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RESEARCH ARTICLE
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HYPONATRIMIA AND HYPOKALEMIA: A COMPARIVE STUDY ON ESCITALOPRAM AND SERTRALINE IN DEPRESSIVE PATIENTS

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ABSTRACT

Background: Depressive illness is assumed the third major cause of disability around the globe. There many groups of drugs for the treatment but SSRIs (selective serotonin reuptake inhibitors) are the most commonly used class of drugs in this disorder.Like other categories of drugs SSRIs also has some adverse effects, aim of this study was to focus on comparing the electrolyte related side effects of escitalopram and sertraline. Hyponatremia (Na < 135mmol/l) and hypokalemia (K<3.5mmol/l)**.**

STUDY DESIGN AND SETTINGS: This comparative cross-sectional study was conducted at Pharmacology department of Jinnah Postgraduate Medical Centre (JPMC) Karachi, Pakistan over in one year.

METHODOLOGY: Samples of blood were collected from128 patients were categorized in four groups with each group consisting of 32 patients on the basis of duration of taking the antidepressants. Group-A patients were on SSRIs from 1-3 month, Group-B patient were taking SSRIs from6-9 months, Group-C patients were taking SSRIs from 1-2 years while Group-D patients were taking SSRIs from 2-5 years. Each group was further divided into two sub groups consisting 16 patients on Escitalopram 10-20mg therapy while other 16 patients on Sertraline 50mg therapy. The male female ratio is this study was 1:1 in all groups.

RESULTS: Escitalopram users samples mean and Standard deviation for Na was 128.23±1.62, for K 2.89±0.19, whereas in treatment group Sertraline mean and Standard deviation for Na was 133.02±1.71 for K 3.30±0.25, there was significant mean difference observed for Na and K between two treatment groups with significant p-value less than 0.01.
CONCLUSION: Escitalopram and Sertraline cause hyponatremia and hypokalemia when used for longer period. These effects are comparatively lesser in Sertraline than Escitalopram.

KEY WORDS: SSRIs (Selective serotonin reuptake inhibitors), Hypokalemia, hyponatremia, Depression

Introduction:

Depression is a metal disorder characterized by sadness, loss of interest in daily activities, pessimism, loss of social contacts, loss of memory, disturbed sleep and eating habits if these symptoms persist for more than two weeks it is called major depression[1]. Depression impairs the quality of life, disturbing the whole family and may end one's life with Suicide if left untreated[2]. It is estimated by the WHO (World Health Organization) that by the end of year 2030 major depressive disorder will become the 2nd major cause of social and economic instability[3]. Currently depression is the 3rd common most cause of disability which affects almost 350 million individuals globally irrespective of age and gender having 7% lifetime risk[4]. Mental disorders are usually missed and remain unrecognized and untreated at primary health care level. Pakistan has a prevalence of depression around 34% which may be attributed to socio-economic conditions[5]. Treatment modalities for depression can be divided into non-pharmacological management and pharmacological management. SSRIs are the most commonly used and relatively safer antidepressants as compared to other antidepressants like TCA (tricyclic antidepressants), MAOIs (Mono Amine Oxidase Inhibitors) and SNRIs (Selective Serotonin/Norepinephrine Inhibitors)[6.] SSRIs include Escitalopram, Citalopram, Fluoxetine and Sertraline etc, they work by blocking the re-uptake of serotonin into the presynaptic terminal thus increasing the concentration of this neurotransmitter in the synaptic space7. Some common adverse effects of SSRIs include GI upsets, weight gain, erectile dysfunctions and electrolyte imbalance in particular hyponatremia and hypokalemia are of utmost importance[8]. Sodium (Na) facilitates the cellular regulation of water balance and helps in maintaining the normal blood pressure, nerve and muscle function along with the fluid balance[9.] The normal value for sodium in the serum ranges between 135 -145 mmol/L level <135mmol/L is termed as hyponatremia[10]. Normal serum potassium (K) concentration is from 3.5-4.5mmol/L and less 3.5 is termed as hypokalemia which is characterized by weakness of all body muscles (skeletal, smooth, cardiac) resulting into and rhabdomyolysis, constipation, ileus and cardiac arrhythmias along with metabolic disturbances like hypomagnesemia, alkalosis, carbohydrate intolerance and polyuria[11.]SSRIs have previously been reported to induce hyponatremia and hypokalemia that may prove fatal sometimes[12]. This study will evaluate and compares these effects of the two well-known SSRIs the Escitalopram and Sertraline.

METHODOLOGY: Patients were selected as a total of128 known cases of depression with randomization for this comparative study at BMSI postgraduate center Karachi under strict inclusion criteria (Patients on Escitalopram for more than1 month and less than 5 years) and exclusion criteria (Non-depressive illness, patients using SSRIs other than Escitalopram and Sertraline, Renal failure patients). Once selected patients were categorized in four groups with each group consisting of 32 patients on the basis of duration of taking the antidepressants. Group-A patients were on SSRIs from 1-3 month, Group-B patient were taking SSRIs from6-9 months, Group-C patients were taking SSRIs from 1-2 years while Group-D patients were taking SSRIs from 2-5 years. Each group was further divided into two sub groups consisting 16 patients on Escitalopram 10-20mg therapy while other 16 patients on Sertraline 50mg therapy. The male female ratio is this study was 1:1 in all groups. Patients were followed up and blood samples were taken after every 6 weeks under standard protocols after written consent. The first sample served as the

baseline. Serum Sodium(Na) and Potassium (K) concentrations were measured on automatic chemistry analyzer. (Easylyte plus-Medica 001384-001 R4). The mean serum Na and K levels were compared among themselves and among the different groups on student's t-test and ANOVA using SPSS Version 22.

RESULTS

Mean age of Escitalopram group patients was 38.69±11.58 and it was 39.52±11.77 years in sertraline group. Serum sodium concentrations in users of Escitalopram at an interval of 2-3 months, 6-9 months, 1-2 years and 2-5 years were 129.90+2.24,128.81+2.12,128.79+2.27 and 128.23+1.62 the difference was no significant statistically p-value 0.578. Serum Potassium concentrations in Escitalopram user after 2-3 months, 6-9 months, 1-2 years and 2-5 years were 3.01+0.17, 2.91+0.16, 2.99+0.20 and 2.89+0.19 respectively and it was noted that there was no statistically significant difference at different levels of usage (p- 0.176). Serum Na concentration in Sertraline groups after different durations like 2-3 months, 6-9 months, 1-2 years and 2-5 years were as 133.10+2.47,130.21+11.09,131.98+2.41 and 133.02+1.71 respectively the difference was not statistically significant p-value 0.476. Serum Potassium concentrations in Sertraline users at 2-3 months, 6-9 months, 1-2 years and 2-5 years were observed as 3.36+0.18, 3.26+0.21, 3.29+0.23 and 3.30+0.25 respectively with a non-significant difference, p-0.626 [Table-1]. Sodium concentration of Escitalopram and Sertraline groups at 1-3 Months were129.90+2.24 and 133.10+2.47 respectively and the difference was significant statistically p- 0.0005. Sodium concentrations in Escitalopram and Sertraline user at 6-9Months were128.81+2.12 and 130.21+11.09 respectively when compared the difference was statistically significant p-0.086. Sodium concentration of Escitalopram and Sertraline users at 1-2Years were 128.79+2.27 and 131.98+2.41 respectively the difference was statistically significant at p-value 0.0007. Sodium concentration of Escitalopram and Sertraline groups at 2-5Years were 128.23±1.62 and 133.02+1.71 respectively when compared the difference was observed as statistically significant with a p-value 0.0001[Table-2]. Similarly, serum potassium concentrations of Escitalopram and Sertraline groups were compared at different levels of time durations and it was observed that significant difference exist between the two groups[Table-2].

Table-1: Comparison of serum Na and K concentration at different levels of use

Parameter	Escitalopram Group-A (1-3moths)	Escitalopram Group-B (6-9months)	Escitalopram Group-C (1-2Years)	Escitalopram Group-D (2-5Years)	P-Value
Na	129.90±2.24	128.81±2.12	128.79±2.27	128.23±1.62	0.578
K	3.01±0.17	2.91±0.16	2.99±0.20	2.89±0.19	0.176
Parameter	**Sertraline Group-A (1-3 months)**	**Sertraline Group-B (6-9 months)**	**Sertraline Group-C (1-2Years)**	**Sertraline Group-D (2-5Years)**	**P-Value**
Na	133.10±2.47	130.21±11.09	131.98±2.41	133.02±1.71	0.476
K	3.36±0.18	3.26±0.21	3.29±0.23	3.30±0.25	0.626

Table-2: Comparison between Escitalopram and Sertraline groups

Parameter	Escitalopram	Sertraline	P-Value
Sodium(1-3Months)	129.90±2.24	133.10±2.47	0.0005
Sodium(6-9Months)	128.81±2.12	130.21±11.09	0.086
Sodium(1-2Years)	128.79±2.27	131.98±2.41	0.0007
Sodium(2-5Years)	128.23±1.62	133.02±1.71	0.0001
Parameter	**Escitalopram**	**Sertraline**	**P-Value**
Potassium (1-3Months)	3.01±0.17	3.36±0.18	0.0003
Potassium (6-9Months)	2.91±0.16	3.26±0.21	0.0001
Potassium (1-2Years)	2.99±0.20	3.29±0.23	0.0004
Potassium (2-5Years)	2.89±0.19	3.30±0.25	0.0001

DISCUSSION

Both the Escitalopram and Sertraline cause hyponatraemia as well as hypokalemia but these effects are reversible[13]. Gandhi et al, (2017) reported strong association between hyponatremia and SSRIs use falling consistent with our findings[14]. Letmaier et al (2012) also reported hyponatremia in patients on SSRI treatment and SNRIs comparable results to our findings[15]. Viramontes et al (2015) in their study results reported hyponatremia in patients using SSRIs which is consistent with our results[16]. Izgi et al (2013) reported hypokalemia in patients using Sertraline. Guzman (2018) also noticed hypokalemia as a consequence of SSRIs treatment[17.] Likasitwattanakul (2005) results fell inconsistent with our finding as he reported hypernatremia in his study finding due to Serotonin syndrome [18]. Patients on SSRIs should be monitored for electrolyte imbalances as any of the SSRIs may cause hyponatremia or hypokalemia. Although both are sustained conditions as per our observation as no significant difference was observed over increased time of use from month to years but milder symptoms may be associated with this imbalance. Our study has some limitations as considering only the sodium and potassium were considered as parameters of study while other electrolytes were missed secondly the prior status of the patients like electrolyte levels before starting the SSRIs therapy may have some important impact on study, so a detailed study is recommended on this topic to cover the pointed out gapes.

CONCLUSION:

Both Escitalopram and Sertraline cause hyponatremia and hypokalemia. Sertraline has more potential to cause hyponatremia and hypokalemia as compared to Escitalopram

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