



HYPONATREMIA AMONG ADULT PATIENTS ON ANTIDEPRESSANTS: A CROSS-SECTIONAL STUDY

Psychiatry

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ABSTRACT

Background And Objective: Antidepressant-induced hyponatremia is a potentially life-threatening complication associated with antidepressants use. However, ongoing debate and conflicting evidence regarding which specific antidepressants are more likely to cause hyponatremia, create uncertainty in clinical practice. Understanding the relative risk of hyponatremia associated with different antidepressant classes is crucial for informed prescribing decisions and patient safety. Therefore, this study aimed to estimate the prevalence of hyponatremia associated with antidepressant medications and identify the risk factors contributing to its development in the Indian population. **Methods:** A cross-sectional observational study was conducted over a period of 2 months. Patients visiting the psychiatry department who met the inclusion criteria were recruited after obtaining written informed consent. Patient data was collected in a case report form and analyzed. Abnormal electrolyte levels were closely examined for associations with the class of antidepressants prescribed, individual drugs, patient gender, and any concomitant medical illness or medications. Possible associations and correlations were documented. **Results:** Among the various side effects of antidepressants, hyponatremia showed a notable association with the selective serotonin reuptake inhibitors (SSRIs) class of antidepressant drugs. Among individual drugs, paroxetine exhibited the highest number of cases causing hyponatremia. Interestingly, hyponatremia was observed only in female patients and not in males. No significant association was found between hyponatremia and concomitant medical illnesses or medications. The prevalence of hyponatremia was 2.65% in patients taking any antidepressant medication and 3.51% in those specifically prescribed SSRIs. **Conclusion:** Antidepressant-induced hyponatremia, particularly with SSRIs, is an important adverse effect. Further studies are needed to explore associated risk factors and prevent serious complications.

KEYWORDS

Antidepressants, hyponatremia, selective serotonin reuptake inhibitors, serotonin-noradrenaline reuptake inhibitors, tricyclic antidepressants.

INTRODUCTION:

Selective serotonin reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs), are recommended as first-line treatments due to their perceived safety compared to the older tricyclic antidepressants (TCAs). Still, recent studies have highlighted that some new-generation antidepressants may have more deleterious adverse effects.^[1,2,3,4] One such effect is hyponatremia which is the most commonly encountered electrolyte disorder with symptoms varying from anorexia and mild lethargy to coma and severe seizures.^[5,6] Because of similarity of these symptoms with those of depression, antidepressant-induced hyponatremia often remains masked. So, the identification of antidepressants with a lower propensity to induce hyponatremia holds significant importance.

Despite extensive recent research into the correlation between antidepressants and hyponatremia, a consensus remains elusive due to conflicting evidence.^[7,12] Several studies demonstrated a reduced risk of hyponatremia for noradrenergic and specific serotonergic antidepressants (e.g., mirtazapine).^[8-11] Though, contradictory results have indicated mirtazapine as having the highest reported risk of hyponatremia.^[12] Findings of within the same antidepressants class are also conflicting.^[7,11]

Methods

A total number of 101 patients aged 18 to 79 years, visiting the psychiatry department and taking antidepressant medications for at least three weeks were recruited in the study ok obtaining written informed consent. Patients who had experienced vomiting along with diarrhea and abdominal pain due to any cause within the last three weeks and were unwilling to participate were excluded.

Serum electrolyte levels of all the enrolled patients were recorded. Patients with serum sodium levels between 135 - 145 mEq/L were considered as normal levels. Those with serum sodium levels lower than 135 mEq/L were classified as having hyponatremia, while those with sodium levels exceeding 145 mEq/L were classified as having hypernatremia. Further, based on the obtained patient data, common antidepressant drugs associated with hyponatremia and hypernatremia based on the patient data obtained. Any confounding factors contributing to hyponatremia were studied. All the data was then analysed to estimate the hyponatremia among patients taking

antidepressant medications. The study also investigated any confounding factors contributing to hyponatremia. Patient identities were kept confidential throughout the study, and all patient-related data were used only after obtaining informed consent.

Statistical Analysis

The collected data was tabulated using Microsoft Excel software and analyzed using SPSS software. Sodium levels corresponding to various classes of antidepressants were documented, and a comparative study was conducted to identify the most common drugs or groups of antidepressants causing hyponatremia. Additionally, factors like age, gender, or concomitant medications contributing to hyponatremia were noted and analyzed.

RESULTS

Of the total 101 patients, 65 were female and 36 were male. All patients were being treated with antidepressants for a variety of diseases including depression, panic disorders, anxiety disorders, and dissociative disorders.

Among the patients, SSRIs were the commonly prescribed class of antidepressants (75.5%) followed by TCAs (16.6%), NaSSAs (5.3%) and SNRIs (2.6%). The most commonly prescribed drugs were paroxetine (25.2%) and escitalopram (25.2%), followed by sertraline (18.5%), amitriptyline (15.9%), fluoxetine (7.3%), mirtazapine (5.3%), venlafaxine (1.3%) and duloxetine (1.3%).

Most drugs showed an average serum sodium level of 140 mEq/L except for duloxetine which showed an average serum sodium of 137.5 and amitriptyline which showed a level of 141.7 mEq/L.

Table 1: Serum Electrolyte Levels

Parameters	Number of Patients n (%)
Normal serum sodium levels	140 (92.7)
Hyponatremia	4 (2.64)
Hypernatremia	7 (4.63)
Normal serum potassium levels	146 (96.6)
Hypokalaemia	2 (1.32)
Hyperkalaemia	3 (1.98)
Normal serum chloride levels	97 (64.2)

Hypochloremia	1 (0.66)
Hyperchloremia	53 (35.1)

Table 1 represents serum electrolyte level. The majority of the patients (92.7%) had normal serum sodium levels (140mEq/L) while 2.64% patients developed hyponatremia and 4.63% patients developed hypernatremia. Similarly, the majority of the patients (96.6%) showed normal potassium levels except for 1.32% patients who developed hypokalemia and 1.98% patients developed hyperkalemia. About 64.2% patients had normal serum chloride levels while 0.66% patient developed hypochloremia and 35.1% patients developed hyperchloremia.

Hyponatremia was observed in four patients taking SSRIs. Of these four cases, three patients were taking paroxetine and one patient was taking sertraline (Table 2).

Table 2: Characteristics Of The Patients Who Developed Hyponatremia

Sr. No	Age (Years)	Gender	Sodium levels (mEq/L)	Diagnosis	Class of drug	Drugs used	Drug Dose (mg)
1	46	Female	128	Anxiety	SSRI	Sertraline	25
2	36	Female	133	Dissociative disorder	SSRI	Paroxetine	12.5
3	24	Female	133	Depression	SSRI	Paroxetine	12.5
4	61	Female	134	Depression	SSRI	Paroxetine	12.5

Hypernatremia was observed in a total of seven patients, with five of them taking SSRIs class of antidepressants and two on TCAs. Among those taking SSRIs, three were on paroxetine, and two were on escitalopram. Both patients with hypernatremia and taking TCAs were on amitriptyline (Table 3).

Table 3: Characteristics Of The Patients Who Developed Hypernatremia

Sr No	Age (Years)	Gender	Sodium levels (mEq/L)	Diagnosis	Class of drug	Drugs used	Drug dose (mg)
1	48	Female	147	Depression	SSRI	Escitalopram	10
2	38	Female	146	Depression	SSRI	Escitalopram	10
3	53	Female	147	Dysthymia & panic attack	TCA	Amitriptyline	25
4	45	Male	147	Depression	TCA	Amitriptyline	25
5	25	Male	151	Depression	SSRI	Paroxetine	12.5
6	41	Male	147	Depression	SSRI	Paroxetine	12.5
7	46	Male	152	Depression	SSRI	Paroxetine	12.5

The prevalence of hyponatremia due to antidepressant medications was found to be 2.65%. Whereas the prevalence of hyponatremia among patients who were only prescribed SSRI, which was the most widely prescribed antidepressant was 3.51%.

DISCUSSION

Antidepressant therapy has proven to be effective for numerous patients of depression and related disorders. However, it does present its own set of complexities, and proper preparation of subjects to manage potential complications is crucial for ensuring a positive outcome^[8-11]. One such complication is the possibility of hyponatremia. In light of these concerns, this study aimed to determine the prevalence of hyponatremia among patients using antidepressant drugs^[9-12].

This study revealed that hyponatremia was only observed in patients using SSRIs and not in those prescribed any other class of antidepressants. This finding aligns with a previous study by Moving KL et al.^[13], which also identified that SSRIs carries three-fold higher risk of developing hyponatremia, than other antidepressants. In contrast to their findings, this study did not find old age to be a significant risk factor for hyponatremia, which can be attributed to the small sample size of the study, with only 5.3% being elderly patients (> 65 years). Additionally, no association between abnormal potassium levels and hyponatremia was found, as all cases in this study exhibited normal potassium levels (3.5 - 5.5 mEq/L).

Confound factors included no correlation between concomitant

medications, medical illnesses, and the development of hyponatremia in patients taking antidepressants. This goes in sync with the conclusions of Kirby D et al.'s study,^[16] suggesting that such factors may not significantly impact the development of hyponatremia in this context.

And also, all cases of hyponatremia in our study occurred exclusively in female patients, corroborating findings from other studies conducted by De Picker L et al. and Giorlando F et al., which also reported a higher incidence of hyponatremia in females compared to males.^[17,18]

The prevalence of antidepressant-induced hyponatremia in this study was relatively low (2.65%), with SSRIs showing a slightly higher incidence (3.51%) compared to other antidepressant classes. However, it is worth noting that a study by Manesse CK et al. reported a higher prevalence (9.3%), emphasizing the importance of continued research in this area.^[19]

CONCLUSION

The study concludes that SSRIs are associated with a higher risk of causing hyponatremia compared to other classes of antidepressant drugs. Among SSRIs, paroxetine and sertraline were found to have a higher propensity to cause hyponatremia than other SSRIs. Additionally, the risk of developing hyponatremia was higher in females compared to males. The prevalence of hyponatremia in patients taking antidepressant drugs was found to be 2.65%, and among those specifically on SSRIs, the prevalence was 3.51%. However, further research is needed to better understand the role of concomitant medications and medical conditions leading to such complications.

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