Recurrent SIADH after Switching Citalopram to Very Low Dose Duloxetine in the Elderly

Dae Hyoun Jeong MD, Patrick Doggett MD, Kristine Swartz MD, Lauren Hersh MD, Brooke Salzman MD
Division of Geriatrics and Palliative Care, Department of Family and community Medicine
Thomas Jefferson University, Philadelphia, PA

OBJECTIVE

- Duloxetine-induced SIADH has been seldom reported
- This case study emphasizes the importance of suspecting rare adverse effects of recurrent SIADH after switching an SSRI to duloxetine in older adults

BACKGROUND

❑ **Hyponatremia** : serum sodium < 135 mmol/L [1,2]

- Symptoms: anorexia, nausea/vomiting, poor concentration, confusion, lethargy, agitation, headache, seizures, coma
- Associated with considerable morbidity and mortality

❑ **Syndrome of inappropriate antidiuretic hormone secretion (SIADH)** [1,2]

- Accounts for nearly 60% of all hyponatremias
- Euvolemic, Serum osm < 275, Urine osm > 100, Urine Na > 30

❑ **Drug-induced Hyponatremia** [2]

Common causes	Rare causes
Thiazide diuretics	ACE inhibitor
SSRI	Amlodipine
TCA	Immunoglobulin (IV)
MAO inhibitor	Bactrim, Ciprofloxacin
Typical Antipsychotics	Amiodarone
Antiepileptic drugs	Proton pump inhibitors
Anticancer agents	Duloxetine
Venlafaxine	Bupropion

- Characterized by an excess of ADH, most frequently caused by SIADH or effective circulating volume depletion
- SSRIs are well recognized for causing SIADH and hyponatremia [1,5]

❑ **Duloxetine** : serotonin-norepinephrine reuptake inhibitor (SNRI)

- Indications : major depressive disorders, diabetic neuropathy, fibromyalgia, urinary stress incontinence
- Theoretically, duloxetine confers high risk for causing SIADH and hyponatremia because it inhibits the reuptake of both serotonin and norephinephrine, which can stimulate ADH release [4]

❑ **Risk factors for duloxetine-induced SIADH** [3,4,6]

- Female gender, polypharmacy, lower baseline serum sodium concentration, low body weight and old age

❑ **Management of duloxetine-induced SIADH** [1,2,5]

- Discontinuation of suspected drugs, fluid restriction, salt intake, tolvaptan, demeclocycline, 3% normal saline (if severe)

CASE PRESENTATION

❑ **HPI** : 86 year-old male with mild dementia and alcoholism who suffered a right hip fracture following a fall

- He underwent R hip repair in April 2015 and was discharged to a rehab facility where his course was complicated by pneumonia
- He developed depression and attempted suicide by hanging in August 2015
- He was transferred to a Geriatric psychiatric unit

- **PMH** : TIA, alcoholism, a-fib, dementia, recurrent falls, restless leg syndrome, GERD, h/GI bleed, IBS, mild anemia
- **Medications** : Ropinirole, zolpidem, thiamine, percocet, ativan, memantine, Donepezil, Atenolol, FeSO4
- **V/S** : BP 122/82, HR 70, RR 18, T 98.0, Ht 5'9",Wt 140lb,BMI 20.7
- **P/E** : unremarkable. Neurologic: AAO x 3 , mild BLE weakness Psychiatric: (+)depressed mood, (-) suicidal ideation or plan.
- **Labs** (on admission) : Hb 10.6, TSH 2.34, B12 596, folate 21 CMP : Na 135 K 3.8 BUN 16 Cr. 0.5

❑ **Clinical course during the hospitalization**

HD 1
- Started on citalopram 10mg QD
- Baseline serum: **Na 135** mM on admission
- The dose was increased to 30mg q daily within 1 week

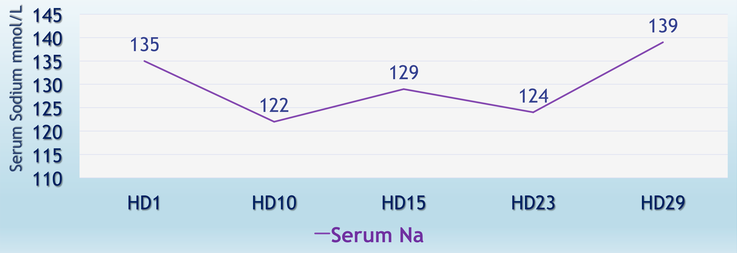
HD10
- Patient reported feeling weaker and drowsy
- Serum **Na 122** mM (Se Osm 258,Ur Osm 771,Urine Na 47)
- Workup for hyponatremia suggested **SIADH**

HD15
- Citalopram was switched to **duloxetine 20mg QD**
- Initiated fluid restriction
- Serum **Na 129** mM (3days after citalopram was discontinued)

HD23
- Patient increasingly lethargic and reported vivid dreams
- Serum **Na 124** mM (10 days after a trial of duloxetine 20mg)

HD29
- Duloxetine was discontinued. Fluid restriction was stopped
- Serum **Na 139** mM(10 days after duloxetine was discontinued)
- Symptoms improved significantly

Trend of serum sodium level during hospitalization



DISCUSSION

❑ **Risk factors for duloxetine-induced hyponatremia**

(1) Old age (2) low body weight (3) low baseline serum sodium level

❑ **Significance of our case**

- Our patient was using the lowest dose of duloxetine (20mg QD) (duloxetine was used for MDD at 30 to 120 mg QD in other cases)
- There is only one other case reported on recurrent hyponatremia after substitution of citalopram with duloxetine [5]

❑ **Consideration**

- We should be aware of duloxetine-induced SIADH while treating older adults with lower duloxetine dosages because serious hyponatremia may be mistaken for worsening of depression
- Older adults started on duloxetine should be closely monitored for hyponatremia, especially within a week of the treatment [5]

CONCLUSION

- **Duloxetine-induced hyponatremia is rare but can occur, even with doses as low as 20mg/day in the elderly.**
- **SNRI may induce hyponatremia in patients with SSRI-induced hyponatremia**
- **Closer monitoring of serum sodium level is required after initiating duloxetine in older adults**

REFERENCES

1. Liamis et al, A Review of Drug-Induced Hyponatremia, Am J Kidney Disease 52(1) 2008:144-153
2. Lee et al, Management of Hyponatremia, CMAJ, May 13, 2014, 186(8)
3. Nakamura et al, Duloxetine-induced Hyponatremia in the Elderly, CNPT3(2012)
4. Beydilli et al, Low Dose Duloxetine Induced Hyponatremia in an Elderly Patient: A Case Report, Bulletin of Clinical Psychopharmacology 2012;22(3):283-5
5. Dirks, et al, Recurrent Hyponatremia After Substitution of Citalopram With Duloxetine, J. of Clinical Psychopharmacology, 27(3) June 2007
6. Amoako et al, Syndrome of inappropriate antidiuretic hormone secretion: a story of duloxetine-induced hyponatraemia, BMJ Case Rep 2015

CONTACT

❑ For additional information, please contact:

Dae Hyoun "David" Jeong, MD
Geriatric Medicine Fellow
Division of Geriatrics and Palliative Care
Department of Family and Community Medicine
Thomas Jefferson University, Philadelphia, PA 19106