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Dose-dependent mirtazapine-induced hyponatraemia: a case report

Abstract

Mirtazapine is a heterocyclic antidepressant having noradrenergic and serotonergic activity. The pharmacodynamic is similar to selective serotonin reuptake inhibitor (SSRI) and tricyclic antidepressant (TCA). Hyponatraemia with mirtazapine can be seen in elderly population with other comorbidities. We present a rare case of hyponatraemia induced after increasing the dose of mirtazapine in a middle-aged woman, without any medical comorbidities.

Keywords: Antidepressant, Noradrenergic, Serotonergic.

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INTRODUCTION

Antidepressants, especially selective serotonin reuptake inhibitors (SSRIs) are known to cause hyponatraemia. Incidence of which is suggested to be minimal with duloxetine, venlafaxine, and mirtazapine.[1] Mirtazapine is a comparatively newer heterocyclic antidepressant having both noradrenergic and serotonergic activity through alpha-2 adrenergic blockade activity. Elderly people with multiple physical comorbidities like hypertension, diabetes mellitus, advancing age, and combination of drugs were found to be more vulnerable in reported cases of mirtazapine-induced hyponatraemia.[2-5] Here, we are presenting a case of dose-dependent mirtazapine-induced hyponatraemia in an adult without any medical comorbidities. The patient has provided permission to publish these features of her case.

CASE REPORT

A 48-year-old woman of low socioeconomic status, who was premorbidly well-adjusted, presented to psychiatry outpatient department with the complaints of persistent sadness of mood, lethargy, anhedonia, depressive cognition, and decreased sleep, precipitated by a family stress in the form of death of her husband seven months back. Her past history did not reveal any significant medical or psychiatric illness, without any family history of mental illness. Her body weight was 46 kg, body mass index (BMI) = 18.42 kg/m^2, and blood pressure (BP) was within normal limits. She was diagnosed with moderate depressive episode without somatic syndrome according to the International Classification of Diseases (ICD-10). Because of her marked sleep disturbance, tablet mirtazapine 7.5 mg/day for one week and later 15 mg/day along with tablet clonazepam 0.5 mg was given. Meanwhile, routine investigations like complete haemogram, serum electrolytes, renal function test, liver function test, thyroid function test, random blood sugar, and fasting lipid profile were done which did not reveal any abnormality. Subjective improvement was 20-30% and the Hamilton-Depression Scale score was reduced from 16 to 14; hence, the dose of tablet mirtazapine was increased to 30 mg/day. However, within three days after increasing the dose, patient reported of headache, nausea, vomiting, fatigability, giddiness, excessive thirst, and irritability following which patient was brought to the casualty. Physical examination did not reveal any significant abnormality and vitals were stable. Patient was admitted and investigated, and noted to find hyponatraemia (Na^+ = 122 mEq/L). Tablet mirtazapine was stopped immediately. Patient was managed with fluid restriction and isotonic saline infusion. Patient was better in next two days. Her mental state improved and serum sodium was normalised (136 mEq/L). After one week, serum sodium was repeated and was within normal limits. Patient was started on tablet desvenlafaxine 25 mg, which she tolerated well. Her depressive symptoms remitted and patient was maintaining well with tablet desvenlafaxine 50 mg since past four months.

DISCUSSION

Table 1 showing the Naranjo adverse drug reaction probability scale score as six indicating probable association between mirtazapine and hyponatremia.[6] There are not many case reports of hyponatraemia after mirtazapine treatment. Most of which had risk factors like hypertension, diabetes mellitus, advanced age, renal dysfunction, low body weight, and other

Table 1: Naranjo adverse drug reaction probability scale[6]

Question	Yes	No	Do Not Know	Score
1. Are there previous conclusive reports on this reaction?	+1	0	0	0
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	+1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0	+1
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	+1
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	+1
			Total Score:	6

comorbidities.[3-4,7] No comorbidities were present in this case. Patient became symptomatic for hyponatraemia immediately after increasing the dose of mirtazapine from 15 mg/day to 30 mg/day. Evidence for dose-dependent mirtazapine-induced hyponatraemia is less.[2] Proposed reasons for hyponatraemia following SSRI are due to action of serotonin on hypothalamus, thereby increasing the secretion of antidiuretic hormone (ADH).[8]

Conclusion

Mirtazapine-induced hyponatraemia can develop in individuals without any risk factors as evidenced in this case and hence, serum sodium levels should be monitored like with any other SSRIs.

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