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

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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
- **Drug-induced Hyponatremia**
  - Common causes
    - Thiazide diuretics
    - SSRI
    - TCA
    - MAO Inhibitor
    - Venlafaxine
  - Rare causes
    - ACE Inhibitor
    - Amlodipine
    - Immunoglobulin (IV)
    - Bacitracin
    - Proton pump inhibitors
    - Duloxetine
    - Bupropion
  - Characterized by an excess of ADH, most frequently caused by SIADH or effective circulatory volume depletion
  - SSRIs are well recognized for causing SIADH and hyponatremia
- **Duloxetine**
  - Serotonin-norepinephrine reuptake inhibitor (SNRI)
  - Indications: major depressive disorders, diabetic neuropathy, restless leg syndrome, GERD, h/GI bleed, IBS, mild anemia
  - Theoretically, duloxetine confers high risk for causing SIADH and hyponatremia because it inhibits the reuptake of both serotonin and norepinephrine, which can stimulate ADH release

HYponatremia
- serum sodium < 135 mmol/L
  - 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)**
  - Accounts for nearly 60% of all hyponatremias
  - Euvolemic, Serum osm < 275, Urine osm > 100, Urine Na > 30
  - Accounts for nearly 60% of all hyponatremias

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, FosFO4
  - V/S: BP 122/82, HR 70, RR 18, T 98.0, Ht 5’9”,Wt 140lb,BMI 20.7
  - **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**
  - Started on citalopram 10mg QD
  - Baseline serum: Na 135 mmol on admission
  - The dose was increased to 30mg q daily within 1 week
  - Patient reported feeling weaker and drowsy
    - Serum Na 122 mmol (5e Osm 258, Ur Osm 771, Urine Na 47)
    - Workup for hyponatremia suggested SIADH
      - Citalopram was switched to duloxetine 20mg QD
      - Initiated fluid restriction
      - Serum Na 125 mmol (3 days after citalopram was discontinued)
        - Patient increasingly lethargic and reported vivid dreams
          - Serum Na 124 mmol (10 days after a trial of duloxetine 20mg)
            - Duloxetine was discontinued. Fluid restriction was stopped
              - Serum Na 139 mmol (10 days after duloxetine was discontinued)
                - Symptoms improved significantly

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
- **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

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

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