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A Clinical Study to Compare Hyponatremia Induced By the Use of Two Different Tricyclic Antidepressants – Amitriptyline and Imipramine

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ABSTRACT

Aims & Objectives: To compare the occurrence of hyponatremia in the patients receiving two different Tricyclic Antidepressants (TCAs)–Amitriptyline and Imipramine **Methodology:** Fifty OPD patients attending the Psychiatry outpatient clinic of Mahatma Gandhi Institute of Medical Sciences, Sewagram having diagnosis of Depressive episode as per DSM-IV-TR criteria were included in the study. Patients with normal serum sodium levels before treatment with antidepressant were included in the study. Repeat serum Sodium levels were done after one month of being on treatment. EPI Info-6 software was used to analyze the data. **Results:** Average serum sodium concentrations of the patients receiving different TCAs before treatment were 139.4+2.45 (Mean+SD). Out of the 44% patients who developed hyponatremia, 45.45% were amongst the Imipramine group and 54.54% were amongst the Amitriptyline group. Although of mild severity only, hyponatremia was more in patients receiving Amitriptyline compared to those receiving Imipramine. **Conclusion:** Patients receiving Amitriptyline have fairly more chance of developing hyponatremia than Imipramine receiving patients. Hence precaution should be observed while using TCA group of antidepressants.

Key words: Amitriptyline, Antidepressant, Imipramine, TCA induced hyponatremia.

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INTRODUCTION

Medications induced hospital hyponatremia (serum sodium concentration below 135 mmol/L) is responsible for around 15-30% hospital mortality.¹ Disruption in the water and electrolyte balance in the body can even prove lethal at times. The anti-diuretic hormone maintains the tonicity and total body water with the help of thirst mechanism and renin-angiotensin aldosterone system.^{2,3,4} Hypo or hypernatremia can be the manifestation of this water balance abnormalities. Hyponatremia may present in the form of nausea, fatigue, weakness, anorexia, confusion and disorientation. Severity of clinical symptom depends on the severity of hyponatremia.⁵ Rapid development of hyponatremia may present with severe neurological symptoms as well. Various drugs like opiates, cytotoxic, chlorpropamine, psychotropics have been implicated in developing hyponatremia, of which psychotropics are the most common ones leading to drug induced hyponatremia.

Various studies have shown that 3-12 % of the psychiatric patients can develop hyponatremia.⁶

Tricyclic antidepressants (TCAs) have been used since number of years for their efficient anti-depressant action and more sedative properties. In the present days newer anti-depressants like the SSRIs are more widely used compare to older tricyclic anti-depressants.^{7,8,9} Much of the research has been done on hyponatremia caused by SSRIs but not enough clinical data is available with TCAs causing hyponatremia.¹⁰ Hence, this study was planned to compare the development of hyponatremia by the use of two different TCAs - Amitriptyline and Imipramine.

MATERIAL AND METHODS

Present clinical, longitudinal prospective observational comparative study was done in Psychiatry outpatient department of a

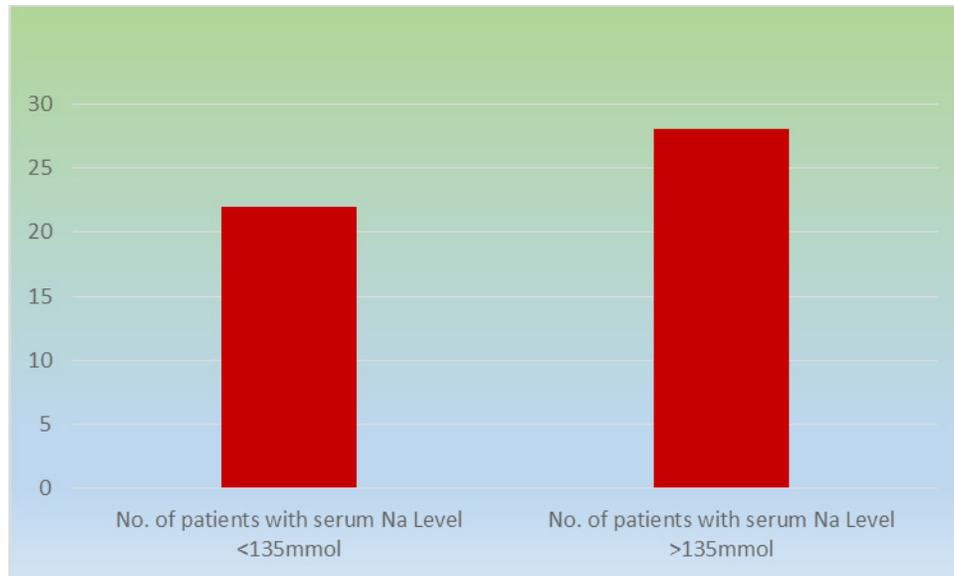


Figure 1: Chart showing development of hyponatremia with TCAs (Total 50 Patients)

medical college & hospital based in rural area. Total duration involved in the study was approximately 18 months. Detailed history of patients attending psychiatry outpatient department was taken and fifty consecutive patients fulfilling DSM-IV-TR criteria for depression were selected. The fresh cases selected who were not exposed to any antidepressant or to any other medication responsible to produce hyponatremia. Inclusion criteria also included absence of any medical or surgical illness. Also the patients with below normal baseline serum sodium level due to any reason were excluded from the study. Ethical clearance was obtained from Institutional Ethical Committee. Consent form was used to obtain patients willingness for participation in the study. For every patient baseline serum sodium levels were calculated before starting either of the TCAs. After starting the patients on TCAs, serum sodium levels were calculated again after a month. Results were tabulated and was subjected to statistical analysis (EPI Info-6 software).

RESULTS

Chart showing development of hyponatremia with TCAs (Total 50 Patients) (Figure 1). Table 1 showing average levels of Serum sodium concentration before and after treatment Table 2 showing the distribution of the patients who developed hyponatremia in the TCA group with respect to the individual drug used.

DISCUSSION

Of the total 25 patients who were receiving Imipramine, 10 patients (40%) developed hyponatremia and 15 patients (60%) did not develop hyponatremia whereas out of 25 patients who were on Amitriptyline, 12 patients (48%) developed hyponatremia whereas 13 patients (52%) didn't develop any hyponatremia. On comparing the results it was found that more number of patients who were receiving Amitriptyline devel-

Table 1 : Average levels of Serum sodium concentration before and after treatment

Serum sodium levels	TCA (Mean±SD)
Before treatment	139.4+2.45
After one month of treatment	135.6+4.11
Average difference	3.82±3.67

Table 2 : distribution of the patients who developed hyponatremia in the TCA group with respect to the individual drug used

Name of the drug	Patients who developed hyponatremia	Patients who did not develop hyponatremia	Total	P Value
Imipramine	10(40%)	15(60%)	25	P> 0.05
Amitriptyline	12(48%)	13(52%)	25	
Total	22	28	50	

oped hyponatremia as compared to Imipramine. Although the difference was statistically insignificant ($p>0.05$).

Researchers did a meta-analysis of the literature prior to March 2013 utilizing data from Web of Science and PubMed on antidepressants and SIADH. They found that incidence rates varied between 0.06% to 40% for SSRIs and 0.08% to 70% for Venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI). However, researchers also observed that evidence and frequency with TCAs were lower. On comparing Odd ratios between SSRIs and TCAs, odd ratio for SSRIs were consistently higher.¹¹

CONCLUSION

As seen in the present study TCAs like other antidepressants can lead to hyponatremia. Although the hyponatremia observed is not much severe in the subjects studied for Amitriptyline and Imipramine but one has to be careful while prescribing them as they may lead to complications in medically compromised, elderly patients and patients with renal impairment. Till date not much research has been done on various TCAs leading to hyponatremia.¹¹ Further study to evaluate the development of hyponatremia between various groups of anti-depressants (e.g. SSRIs vs TCAs) with larger sample size is suggested.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS USED

TCA- Tricyclic Antidepressant ;SSRI- Selective Serotonin Re-uptake Inhibitors ; SIADH- Syndrome of Inappropriate Antidiuretic Hormone (ADH) Secretion

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