



Research Paper

Hyponatremia and Antidepressants -A Perspective

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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. 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.

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Approximately 800 million people worldwide are affected by mental disorders, with depression and anxiety being the most prevalent among them.^[1] According to WHO, approximately 5% of adults and 5.7% of the elderly population suffer from depression, and the global prevalence reaches around 3.8% (280 million people).^[2]

New-generation antidepressants, including 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)^[3]. However, recent studies have revealed that some new-generation antidepressants may have more pronounced adverse effects.^[3,4] One such effect is hyponatremia which is the most frequently encountered electrolyte disorder with symptoms varying from anorexia and mild lethargy to coma and severe seizures.^[5,6] Due to similarity of these symptoms with those of depression, antidepressant-induced hyponatremia might remain undetected, posing serious risks. Thus, 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 illustrated a reduced risk of hyponatremia for noradrenergic and specific serotonergic antidepressants (e.g., mirtazapine).^[8-11] However, contradictory results have indicated mirtazapine as having the highest reported risk of hyponatremia.^[12] Findings of within the same antidepressants class are also conflicting; For instance: among SSRIs, lowest risk of hyponatremia was evident with escitalopram in a population-based cohort study,^[8] whereas, the findings were totally contradictory in other studies depicting highest risk of hyponatremia with escitalopram.^[7,11]

Given the conflicting findings related to individual antidepressants, identifying those less likely to induce hyponatremia remains a challenge. Enhancing awareness and understanding of the relationship between specific antidepressant drugs class and hyponatremia could potentially lead to safer treatment strategies for vulnerable patients. Nevertheless, due to the inconsistencies present in the literature, a broad association between most antidepressants and hyponatremia is apparent, and the classification of hyponatremia as a "class-specific adverse effect," particularly in the Indian population has yet to be definitively established.^[13-18] Among SSRIs, paroxetine and sertraline were identified as having a higher propensity to cause hyponatremia than other SSRIs. Additionally, the risk of developing hyponatremia was higher in females compared to males. However,

further research is needed to better understand the role of concomitant medications and medical conditions in contributing to antidepressant-induced hyponatremia.

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