Inpatient Hyponatremia: Opportunity for Pharmacists to Improve Patient Care

A knowledge-based CPE activity presented during the
2013 ISHP Spring Meeting

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Boise, Idaho

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Inpatient Hyponatremia:
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ACTIVITY FACULTY

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Dr. Pepin earned her Bachelor of Science degree in pharmacy from Ohio Northern University in Ada, Ohio, and her Doctor of Pharmacy degree from The University of Texas in Austin. Since 1987 she has assumed a variety of practice and management roles, including home health care pharmacy, acute care adult medicine, critical care, and clinical leadership. She serves as chair for the Seton Pain Management Team.

Dr. Pepin is a member of the Texas Pain Advocacy and Information Network (TxPain) Steering Committee. She also is a member of local and national pharmacy organizations, including the American Society of Health-System Pharmacists and Society of Critical Care Medicine. She is certified in Anticoagulation Management and is a fellow of the Patient Safety Improvement Corps (PSIC) supported by the Agency for Healthcare Research and Quality (AHRQ) and the U.S. Department of Veterans Affairs.

At Seton, Dr. Pepin has served as a team leader for TeamSTEPPS, which is an evidence-based teamwork system developed by AHRQ and the U.S. Department of Defense to improve patient safety and communication among health professionals. She has authored several publications and is currently involved in several patient safety initiatives and clinical research projects.

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ACTIVITY OVERVIEW

Hyponatremia is an often overlooked and undertreated electrolyte disorder with serious clinical and economic outcomes in hospitalized patients. This activity will provide an overview of hyponatremia management in hospitalized patients, including normal sodium regulation and the pathophysiology, prevalence, and outcomes associated with hyponatremia. Traditional treatment strategies, such as fluid restriction and hypertonic sodium chloride, and treatment with arginine vasopressin receptor antagonists (also called vaptans) will be reviewed. Patient vignettes will reinforce the application of important concepts to clinical practice.

There will be time for questions and answers at the end of the presentation.

LEARNING OBJECTIVES

At the conclusion of this knowledge-based CPE activity, attendees should be able to

- Describe the clinical and economic impact of hyponatremia in hospitalized patients.
- Identify different forms of hyponatremia.
- Describe the safety and efficacy of options for managing hyponatremia in hospitalized patients.
- Outline a plan for monitoring hospitalized patients for development and resolution of hyponatremia.

CONTINUING EDUCATION ACCREDITATION

The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1 hour (0.1 CEU) of continuing pharmacy education credit (ACPE activity # 0204-0000-12-434-L01-P).

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Date of Activity	Activity Title	Enrollment Code	Credit Hours
04-06-2013	Inpatient Hyponatremia: Opportunity for Pharmacists to Improve Patient Care	_ _ _ _ _	1.0

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Hyponatremia: Definition

- One of the most common electrolyte disorders seen in clinical practice
- Commonly defined as serum sodium concentration <136 mEq/L, but cut-off values vary

Serum Sodium Concentration (mEq/L)		
Mild	Moderate	Severe
131-135	120-130	<120

Upadhyay A et al. *Am J Med*. 2006; 119(Suppl 1):S30-5.
Kumar S et al. *Lancet*. 1998; 352:220-8.

Hyponatremia: Prevalence

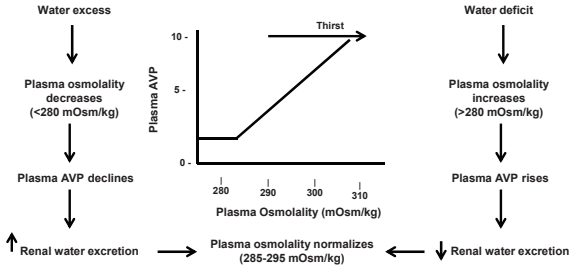
- 3.2−6.1 million persons annually
- 1 million hospitalizations annually with 1° or 2° diagnosis
  - Up to 15% of hospitalized patients, 30-40% of patients in intensive care unit (ICU)
  - Independent predictor of ICU mortality
- Incidence increases with age
- Significant morbidity and mortality
  - Preoperative hyponatremia: higher risk of 30-day mortality and 1-day adjusted increased length of stay (LOS)
- 60% of hyponatremia goes unreported
- No firm causality between hyponatremia and outcomes

Boscoe A et al. *Cost Eff Resour Alloc*. 2006; 4:1-11;
Friedman B et al. *J Crit Care*. 2012 Aug 8; Cawley MJ. *Ann Pharmacother*. 2007; 41:840-50;
Leung AA et al. *Arch Intern Med*. 2012 Sep 10; Movig KL et al. *J Clin Epidemiol*. 2003; 56:530-5.

Hyponatremia: Pathophysiology

- Excessive water retention
- Hypertonic urinary losses
- Impaired ability to excrete free water
- Plasma osmolality is regulated by thirst and the release of arginine vasopressin (AVP)
  - Also known as antidiuretic hormone (ADH)

AVP: Regulates Water and Electrolyte Balance



Kumar S et al. In Berl T, Bonventre JV, eds. Vol. 1. 1999:1.1-1.22.
Robertson GL et al. *Am J Med*. 1982; 72:339-33.
Rossi NF et al. *Crit Care Clin*. 1987; 3:759-77.

AVP: Receptor Subtypes

Receptor Subtype	Site of Action	Activation Effects
V_{1A}	Vascular smooth muscle cells Platelets Lymphocytes and monocytes Hepatocytes	Vasoconstriction Platelet aggregation Coagulation factor release Glycogenolysis
V_{1B}	Anterior pituitary	ACTH and β-endorphin release
V_2	Renal collecting duct cells	Free water absorption

ACTH = adrenocorticotropic hormone

Adapted from Lee CR et al. *Am Heart J*. 2003; 146:9-18.
Verbalis JG. *J Mol Endocrinol*. 2002; 29:1-9.

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Hyponatremia: Classification

Dilutional Hyponatremia
Total body water INCREASED

Hypervolemic
(edema)
Total body sodium INCREASED
Heart failure
Cirrhosis
Nephrotic syndrome

Euvolemic
(no edema)
Total body sodium UNCHANGED
SIADH
Hypothyroidism
Secondary adrenal insufficiency

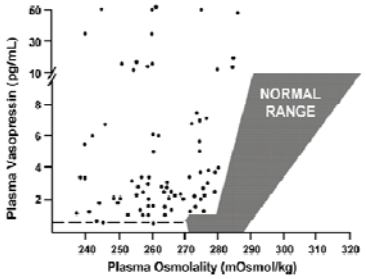
Depletional Hyponatremia
Total body water DECREASED

Hypovolemic
Sodium lost
Total body sodium DECREASED
Diarrhea
Vomiting
Burns
Trauma
Pancreatitis
Diuretic excess
Renal salt wasting
Primary adrenal insufficiency

SIADH = syndrome of inappropriate antidiuretic hormone

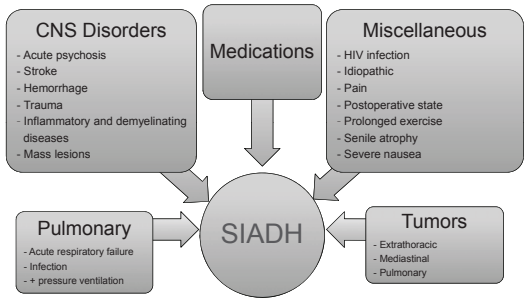
Cawley MJ. *Ann Pharmacother.* 2007; 41:840-50.

AVP: Concentrations Inappropriately Elevated in Patients with SIADH

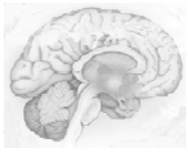


Zerbe R et al. *Annu Rev Med*. 1980; 31:315-27.

Various Causes of SIADH



Mechanisms of Drug-Induced Hyponatremia

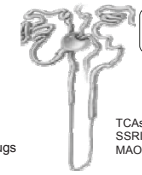


↑ Hypothalamic production of vasopressin

- Antidepressants (TCAs, SSRIs, MAOIs)
- Antipsychotics (phenothiazines, haloperidol)
- Antiepileptics (carbamazepine, valproic acid)
- Antineoplastic agents
- Opiates

↑ Vasopressin effect at renal tubule level

- Antidiabetic drugs (chlorpropamide, tolbutamide)
- Antiepileptics (carbamazepine, lamotrigine)
- IV cyclophosphamide
- Nonsteroidal anti-inflammatory drugs



Alter sodium and water homeostasis

- Thiazide diuretics and indapamide
- Amiloride
- Loop diuretics

TCAs = tricyclic antidepressants
SSRIs = selective serotonin reuptake inhibitors
MAOIs = monoamine oxidase inhibitors

Adapted from Liamis G et al. *Am J Kidney Dis*. 2008; 52:144-53.

Thiazide-induced Hyponatremia

- In observational study, occurred in 13.7% of treated patients
- Thiazides implicated in 26% of patients with hyponatremia
- Risk factors
  - Increasing age
  - Female gender
  - Low body weight
  - Increased incidence in summer

Note: thiazide-induced hyponatremia may be hypovolemic or euvolemic

Foote EF. In: Tisdale JE et al. Drug-induced diseases. 2012:885-902.

SSRI-induced Hyponatremia

- Incidence 0.5%–32%
- Occurs most often during 1st few weeks
  - Normal serum sodium usually achieved within 2 weeks of discontinuing drug
- Risk factors
  - Older age
  - Concomitant diuretic therapy
  - Low body weight
  - Baseline serum sodium concentration <133 mEq/L

Liamis G et al. *Am J Kidney Dis*. 2008; 52:144-53.
Jacob S et al. *Ann Pharmacother*. 2006; 40:1618-22.
Bouman WP et al. *Int J Geriatr Psychiatry*. 1998; 13:12-5.

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Role of the Pharmacist in Drug-induced Hyponatremia

- Thoroughly review home medications and those started in the hospital
- Critically evaluate the literature
- Know the elimination half life of the offending drug
  - Many have long half lives
  - Estimate the duration of drug effect on changes in sodium
  - May need other interventions during time of drug elimination

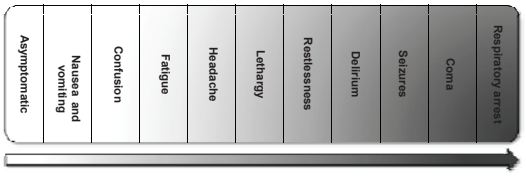
Common Symptoms Associated with Severity of Hyponatremia

Serum sodium concentration 130–135 mEq/L	Serum sodium concentration 120–130 mEq/L	Serum sodium concentration <120 mEq/L
• Asymptomatic • Headache • Nausea • Vomiting • Fatigue • Confusion • Anorexia • Muscle cramps • Depressed reflexes	• Malaise • Unsteadiness • Headache • Nausea • Vomiting • Fatigue • Confusion • Anorexia • Muscle cramps	• Headache • Restlessness • Lethargy • Seizures • Brainstem herniation • Respiratory arrest • Death

Bagshaw SM et al. *Can J Anaesth*. 2009; 56:151-67.
Ghali JK. *Cardiology*. 2008; 111:147-57.

Symptom Correlation with Declining Sodium Concentrations

- Asymptomatic presentation common
- May present with mild, nonspecific symptoms
- Degree of symptomatology is marker for duration of hyponatremia
- Symptoms from underlying disease process also common



Increasing rate of serum sodium decline and severity of hyponatremia

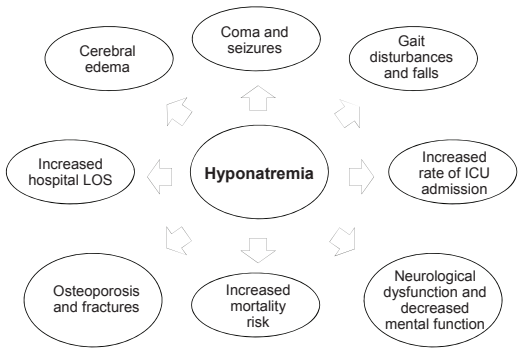
Bagshaw SM et al. *Can J Anesth*. 2009; 56:151-67; Ghali JK. *Cardiology*. 2008; 111:147-57.

Outcomes Associated with Declining Sodium Concentrations

- Defined as serum sodium <138 mEq/L on admission and decline ≥2 mEq/L over first 48 hr
- Occurs in 6% of community-acquired and 38% with hospital-acquired hyponatremia
- Inpatient mortality
  - OR 2.30 (1.75-3.02) with decline
  - OR 1.46 (1.31-1.64) with no decline
- Prolonged length of stay
  - OR 1.40 (1.32-1.49)
- Sets stage for impact of therapies

Wald RW et al. *Arch Intern Med*. 2010; 170:294-302.

Hyponatremia: Consequences



Patient: Mona Lisa

- 78-year-old woman presents to ED via EMS with altered mental status with mechanical fall
- Daughter reports mother "not acting right" recently
- Medication history includes "water pill and mood pill"
- Pertinent laboratory tests and imaging
  - Head CT: no acute findings
  - Urine drug screen: negative
  - Na=113 mEq/L, BUN=26 mg/dL, Scr=1.7 mg/dL
- What are issues surrounding her fall?

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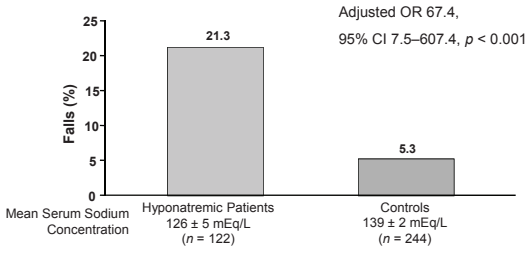
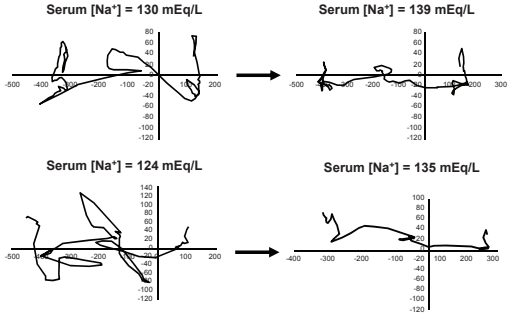
Falls: Common Symptom of Chronic "Asymptomatic" Hyponatremia



Patients with chronic "asymptomatic" hyponatremia admitted for falls significantly more frequently than patients with normal serum sodium

Renneboog B et al. *Am J Med.* 2006;119:71.e1-8.

Gait in Patients Before and After Correcting Hyponatremia



Renneboog B et al. *Am J Med.* 2006;119:71.e1-e8.

At your health system, does the falls team include a pharmacist?

?

a. Yes
b. No
c. I don't know

Role of the Pharmacist in Managing Falls

- Review complete list of medications taken at home
- Participate as member of falls team
  - Detect, report, and manage adverse drug events (ADEs)
  - Manage pharmacotherapy regimens and electrolyte disorders
  - Help to reduce CMS "Never Events" related to falls
- Confirm normonatremia in critically ill patients participating in early mobilization as part of delirium-reduction bundles
- Become involved in discharge medication reconciliation
  - Reduce or eliminate medications known to cause hyponatremia in at-risk patients

Principles to Guide Management

- Weigh risks and benefits
  - Neurologic consequences can follow both failure to promptly treat and excessively rapid rate of correction
  - Even modest improvement in serum sodium has survival benefits
- Monitor serum sodium frequently
- Address underlying disease and stop offending medications
- Identify acute vs. chronic hyponatremia

Adrogue HJ et al. *N Engl J Med.* 2000; 342:1581-9.
Verbalis JG et al. *Am J Med.* 2007; 120(Suppl 1):S1-S21.

Hyponatremia: Strategies for Correction

Add to the numerator (traditional approach)

$$\text{Serum sodium concentration} \sim \frac{Na^+_E + K^+_E}{\text{Body water}}$$

Subtract from the denominator (rational approach)

Verbalis JG et al. *Am J Med.* 2007; 120(Suppl 1):S1-S21.

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Patient: Jim Whistler

- 62-year-old man admitted to CCU for acute heart failure
- In ER given furosemide 40 mg IV and started nitroglycerin infusion 5 mcg/min to treat dyspnea
- Is slightly disoriented
- Abnormal labs in CCU
  - Potassium 3.3 mEq/L, sodium 120 mEq/L
- Drug orders in CCU
  - Potassium IV 20 mEq given over 30 minutes
  - 0.9% Sodium chloride at 100 mL/hr
- What are the problems surrounding the use of sodium chloride to increase Mr. Whistler's sodium concentration?

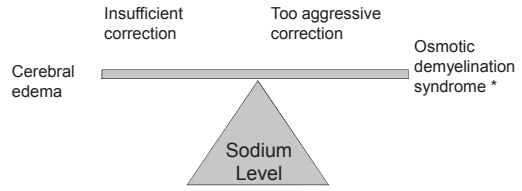
Acute vs. Chronic Hyponatremia

Acute (≤ 48 hr)	Chronic (> 48 hr)
Symptoms • Cerebral edema • Seizures • Increased mortality risk	**Symptoms** • Nausea and vomiting • Confusion or personality changes • Neurologic dysfunction • Gait disturbances • Seizures (with very low serum sodium levels)
Rapid correction reverses cerebral edema without sequelae	Rapid correction may cause brain dehydration and osmotic demyelination syndrome (ODS)

Apply pharmacotherapeutic knowledge to avoid overcorrection

Ghali JK. *Cardiology*. 2008;1 11:147-57.
Verbalis JG et al. *Am J Med*. 2007; 120(Suppl 1):S1-S21.

Increase Serum Sodium to More Normal Level at Appropriate Rate



*Patients with severe malnutrition, alcoholism, or advanced liver disease may be especially susceptible, and slower rates of correction may be advisable

Verbalis JG et al. *Am J Med*. 2007; 120(Suppl 1):S1-S21.
Adrogué HJ et al. *N Engl J Med*. 2000; 342:1581-9.

Principles of Sodium Correction

- Overly rapid increase in serum sodium (>12 mEq/L/24 hr) may result in serious sequelae
- Chronicity of hyponatremia impacts the rate at which correction should be undertaken
- Presence or absence of significant neurologic signs and symptoms must guide management

Janicic N et al. *Endocrinol Metab Clin N Am*. 2003; 32:459-81.
Kumar S et al. In Berl T, Bonventre JV, eds. Vol. 1. 1999:1.1-1.22.

Sodium Administration

- 0.9% Sodium chloride (normal saline)
  - Not for acute/severe symptoms correction – only 154 mEq Na/L
  - Not for edematous patients
- 3% Sodium chloride (hypertonic saline) +/- loop diuretic
  - Use for symptomatic or acute hyponatremia (seizure, coma)
  - Requires vigilant monitoring to avoid overcorrection
  - Discontinue when serum sodium reaches 120-130 mEq/L or symptoms subside
    - Exception: cerebral edema with sodium augmentation
- Safety concerns: requires ICU monitoring
- No randomized trials performed

Fall PJ. *Postgrad Med*. 2000; 107:75-82.
Zietse R et al. *NDT Plus*. 2009; 2(Suppl 3):iii12–iii19.

Fluid Restriction (500-900 mL/day)

- Can be used in asymptomatic hyponatremic patients or patients with less serious hyponatremia
- Raises serum sodium approximately 1 to 2 mEq/L/day
  - May be too slow
- Patient adherence limited due to thirst
- Pharmacist may not know about a fluid restriction order
- Difficult to implement
  - Must account for all fluids
  - Patients in ICU: often receiving 8-12 IV drugs with volume of 4-8 L/day

Munger MA. *Am J Health-Syst Pharm*. 2007; 64:253-65; Cawley MJ. *Ann Pharmacother*. 2007; 41:840-50; Goldsmith SR. *Am J Cardiol*. 2005; 95(Suppl):14B-23B.

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Myth: Fluid Restriction Is Cheap

- Assumption is that giving less costs less
- Most expensive therapy is the one that does not work
- Cost implications when concentrating IV drugs in a patient with hyponatremia
  - Takes time to change drug concentration
  - Can increase pharmacy workload
  - Potential for drug waste
  - Potential for errors if pump is not re-programmed

At your health system, are pharmacists routinely notified of orders for fluid restriction?

a. Yes
b. No
c. I don't know

Demeclocycline 600 mg/day

- Tetracycline antibiotic that blocks effect of AVP
- Leads to increased urine volume, decreased urine osmolality, and increased serum sodium concentration
- Not FDA approved for treatment of hyponatremia
  - Can be used in chronic asymptomatic hyponatremia if loop diuretics and fluid restriction have failed and in non-acute SIADH
- Slow onset of action (3-6 days)
- Adverse effects: nephrotoxicity, neurotoxicity, polyuria, and photosensitivity
- Renal function monitoring required, particularly in patients with cirrhosis
  - Adds to cost of care

Goldsmith SR. *Am J Cardiol.* 2005; 95(Suppl):14B-23B.

AVP-Receptor Antagonists*

Agent	Receptor Selectivity	Formulation	Half-life, hr	Urine Volume	Urine Osmolality	FDA Approval Status
Conivaptan	Mixed (V_{1a}+V_2)	IV	5	↑	↓	Approved 2004
Tolvaptan	V_2	Oral	12	↑	↓	Approved 2009
Lixivaptan	V_2	Oral	7–10	↑	↓	In review

- Induce highly hypotonic urine and diuresis without substantially affecting electrolyte excretion, referred to as aquaresis
- Indicated for treatment of euvolemic and hypervolemic hyponatremia only
  - Use in mild asymptomatic hyponatremia is questionable

*Also called vaptans.

Decaux G et al. *Lancet.* 2008; 371:1624-32.
Lee CR et al. *Am Heart J.* 2003; 146:9-18.
Zietse R et al. *NDT Plus.* 2009; 2(Suppl 3):iii12-iii9.

Conivaptan 20–40 mg/day (IV)

- Indicated for euvolemic or hypervolemic hyponatremia in hospitalized patients
- Administer IV via large veins
  - Infusion-site reactions (63–73%), change infusion site every 24 hr
- Available as 20 mg/100 mL premixed in 5% dextrose
- Dosing: 20-mg IV loading dose over 30 min, then 20 mg as continuous infusion over 24 hr
  - Only compatible with 5% dextrose
- Duration of infusion limited to 4 days
- Limited data on IV drug–drug compatibility
- Contraindicated with potent CYP3A4 enzyme inhibitors
  - Examples: ketoconazole, itraconazole, indinavir

Vaprisol (conivaptan hydrochloride) injection prescribing information. 2011 Feb (URL in ref list).

Tolvaptan 15–60 mg/day (Oral)

- Indicated for clinically significant hypervolemic and euvolemic hyponatremia (serum sodium < 125 mEq/L or less marked hyponatremia that is symptomatic and has resisted correction with fluid restriction), including patients with heart failure, cirrhosis, and SIADH
- Available in 15-mg and 30-mg tablets
- Dosing: 15 mg orally once daily
  - May increase at intervals >24 hr to maximum 60 mg once daily
- Should only be initiated and re-initiated in hospital setting
  - Must review FDA-approved medication guide with every patient
- Contraindicated with potent CYP3A4 enzyme inhibitors
  - Examples: ketoconazole, itraconazole, indinavir

Samsca (tolvaptan) prescribing information. 2009 May (URL in ref list).

Adverse Effects of AVP-Receptor Antagonists*

Conivaptan	Tolvaptan
• Nausea/vomiting (3–7%) • Polyuria (6%) • Hypokalemia (10–22%) • Pyrexia (11%) • Headache (10%) • Orthostatic hypotension (14%) • Constipation (8%) • Infusion site reactions (70%) – Phlebitis, pyrexia, swelling – Edema, erythema, pain	• Nausea (20%) • Pollakiuria (11%) • Thirst (16%) • Dry mouth (13%) • Asthenia (9%) • Constipation (7%) • Hyperglycemia (6%) • Pyrexia (4%)

*Data not obtained from comparative clinical trials.

Vaprisol (conivaptan hydrochloride) injection prescribing information. 2011 Feb (URL in ref list).
Samsca (tolvaptan) prescribing information. 2009 May (URL in ref list).

Safety Warning for Tolvaptan: Letter Distributed January 22, 2013

- Safety warning of reversible liver injury with tolvaptan
- Clinical trial, polycystic kidney disease (n = 1400)
  - Significant elevations in liver function tests in 3 patients
  - Reversible following tolvaptan discontinuation
  - Doses of 120 mg/day (higher than in hyponatremia)
- Liver damage not reported in hyponatremia trials
- Cannot exclude similar risk using tolvaptan in hyponatremia

Otsuka. Important drug warning. 2013 Jan 22 (URL in ref list).

Summary of Treatment Options

Treatment	Mechanism	Advantage	Limitations
Saline infusion (isotonic or hypertonic)	Sodium replacement	Rapid response in symptomatic patients Inexpensive	Complex calculations Volume expansion – not for edema-forming disorders
Fluid restriction	Decreases availability of free water	Inexpensive	Noncompliance Slow response Minimal ↑ in sodium
Loop diuretic	Decreases both free water and sodium	Inexpensive	Loss of sodium, potassium, magnesium Contraction alkalosis
Demeclocycline	Targets excess AVP	Unrestricted water intake	Nephrotoxic in heart failure and cirrhosis Slow onset
AVP-receptor antagonists	Targets excess AVP	Available as oral and IV Aquaresis (solute-free urine output)	Drug interactions Not for hypovolemic disorders

Hyponatremia: Often mismanaged

- Prospective review of lab and chart data at a large teaching hospital
  - In 6 months, 104 patients with serum sodium <125 mEq/L
- 42% of diagnoses inconsistent with clinical details
- 33% had "significant" management errors
  - Inadequate investigation (10)
  - Diuretic-induced hyponatremia treated with fluid restriction (6)
  - Fluid restriction + IV sodium chloride (4)
  - Thiazides continued (4)
  - Inappropriate IV sod chloride (4)
  - IV saline in heart failure (1)
  - Desmopressin in SIADH (1)
  - Iatrogenic (4)
- 27% overall mortality rate
  - 20% mortality in patients managed appropriately
  - Mortality rate doubled in patients with management errors

Huda MS et al. *Postgrad Med J*. 2006; 82:216-9.

Role of the Pharmacist in Monitoring of Hyponatremia Strategies

- Verify proper therapeutic choices
  - Overall goal: Avoid overcorrection
- Monitor
  - Basic metabolic panel (e.g., sodium, potassium, chloride)
  - Frequent serum sodium levels
  - Neurologic function
  - Serum osmolality
  - Urine osmolality and sodium concentration
  - Fluid intake and output
- Use free water in cases of overcorrection
- Avoid offending medications

Verbalis JG et al. *Am J Med*. 2007; 120(Suppl 1):S1-S21.

Factors Influencing Therapeutic Decisions

- Safety and efficacy – rate of change in serum sodium
  - Fluid restriction – slow – hard to implement
  - 0.9% sodium chloride correction – medium but cannot use on all patients – heart failure
  - Demeclocycline – slow – nephrotoxicity
  - Vaptans – medium – overcorrection can occur
  - 3% sodium chloride correction – fastest – highest risk
- Total cost of care vs. acquisition cost

Jaber BL et al. *Am J Med*. 2011; 124:977.e1-e9.
Dasta JF et al. *Exp Rev Pharmacoecon Outcomes Res*. 2012; 12:399-410.

Pharmacoeconomic Data Related to the Pharmacotherapy of Hyponatremia

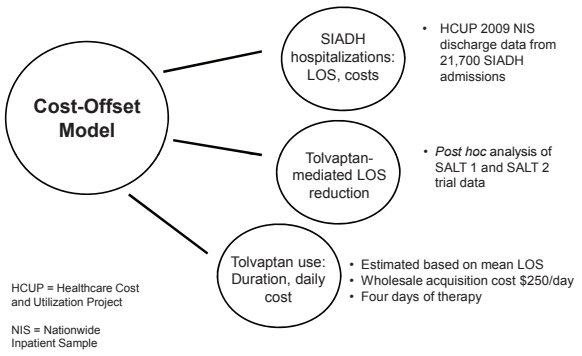
- Fluid restriction – No
- Demeclocycline – No
- 3% Sodium chloride – No
- Furosemide – No
- Conivaptan – No
- Tolvaptan – Yes

Economic Evaluation of New Pharmaceuticals

- Evaluate the balance between
  - Acquisition cost of the drug
  - Effects on total cost of care
- Can use cost-effectiveness and cost-consequence methods
  - Is the cost of the new drug worth the expenditure of funds?

Dasta JF et al. *Exp Rev Pharmacoecon Outcomes Res*. 2012; 12:399-410.

Cost-Offset Model of Tolvaptan: SIADH



Dasta JF et al. *Hosp Prac (Minneap)*. 2012; 40:7-14.

Cost-Offset Model: Results

- Overall cost reduction per admission due to tolvaptan use

Type of Resource	Reduction per Admission	Total Cost of Tolvaptan Use	Total Cost-Offset
Total hospital cost ($)	$1694	$1000	$694
Length of stay (days)	1.11	--	--

- $15 million total cost reduction for HCUP patients
- Cost neutral (cost − offset = $0) threshold for duration of tolvaptan therapy
  - 6.8 days

Dasta JF et al. *Hosp Prac (Minneap)*. 2012; 40:7-14.

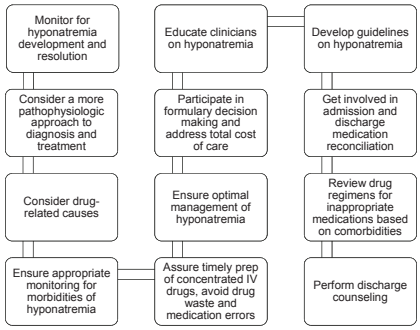
What is known about the real-world use of therapies for hyponatremia?

Hyponatremia Registry: Interim Results

- Observational registry
  - Defined as serum sodium < 130 mEq/L
  - Target enrollment 5000, 1672 enrolled as of April 2012
- Mean entry and discharge serum sodium
  - 126.4 ± 7.5 mmol/L and 131.7±5.0 mmol/L, respectively
  - 41% hyponatremic at discharge
- Monotherapies
  - Fluid restriction (29%)
  - 0.9% sodium chloride (21%)
  - Pharmacologic therapy (5%)
  - Hypertonic saline (1.3%)
- Overcorrection in 29% with hypertonic saline

Dasta J et al. American College of Clinical Pharmacy Annual Meeting; 2012 Oct 20.

Role of Pharmacists in Managing Patients with Hyponatremia



Conclusion

- Hyponatremia is common and complex
  - Often misunderstood and overlooked
- Questions remain about optimal management
- Recent data
  - Address inadequacies of current management
  - Probe into effects of total costs associated with vaptans
- National guidelines on management of hyponatremia in hospitalized patients needed
- Pharmacists can play important role

Inpatient Hyponatremia: Opportunity for Pharmacists to Improve Patient Care

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Inpatient Hyponatremia: Opportunity for Pharmacists to Improve Patient Care

SELF–ASSESSMENT QUESTIONS

1. As shown in a study by Leung et al., how does the risk of 30-day mortality for preoperative patients with hyponatremia compare with that of preoperative patients with normal baseline sodium levels?

   a. Higher.
   b. Lower.
   c. No difference.

2. Which of the following statements best describes hypervolemic hyponatremia?

   a. Both total sodium and water content in the body increase, but the water gain is greater.
   b. Both total sodium and water content in the body decrease, but the sodium loss is greater.
   c. Total water content in the body increases, but the sodium content in the body stays the same.
   d. Total water content in the body decreases, and the sodium content in the body stays the same.

3. As a general principle of sodium correction in hospitalized patients with hyponatremia, the 24-hour increase in serum sodium should be limited to less than _____ to avoid serious sequelae.

   a. 6 mEq/L.
   b. 12 mEq/L.
   c. 18 mEq/L.
   d. 24 mEq/L.

4. A 75-year-old man is brought to the emergency department after a fall, and his family reports that he has acted groggy lately. His medication history includes chlorothiazide and paroxetine. Pertinent laboratory tests and imaging results indicate no head injury, negative urine screen, serum sodium 115 mEq/L, BUN 26 mg/dL, and Scr 1.7 mg/dL. Which of the following should be investigated and monitored as a possible cause of this gentleman's fall?

   a. Kidney function.
   b. Liver function.
   c. Low serum sodium.
   d. Nothing; falling is a natural consequence of aging.

Answers

1. a
2. a
3. b
4. c