Trial 141 patients	30 min of i.v. infusion of furosemide (120–250 mg) + HSS (150 mL of 1.4–4.6% NaCl) twice a day for 6 days versus 30 min of i.v. infusion of furosemide (120–150 mg) twice a day without HSS for 6 days.	Increase in diuresis, weight loss; reduction in the serum markers of atrial stretching, fibrosis and inflammation.
Griffin et al. [54]	2020	Retrospective Study 40 patients	i.v. 150 mL of 3% NaCl over 30 min + high doses of loop diuretics.	Improvements in urine output, weight loss, diuretic efficiency, renal function; increase in serum sodium levels; no discernible deterioration in respiratory status or overcorrection of hyponatremia.
Wan et al. [55]	2017	Randomized Controlled Trial 264 patients	i.v. 1-h infusion of furosemide (100 mg) plus HSS (100 mL) twice a day and severe water restriction (< 500 mL) vs. i.v. furosemide (100 mg) twice a day and severe water restriction (< 500 mL) without HSS.	Increase in urination, reduction of hospitalization time and costs; higher average readmission time; lower mortality rate.
Lafrenière et al. [56]	2017	Prospective Study 47 patients	i.v. infusion of 250 mg furosemide plus 150 mL HSS 3% NaCl twice a day for a mean duration of 2.3 days.	Greater weight loss per day of treatment.
Yayla et al. [57]	2015	Randomized Controlled Trial 43 patients	Continuous infusion of 160 mg furosemide for 16 h/day versus bolus injections of 80 mg furosemide twice a day versus administration of 160 mg furosemide plus HSS as an infusion for 30 min once a day.	Significantly shorter hospitalization.
Paterna et al. [58]	2015	Randomized Controlled Trial 40 patients	i.v. furosemide (125 mg/250 mg/500 mg) diluted in 150 mL of normal saline. (0.9%) versus the same furosemide dose diluted in 150 mL of HSS (1.4%).	Increased total urine output, sodium excretion, urinary osmolality, and furosemide urine delivery.

Journal of *Personalized Medicine*

MDPI

Review

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- Consider ultrafiltration

Table 3. Tolvaptan as an alternative therapy to loop diuretics in chronic and acute failure with hyponatremia

	Udelson 2011 [74]	AQUA-AHF 2020 [75]
Enrolled patients	83	33
Inclusion criteria	Multicenter, randomized, double-blind placebo-controlled. NYHA class II or III HF, systolic dysfunction (EF $\leq$ 40%) and signs of congestion (edema, rales).	Prospective, randomized, open-label, parallel-group, single center study. Acute congestive HF and a serum Na < 135 mmol/L.
Design/tolvaptan dosing	4 groups: tolvaptan 30 mg, furosemide 80 mg, a combination of tolvaptan 30 mg/furosemide 80 mg and placebo for 7 days (+ standard therapy).	Randomized to receive tolvaptan 30 mg orally daily or furosemide 5 mg/h intravenously for 24 h, after which treatment could be escalated.
Primary end point results	Reduction of body weight was similar in all groups.	No significant differences in median urine output or net fluid balance between groups at 24 h.
Secondary end point results	An increase in serum sodium within the normal range was also observed in tolvaptan-treated group when compared with placebo or furosemide group.	Oral tolvaptan was associated with similar, but not superior diuresis compared with intravenous furosemide for acute HF with concomitant hyponatremia. In contrast to conventional diuretics, exacerbation of hyponatremia is unlikely with tolvaptan.

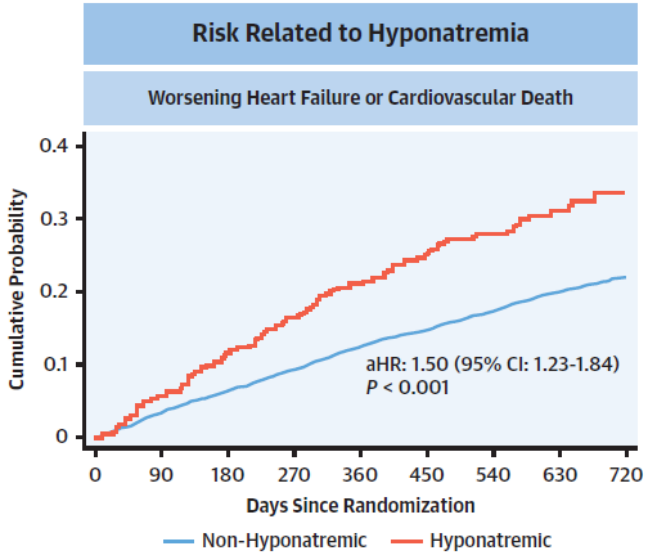
JACC: HEART FAILURE
EDITORIAL COMMENT
MAY 2022:319–320
https://doi.org/10.1016/j.jchf.2022.02.005

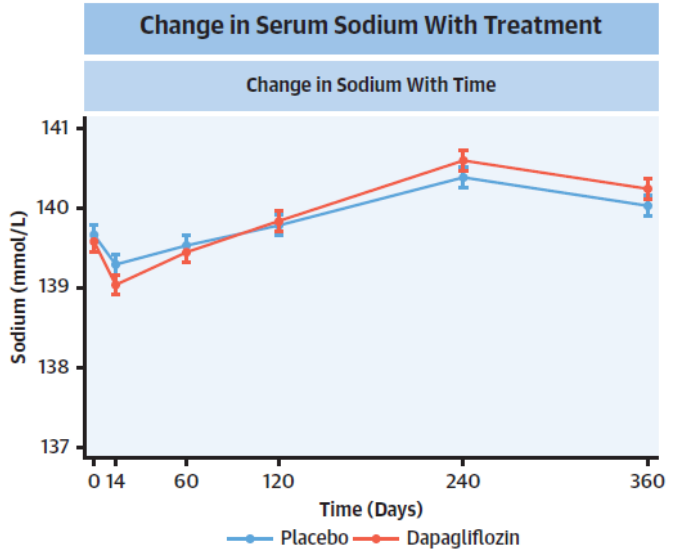
Impact of SGLT2 Inhibitors on Serum Sodium in Heart Failure With Reduced Ejection Fraction*

Song Li, MD, Wayne C. Levy, MD

- ✓ La dapagliflozina tiene un efecto bifásico sobre el sodio sérico, disminuyendo la concentración de sodio más que el placebo en el día 14, seguido de una tendencia creciente que se eleva por encima tanto del valor inicial como del grupo placebo a los 8 meses.
- ✓ Este fenómeno probablemente sea causado por una combinación de efectos natriuréticos y osmóticos de los iSGLT2.
- ✓ A pesar de la naturaleza transitoria de la natriuresis, la iSGLT2 aumenta el suministro de sodio y cloruro a la mácula densa, lo que puede reducir la secreción de renina y posiblemente inhibe el RAAS y el sistema nervioso simpático.
- ✓ Los iSGLT2 aumentan la producción de eritropoyetina y el hematocrito, lo que puede ayudar a mejorar la hiponatremia dilucional.
- ✓ Los beneficios de los iSGLT2 en la IC aún está por dilucidar.

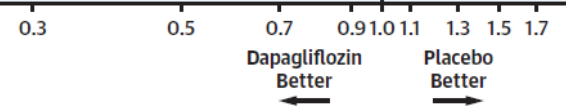
CENTRAL ILLUSTRATION Hyponatremia in the DAPA-HF Trial





Effects of Dapagliflozin According to Baseline Sodium Level

Outcomes	Dapagliflozin	Placebo	HR (95% CI)	Interaction *P* Value
CV Death or HF Hospitalization or Urgent HF Visit				0.54
Overall	386/2,371 (16.3)	501/2,369 (21.1)	0.74 (0.65-0.85)	
Na^+ ≤135 mmol/L	54/205 (26.3)	61/193 (31.6)	0.83 (0.57-1.19)	
Na^+ >135 mmol/L	332/2,166 (15.3)	440/2,176 (20.2)	0.73 (0.63-0.84)	
HF Hospitalization or Urgent HF Visit				0.95
Overall	237/2,371 (10.0)	325/2,369 (13.7)	0.70 (0.59-0.83)	
Na^+ ≤135 mmol/L	29/205 (14.2)	39/193 (20.2)	0.69 (0.43-1.11)	
Na^+ >135 mmol/L	208/2,166 (9.6)	286/2,176 (13.1)	0.70 (0.59-0.84)	
Cardiovascular Death				0.73
Overall	227/2,371 (9.6)	273/2,369 (11.5)	0.82 (0.69-0.98)	
Na^+ ≤135 mmol/L	35/205 (17.1)	38/193 (19.7)	0.89 (0.56-1.40)	
Na^+ >135 mmol/L	192/2,166 (8.9)	235/2,176 (10.8)	0.81 (0.67-0.98)	
All-Cause Death				0.96
Overall	276/2,371 (11.6)	329/2,369 (13.9)	0.83 (0.71-0.97)	
Na^+ ≤135 mmol/L	41/205 (20.0)	47/193 (24.4)	0.85 (0.56-1.29)	
Na^+ >135 mmol/L	235/2,166 (10.9)	282/2,176 (13.0)	0.83 (0.70-0.98)	



Yeoh SE, et al. J Am Coll Cardiol HF. 2022;10(5):306-318.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Acetazolamide in Acute Decompensated Heart Failure with Volume Overload

W. Mullens, J. Dauw, P. Martens, F.H. Verbrugge, P. Nijst, E. Meekers, for the ADVOR Study Group*

DOI: 10.1056/NEJMoa2203094 August 27, 2022, at NEJM.org.

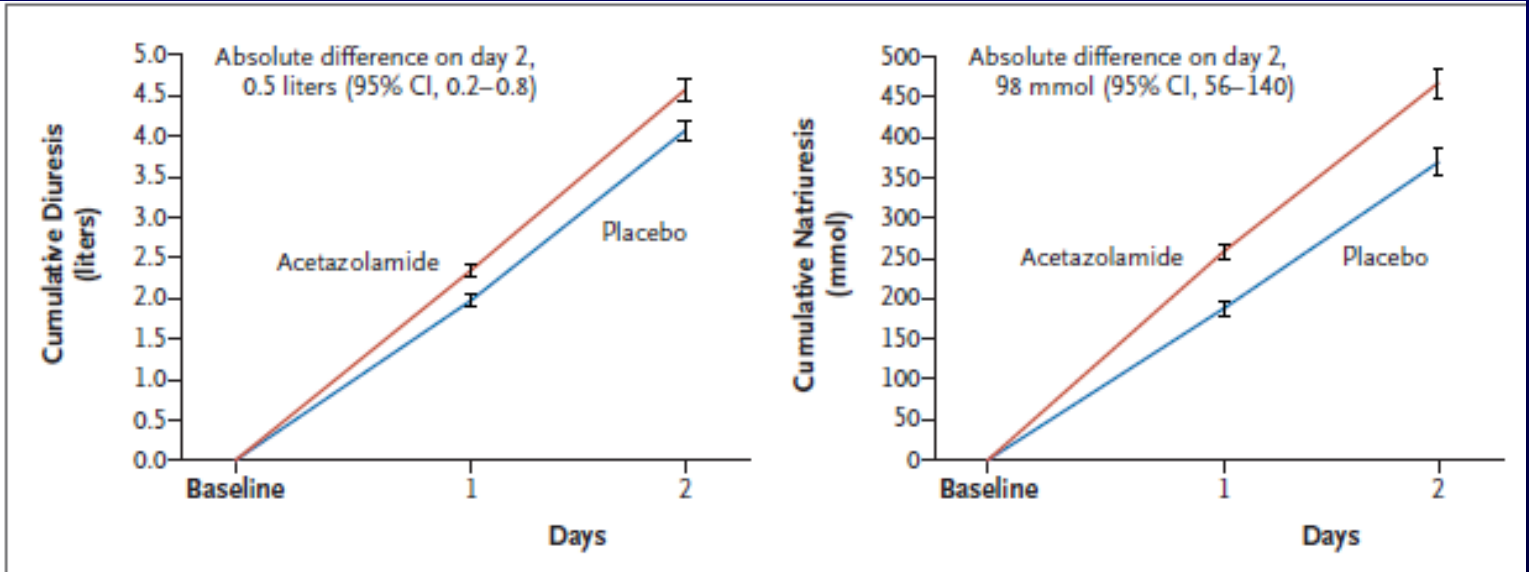


Figure 3. Diuresis and Natriuresis According to Trial Group.

El tratamiento con Acetazolamida se asoció con una mayor producción acumulada en el débito urinario y de natriuresis, hallazgos consistentes con una mejor eficiencia diurética.

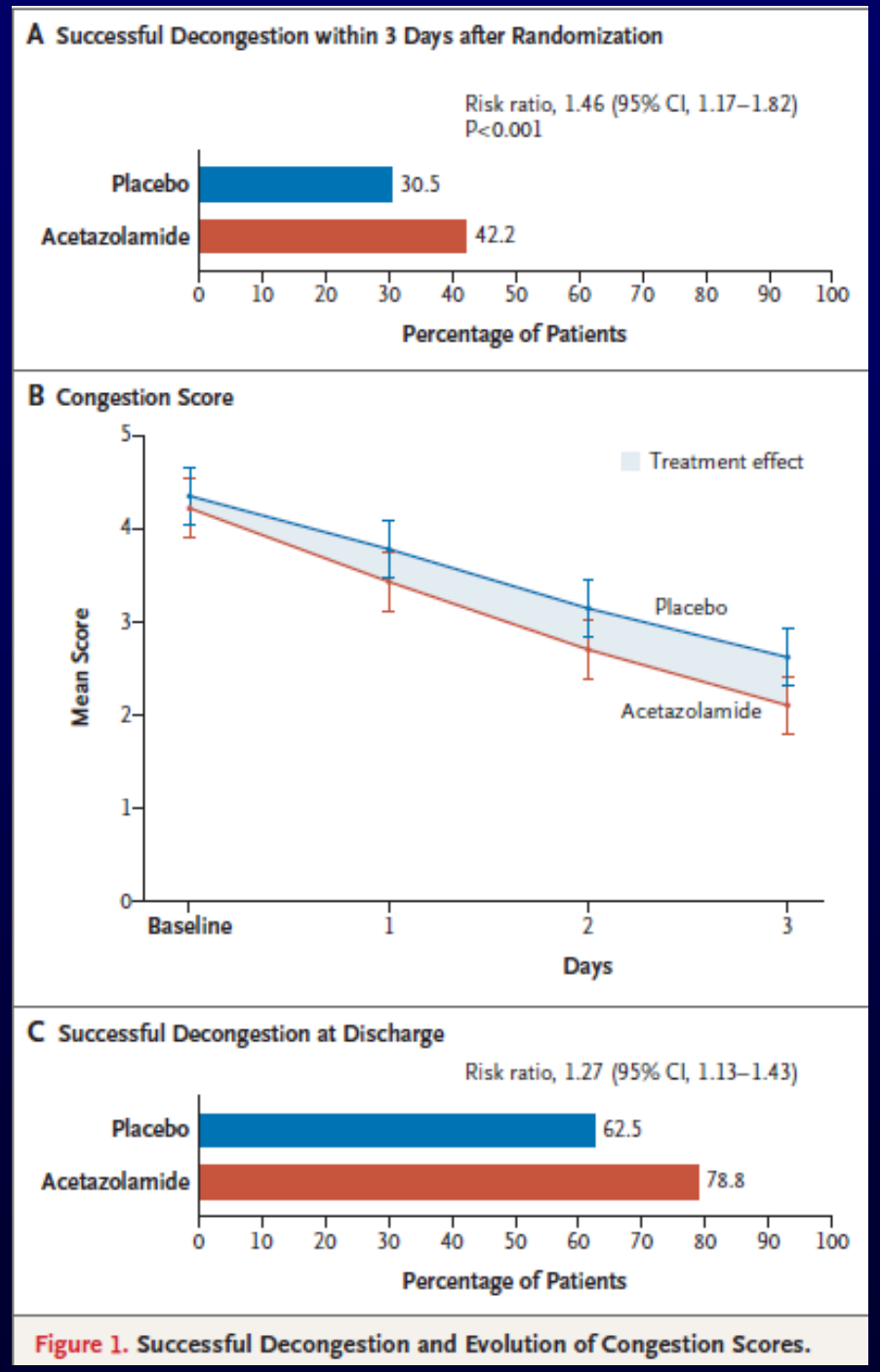


Figure 1. Successful Decongestion and Evolution of Congestion Scores.

MEDICINA CLINICA

www.elsevier.es/medicinaclinica

Original 26 January 2024, https://doi.org/10.1016/j.medcli.2023.08.001

Efectividad de la administración de urea para el tratamiento de la hiponatremia en la insuficiencia cardiaca

Ángel Martínez González[a,*], Pedro Rodeiro Escobar[b], José Llópiz Castedo[b], María Díaz Vázquez[b],

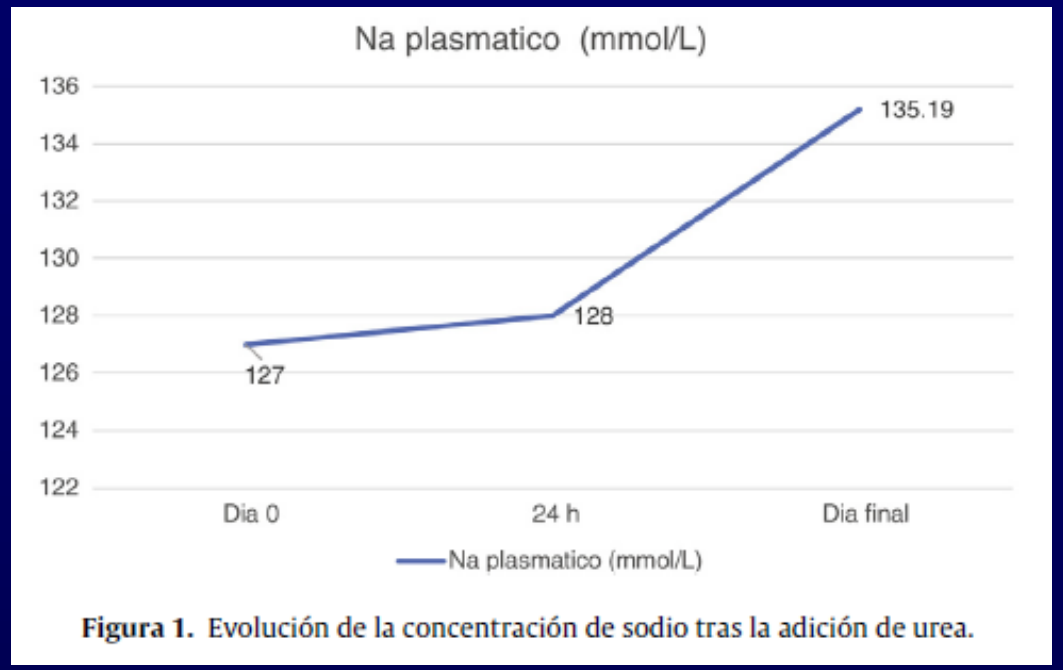


Figura 1. Evolución de la concentración de sodio tras la adición de urea.

Tabla 3
Efectos adversos de la urea

Variables efectos adversos	n (%) (n = 49)
Molestias gastrointestinales leves	4 (8,16%)
Hipotensión arterial asintomática	3 (6,12%)
Taquicardia sinusal leve	2 (4,08%)
Rechazo por mal sabor del preparado	1 (2,04%)

El tratamiento con urea oral añadido al tratamiento estándar, durante cortos periodos de tiempo, es seguro y eficaz para corregir la natremia en pacientes con IC hipervolémica con hiponatremia.

Tabla 2
Evolución de parámetros analíticos

Variables	Día 0	24 horas	p	Día de normalización Na^+	p
Sodio (mmol/l), media (DT)	127 ± 5,22	128 ± 2,47	0,009	135,19 ± 4,23	0,005
Urea plasmática (mg/dl), media (DT)	73,00 ± 46,93	73,46 ± 38,41	0,329	116,05 ± 63,64	0,002
Creatinina plasmática (mg/dl), media (DT)	1,27 ± 0,680	1,04 ± 0,900	0,046	1,30 ± 0,714	0,003
Potasio plasmático (mmol/l), media (DT)	4,67 ± 0,72	4,50 ± 0,734	0,268	4,23 ± 0,568	0,198

Hyponatremia in Heart Failure

Serum Na^+ ≤135 mEq/L

Comprehensive medical history & clinical exam

- Fluid intake
- Extra-renal fluid losses
- Concomitant acute or chronic illnesses
- Alcohol & illicit drug use
- Use of specific medications that interfere with urine dilution or may cause SIADH

Laboratory testing

- Complete set of electrolytes with chloride, potassium & magnesium
- Thyroid-stimulating hormone to exclude significant thyroid disease
- Exclude adrenal insufficiency within suggestive clinical setting
- Plasma osmolality

EXCLUDE:

Pseudohyponatremia

= low serum Na^+ concentration due to laboratory artefact

- Hyperlipidemia
- Abnormally high protein levels (i.e., monoclonal gammopathies, malignancy, chronic hepatitis C or HIV infection)

Hyponatremia with normal or elevated plasma osmolality

- Hyperglycemia
- Uremia
- Contrast agents
- Other source of osmoles

Evaluation and Management of Hyponatremia in Heart Failure
Giulio M. Mondellini[1,2] · Frederik H. Verbrugge[2,3] 27 February 2024

Hypotonic Hyponatremia in Heart Failure
(Plasma osmolality <275 mOsm/L)

Severe symptomatic hyponatremia <120-125 mmol/L

- Coma
- Seizures
- Deep somnolence
- Cardiorespiratory distress

→

- **Admit to intensive care or stepdown unit**
- **150 mL of 3% hypertonic saline in 10-20 min through central or peripheral line**
- **Diuretics if signs of fluid overload**

GOAL: **rapidly increase serum Na^+ with >5 mmol/L or ≥125 mmol/L**

Consider concomitant cause of hyponatremia other than heart failure !!!

Treat depletional hyponatremia

- **Aggressive potassium repletion >4 mmol/L**
- **Aggressive magnesium repletion >0.85 mmol/L**

Signs & symptoms suggestive of hypovolemia?

Serum Na^+ minus serum chloride >40 mmol/L?

- **Pause all diuretics**
- **Consider fluid bolus of isotonic crystalloid (=diagnostic for SIADH)**

Electrolyte-free water excretion predicts serum Na^+ evolution

= (Urine Na^+ plus potassium concentration)
- (Serum Na^+ plus potassium concentration)

Treat dilutional hyponatremia

1. Optimize hemodynamics & renal blood flow

2. Implement guideline-directed medical therapy

Start/uptitrate in particular

- Renin-angiotensin blockers (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin-neprilysin inhibitors)
- Sodium-glucose co-transporter-2 inhibitors that increase distal nephron flux and may cause osmotic diuresis

3. (Consider fluid restriction as adjunctive therapy)

Poor quality evidence, especially in acute heart failure

4. Treat fluid overload with diuretics

- Combination: Acetazolamide 500 mg OD + Adequately dosed loop diuretics
- Avoid: thiazide-like diuretics and amiloride unless diuretic resistance (Urine Na+ <80 mmol/L)
- Consider temporarily interrupting mineralocorticoid receptor antagonists, always restart before discharge

Aim for positive electrolyte-free water excretion with urine Na^+ ≥80 mmol/L

- ✓ Los iSGLT2 *disminuyen la reabsorción tubular proximal*, aumentando así el flujo de la nefrona distal, lo que *mejora la capacidad de excreción de agua libre*.
- ✓ También causan glucosuria como *diuresis osmótica* eliminando así el agua libre de electrolitos.

- ✓ Por lo tanto, los **iSGLT2** son probablemente la **primera terapia médica** dirigida por pautas a considerar en pacientes con **IC e Hiponatremia**.

Clinics in Liver Disease
Volume 26, Issue 2, May 2022, Pages 149-164

Hyponatremia in Cirrhosis

Helbert Rondon-Berrios MD, MS, Juan Carlos Q. Velez

https://doi.org/10.1016/j.cld.2022.01.001

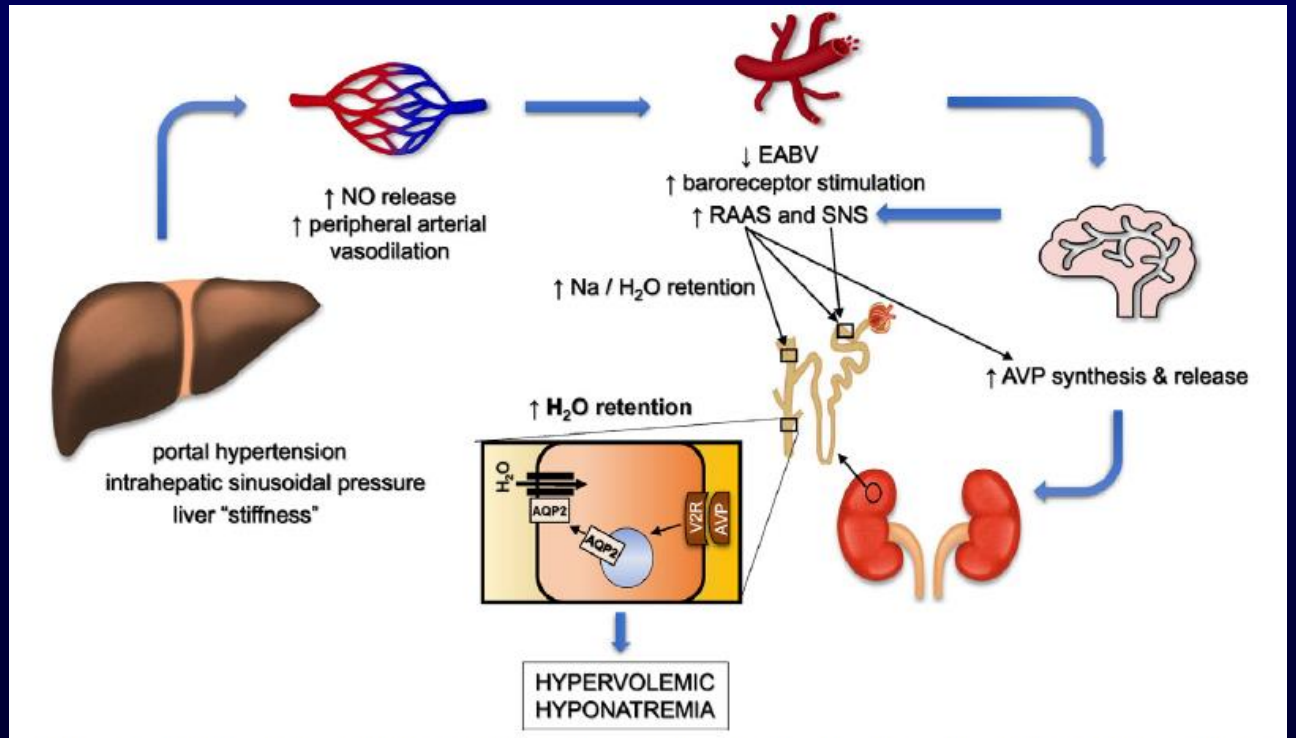


Fig. 2. Pathogenesis of hyponatremia of cirrhosis. ↑, increased; ↓, decreased; AQP2, aqua-

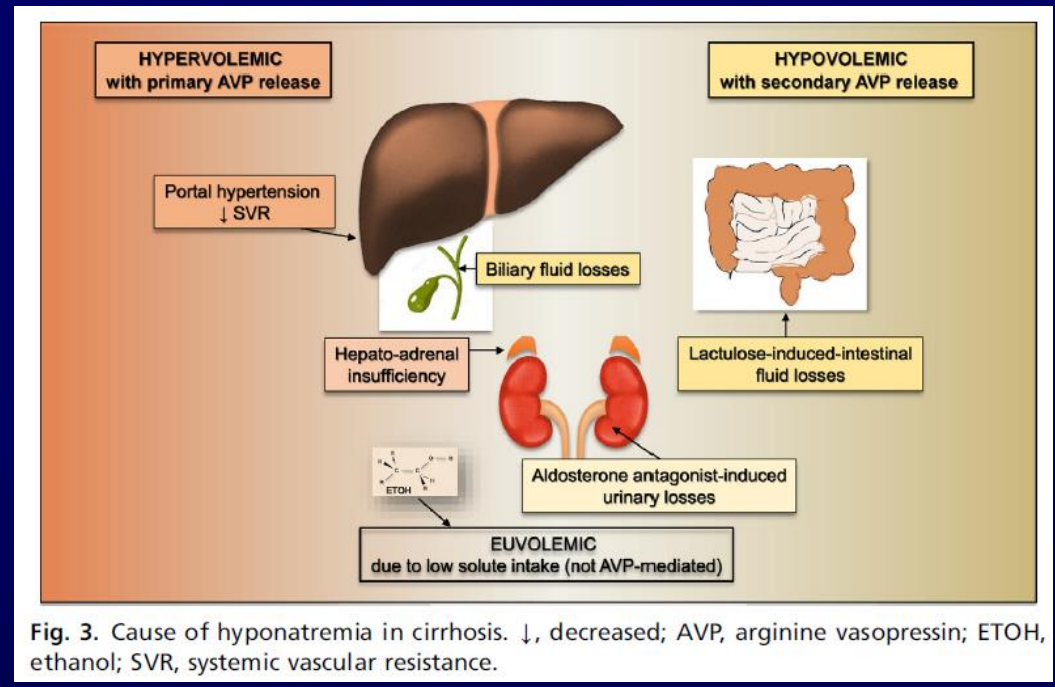


Fig. 3. Cause of hyponatremia in cirrhosis. ↓, decreased; AVP, arginine vasopressin; ETOH, ethanol; SVR, systemic vascular resistance.

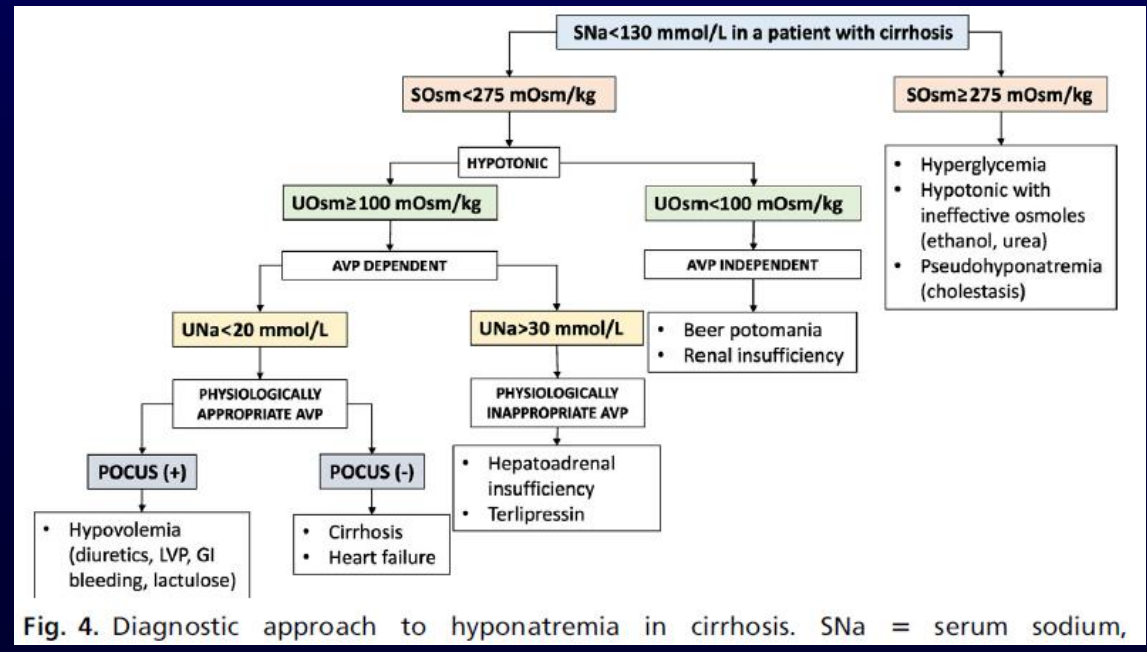


Fig. 4. Diagnostic approach to hyponatremia in cirrhosis. SNa = serum sodium,

Treatment Guidelines for Hyponatremia

Stay the Course

Richard H. Sterns,[1,2] *Helbert Rondon-Berrios*,[3] *Horacio J. Adrogué*,[4] *Tomas Berl*,[5] *Volker Burst*,[6] *David M. Cohen*,[7] *Mirjam Christ-Crain*,[8] *Martin Cuesta*,[9] *Guy Decaux*,[10] *Michael Emmett*,[11] *Aoife Garrahy*,[12] *Fabrice Gankam-Kengne*,[13] *John K. Hix*,[2] *Ewout J. Hoorn*,[14] *Kamel S. Kamel*,[15] *Nicolaos E. Madias*,[16] *Alessandro Peri*,[17] *Julie Refardt*,[8] *Mitchell H. Rosner*,[18] *Mark Sherlock*,[19] *Stephen M. Silver*,[2] *Alain Soupart*,[10] *Chris J. Thompson*,[19] and *Joseph G. Verbalis*,[20] *on behalf of PRONATREOUS Investigators**

Abstract

International guidelines designed to minimize the risk of complications that can occur when correcting severe hyponatremia have been widely accepted for a decade. On the basis of the results of a recent large retrospective study of patients hospitalized with hyponatremia, it has been suggested that hyponatremia guidelines have gone too far in limiting the rate of rise of the serum sodium concentration; the need for therapeutic caution and frequent monitoring of the serum sodium concentration has been questioned. These assertions are reminiscent of a controversy that began many years ago. After reviewing the history of that controversy, the evidence supporting the guidelines, and the validity of data challenging them, we conclude that current safeguards should not be abandoned. To do so would be akin to discarding your umbrella because you remained dry in a rainstorm. The authors of this review, who represent 20 medical centers in nine countries, have all contributed significantly to the literature on the subject. We urge clinicians to continue to treat severe hyponatremia cautiously and to wait for better evidence before adopting less stringent therapeutic limits.

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Hyponatraemia—treatment standard 2024

Goce Spasovski

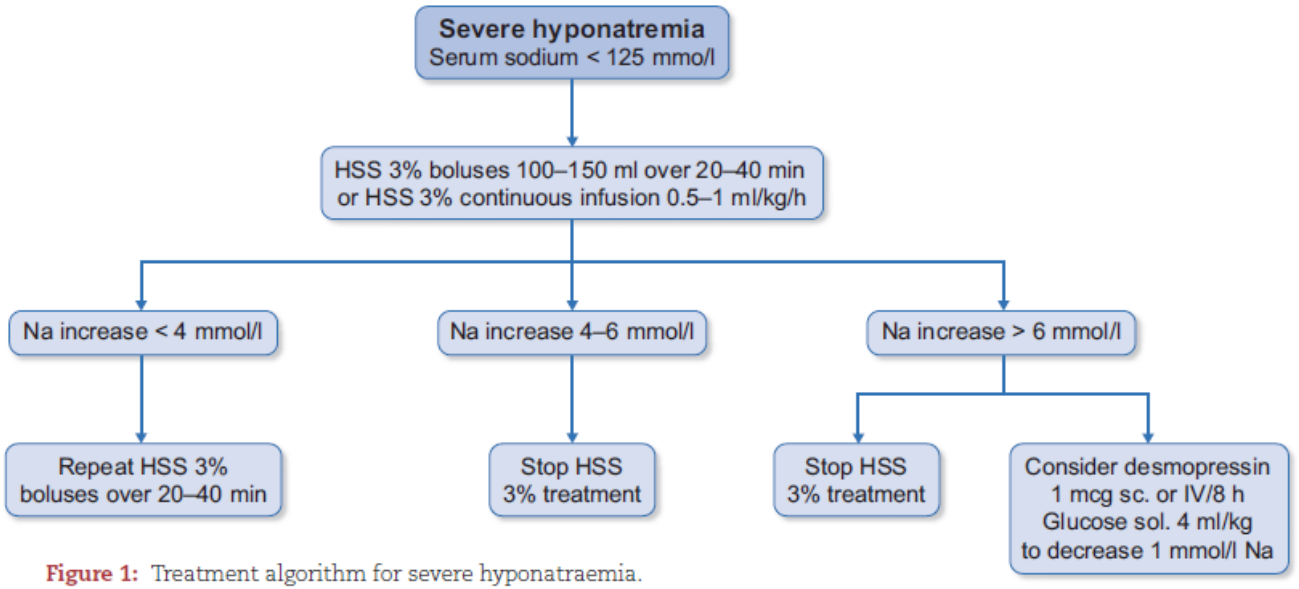
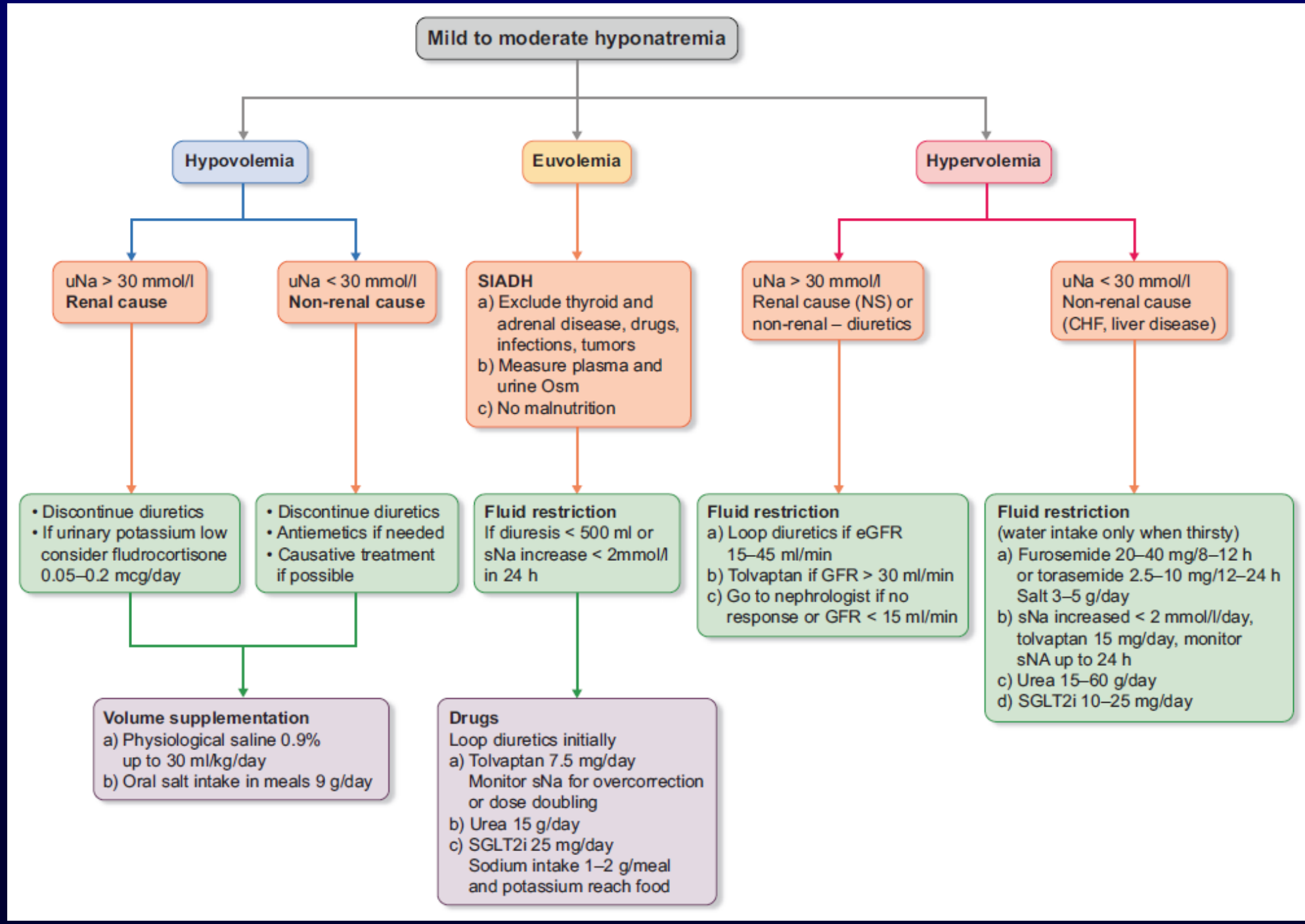


Figure 1: Treatment algorithm for severe hyponatraemia.

Table 1: Pharmacological options for the treatment of hyponatraemia.

Characteristics	Isotonic saline	3% HSS	Loop diuretics	Vaptans	Urea	SGLT2 inhibitor
Indication	Hypovolaemic hyponatraemia	Severe hyponatraemia	SIADH, hypervolaemic hyponatraemia (CHF patients)	SIADH, hypovolaemic hyponatraemia (CHF patients)	SIADH	SIADH
Daily dose	23–30 ml/kg	2–4 ml/kg as boluses or 0.5–1 ml/kg/h continuous infusion	Furosemide 20–40 mg/12 h, torasemide 2.5–10 mg/24 h	Tolvaptan 7.5–60 mg	15–60 g	10–25 mg
eGFR Ineffective response	No limits	No limits		>15 ml/min Water intoxication	>30 ml/min	>60 ml/min uOsm <350 mOsm
Projected Na increase			2–4 mmol/l in the first 2 days	4–6 mmol/l in 24 h	4–6 mmol/l (2–7 days)	
Precautions or contraindications	Hypervolaemia	Hypervolaemia	Hypovolaemia	Pregnancy CYP3A4	CKD, liver disease, dehydration	Hypovolaemia


Mild to moderate hyponatremia
Hypovolemia
Euvolemia
Hypervolemia
uNa > 30 mmol/l
Renal cause
uNa < 30 mmol/l
Non-renal cause
SIADH
a) Exclude thyroid and adrenal disease, drugs, infections, tumors
b) Measure plasma and urine Osm
c) No malnutrition
uNa > 30 mmol/l
Renal cause (NS) or non-renal – diuretics
uNa < 30 mmol/l
Non-renal cause (CHF, liver disease)
• Discontinue diuretics
• If urinary potassium low consider fludrocortisone 0.05–0.2 mcg/day
• Discontinue diuretics
• Antiemetics if needed
• Causative treatment if possible
Fluid restriction
If diuresis < 500 ml or sNa increase < 2mmol/l in 24 h
Fluid restriction
a) Loop diuretics if eGFR 15–45 ml/min
b) Tolvaptan if GFR > 30 ml/min
c) Go to nephrologist if no response or GFR < 15 ml/min
Fluid restriction
(water intake only when thirsty)
a) Furosemide 20–40 mg/8–12 h or torasemide 2.5–10 mg/12–24 h
Salt 3–5 g/day
b) sNa increased < 2 mmol/l/day, tolvaptan 15 mg/day, monitor sNA up to 24 h
c) Urea 15–60 g/day
d) SGLT2i 10–25 mg/day
Volume supplementation
a) Physiological saline 0.9% up to 30 ml/kg/day
b) Oral salt intake in meals 9 g/day
Drugs
Loop diuretics initially
a) Tolvaptan 7.5 mg/day
Monitor sNa for overcorrection or dose doubling
b) Urea 15 g/day
c) SGLT2i 25 mg/day
Sodium intake 1–2 g/meal and potassium reach food

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Hyponatremia and bone pathophysiology: an integrated preclinical and clinical perspective

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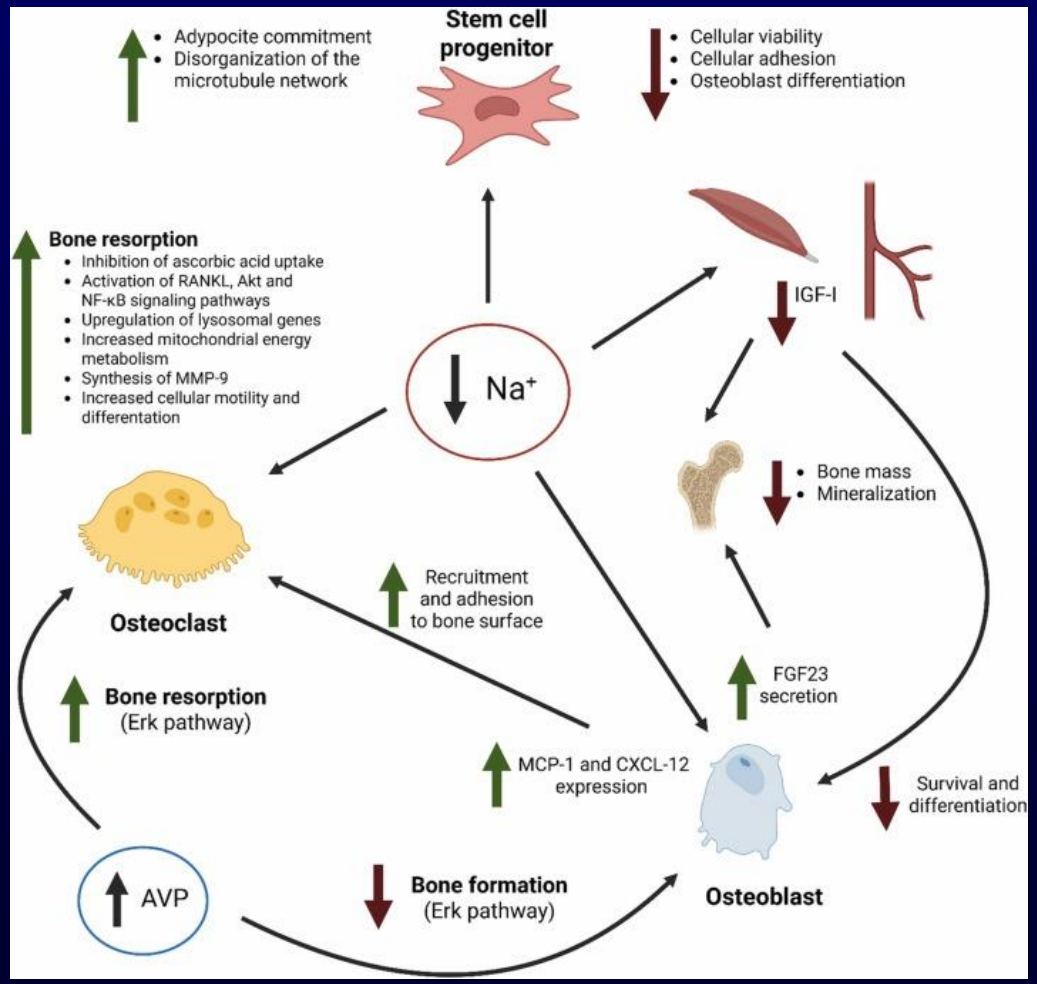
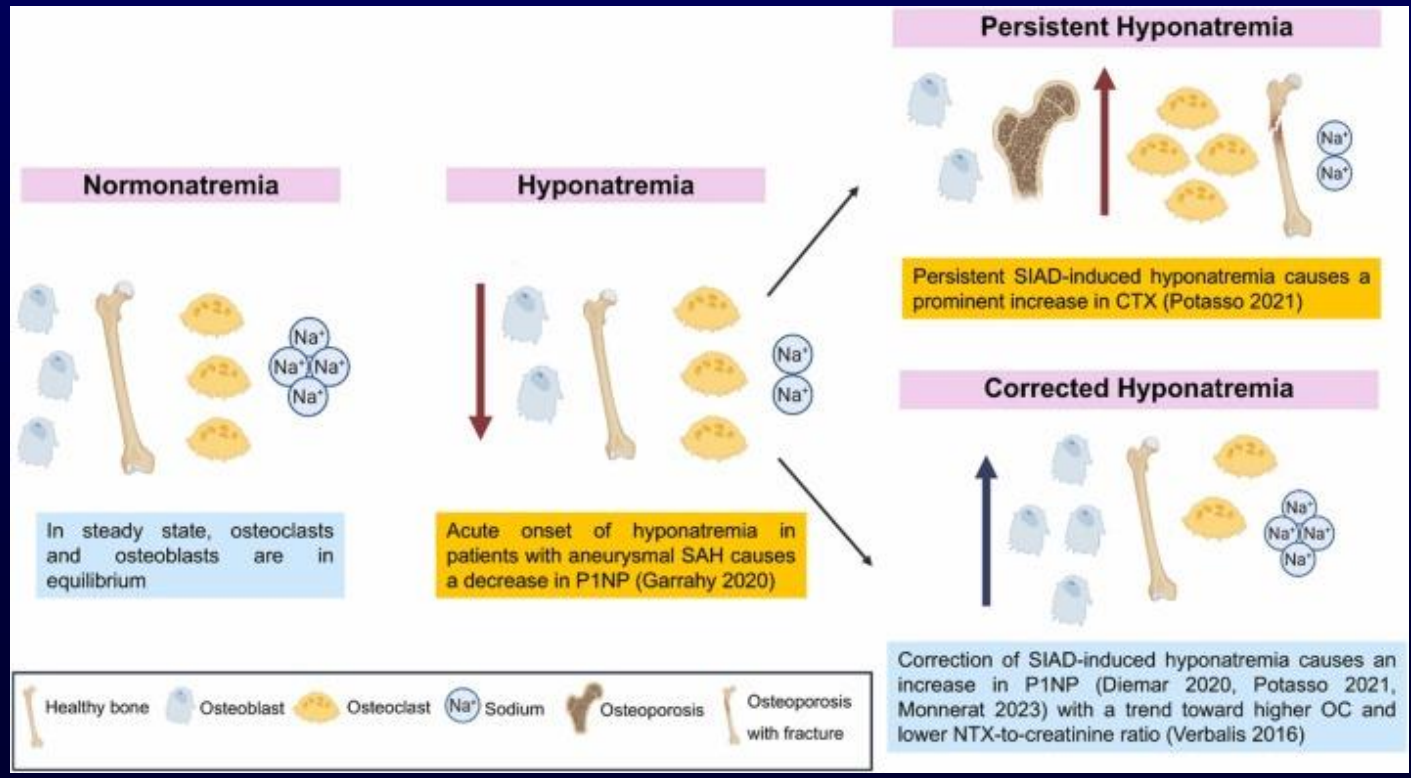
- ✓ La hiponatremia crónica induce resorción ósea ↑ (osteoclastos), formación ósea ↓ (osteoblastos).
- ✓ Asociada a ↑ riesgo de fracturas (OR ~4) y osteoporosis independiente de caídas.
- ✓ La hiponatremia (incluso leve y crónica) debe considerarse un factor de riesgo independiente y modificable para osteoporosis y fracturas.
- ✓ La corrección de Na^+ parece estimular la formación ósea más que reducir la resorción.





Hiponatremia en hospitalización

Vahid Nouri Kandany – República Dominicana
Sonia Indacochea-Cáceda – Perú
Luis García-Carrión – Perú
Pascual Valdez – Argentina

Introducción

El agua corporal se divide en dos compartimentos: el líquido extracelular (LEC) y el intracelular (LIC). En el LEC, el ion más abundante es el sodio, y en el LIC, el potasio. El equilibrio de estos electrolitos es vital y depende del volumen y composición de los líquidos, cuyos valores pueden oscilar por varios factores. Los mecanismos de regulación previenen los desequilibrios electrolíticos, que pueden afectar distintos órganos y sistemas, así como aumentar la morbimortalidad. La concentración de sodio en el plasma es directamente proporcional al equilibrio de líquidos corporales, por lo cual suele reflejar la osmolaridad plasmática (1).

¿Qué aporta este capítulo?

Este capítulo ofrece una revisión actualizada y basada en la evidencia sobre la hiponatremia en pacientes hospitalizados. Se abordan los siguientes aspectos: definición de hiponatremia, epidemiología, etiopatogenia, clasificación, diagnóstico, tratamiento, complicaciones y pronóstico.

Definición

La *hiponatremia* se define como una concentración sérica de sodio inferior a 135 mmol/L, que resulta de un exceso de agua corporal en relación con el sodio total. Se trata del trastorno más frecuente del equilibrio hidroelectrolítico, que plantea desafíos tanto para su diagnóstico como para su tratamiento. Así lo demuestra un registro reciente sobre esta alteración. Esta no constituye una entidad nosológica, sino un proceso fisiopatológico que refleja una alteración en la homeostasis del agua (2-6).

Epidemiología

La hiponatremia es un trastorno común tanto en la población ambulatoria como en pacientes hospitalizados, con una incidencia significativa en ambos grupos. Además, afecta de manera desproporcionada a los ancianos y puede estar relacionada con el uso de medicamentos y diversas enfermedades. La estimación de la prevalencia de hiponatremia en los Estados Unidos varía entre 3,2 millones y 6,1 millones de personas anualmente. Aproximadamente, el 1% de los pacientes presentan hiponatremia aguda y sintomática; el 4%, hiponatremia aguda y asintomática; 15%-20%, hiponatremia crónica y sintomática, y 75%-80%, hiponatremia crónica y asintomática. En cuanto a la atención médica, se encontró que entre el 55% y el 63% de los pacientes son inicialmente tratados como pacientes hospitalizados, el 25% reciben tratamiento en la sala de emergencias y del 13%-20% son atendidos únicamente en el consultorio médico. Se estima que los costos directos asociados al tratamiento de la hiponatremia en los Estados Unidos oscilan entre $1,6 y $3,6 millones (7).

Pero la que tiene valor fisiológico es la *osmolaridad efectiva* o *tonicidad*, que no incluye a la urea en la fórmula (por su facilidad para atravesar las membranas y la improbabilidad de estar de un lado de la misma ejerciendo presión osmótica).

$$\textbf{Osmolaridad efectiva (tonicidad)} = (2 \times Na^{+}) + (\text{glucosa}/18)$$

Inclusive, si la glucemia es estable, se la reemplaza por un valor fijo.

$$\textbf{Osmolaridad efectiva (tonicidad)} = (2 \times Na^{+}) + 10$$

Esta medida permite diferenciar la hiponatremia verdadera, con hipoosmolaridad, de la pseudohiponatremia, con osmolaridad normal o alta. Esto es clave para identificar la causa y el tratamiento de la hiponatremia (17-19).

Osmolaridad urinaria

La osmolaridad urinaria se puede estimar con siguiente fórmula:

$$\textbf{Osmu (mOsm/kg)} = (\text{densidad de la orina (du)} - 1{,}000) \times 35$$

Esta fórmula no es válida si se usa manitol, piperacilina, carbenicilina o carbapenem. La osmolaridad urinaria ayuda a diferenciar las causas de hiponatremia por alteración en la excreción de agua, que tiene una osmolaridad mayor de 100 mOsmol/kg (18).

Para la interpretación de la osmolaridad urinaria, es fundamental considerar que "una osmolaridad superior a 100 mOsmol/kg sugiere una probabilidad significativa de la existencia de causas genuinas de hiponatremia, caracterizadas por una alteración en la excreción de agua" (19). La fórmula de la osmolaridad urinaria requiere correcciones por glucosuria y proteinuria (17).

CONCLUSIONES

1. Para el diagnóstico de hiponatremia se tiene que abordar con un enfoque fisiológico que incluya la confirmación secuencial de la hipotonicidad, la presencia y liberación de arginina vasopresina.
2. En casos agudos primero tratar el alivio de los síntomas para prevenir herniación cerebral.
3. En el tratamiento se debe considerar la prevención de nuevas disminuciones en el sodio.
4. El potasio y el sodio son osmóticamente equivalentes y se debe considerar el ajuste de la velocidad de infusión de solución salina hipertónica cuando se suplementa el potasio.
5. Evitar la corrección demasiado rápida y el SDO.
6. La desmopresina se puede utilizar para prevenir una corrección demasiado rápida de la hiponatremia.
7. La hiponatremia crónica, incluso leve y aparentemente asintomática, se ha asociado con deterioro neurocognitivo que incluye déficit de atención, alteraciones de la marcha, caídas y osteoporosis.
8. Para el tratamiento de la hiponatremia en IC, se prefieren los diuréticos de acción proximal, incluidos los inhibidores de SGLT2, la acetazolamida y los diuréticos de asa, y los diuréticos similares a las tiazidas se reservan para la resistencia grave a los diuréticos.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