The Egyptian Journal of Hospital Medicine (October 2021) Vol. 85 (2), Page 4328-4330

Assessment of Oxytocin Level in Patients with Manic Depressive Disorders

Nihad Shokry Mohamed, Laila Mahmoud Ali, Bassem Murad Mostafa*
Department of Internal medicine, Endocrinology and Metabolism,
Ain Shams University Hospital, Cairo11566, Egypt.
***Corresponding author:** Bassem M. Mostafa, **Mobile:** (+20)01144322070, **E-Mail:** Basemmurad44@med.asu.edu.eg

ABSTRACT

Background: Major depressive disorder (MDD) is a major health concern, with lifetime prevalence. In the United States estimated to be as high as 16.2%. Although, a number of pharmacological agents are available to treat, approximately 30–40% of patients do not respond to treatment. Therefore, a major emphasis in modern psychiatric research is to uncover the underlying etiology of mood disorders, and to develop novel efficacious antidepressant treatments. Oxytocin may be of therapeutic benefit in these patients**.**

Objective: To assess the level of oxytocin in patients with major depressive disorders**.**

Patients and methods: A case-control study was conducted on sixty subjects above eighteen years old. They were classified into: 20 naïve patients during the manic attack of bipolar manic depressive disorder (group I), 20 naïve patients during the depressive attack of bipolar manic depressive disorder (group II) and 20 normal control subjects (group III). All participants were subjected to full history, clinical examination and laboratory measurement of oxytocin, AST, ALT, serum albumin, BUN & creatinine.

Results: On comparing group I (bipolar patients with recent attack of mania) and group 3 (control) regarding serum oxytocin level, there was a significant difference in serum oxytocin being higher in patients with manic symptoms ($p < 0.001$) but with no significant difference between group 2 (bipolar patients with recent attack of depression) and group 3 (control).

Conclusion: The significant difference in the level of oxytocin among the studied groups may suggest a possible role of oxytocin in management of patients with such psychiatric disorder.

Keywords: Oxytocin, Major depression, Mania.

INTRODUCTION

Oxytocin is present in most bony vertebrate species. It is a neuropeptide which has a major role in delivery and lactation, above that it acts as neuromodulator within the brain and interacting with the central oxytocin receptors [(1)].

Oxytocin is present in amygdala and the tegmental area, such brain areas are involved in social emotion. Oxytocin is a key go between of complex passionate and social practices, for example, connection, social acknowledgment, and hostility in people. Many reviews discovered relationship amongst oxytocin and neuropsychiatric issue, such as autism and depression [(2)]. Affective disorders are the most widely recognized psychiatric issues. In the United States and Europe, 8-11 % of male adults and about 18-23% of female adults have a depressive syndrome. Hospitalization is required in 6% of the females and 3% of the males who had severe depression [(3)].

There is hypothesis that many of the manifestation usually reported in depression (i.e. social withdrawal, decreased appetite, cognitive impairment) may be due to changes in central oxytocin function [(4)].

The aim of the present study was to assess the level of oxytocin in patients with major depressive disorders.

PATIENTS AND METHODS

Our case-control study was conducted through the period from 1/5/2016 to 30/7/2016 in Cairo on 60 subjects (males and females) above 18 years old. Cases involved in this study were collected from the Psychiatry Outpatient Clinic and Ward at Ain Shams University Hospital.

Ethical approval:

This study was approved by the Local Ethical Committee and a written consent was taken from every subject to be included in our study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

All participants were subjected to full medical history with special stress on psychiatric assessment of criteria of depression or mania and thorough clinical examination [(5)].

Exclusion criteria:

Other psychiatric disorders e.g. schizophrenia. Pregnancy or lactation. Neurological disorders, which may affect mood e.g. DS. Endocrinal diseases as hypopituitarism, hyperprolactinemia and thyroid disorders. Patients with major illnesses as cancer, IHD, renal failure or liver cell failure. Drugs, which might affect mood e.g. corticosteroids and history of substance abuse.

Subjects enrolled in this study were divided into 3 groups, **group I**: 20 naïve patients during the manic attack of bipolar manic depressive disorder, **group II:**

Received: 05/08/2021
Accepted: 01/10/2021

20 naïve patients during the depressive attack of bipolar manic depressive disorder and **group III:** 20 normal control subjects.

Laboratory studies:
Laboratory studies included serum oxytocin level using ELISA technique, liver function tests (AST, ALT & serum albumin) and kidney function tests (serum BUN & creatinine).

Sampling and analysis:
Subjects were instructed first to fast 8 hours (overnight fasting), 5 ml of venous blood were collected by venipuncture. Serum was separated by centrifugation and the sample was used for measurement of serum oxytocin, AST, ALT, serum albumin, serum BUN & creatinine.

Statistical analysis
After collection of data, revision and tabulation, analysis was performed using PASW statistics 18. Continuous data were expressed as mean ± SD. Comparative analysis of quantitative data was done using student t-test to compare two groups and the one-way ANOVA test was used to compare parametric and quantitative variables between more than two groups. Pearson correlation coefficient (r) was used for correlation of data. $P \leq 0.05$ is significant.

RESULTS
Descriptive statistics of the study groups shown in table (1). According to our study serum oxytocin level was significantly higher in group 1 (patients with manic symptoms) than in group 2 (patients with depressive symptoms) and group 3 (control group) ($P < 0.001$) as shown in table (2). Also, there was no significant difference between group 2 and group 3. On correlating serum oxytocin with different parameters, there was no significant correlation (Table 3).

Table (1): Descriptive statistics of the study groups

	Mean ± SD		
	Group 1	**Group 2**	**Group 3**
Age (year) Range:	42.700 ±6.85 27-52	44.800 ±7.811 24-52	43.900 ±7.247 27-53
Serum oxytocin level **(µg/ml)**	231.850 ±45.828	38.450 ±5.343	93.550 ±22.456
AST (U/L)	14.400 ±2.981	15.400 ±2.981	15.400 ±2.981
ALT (U/L)	14.700 ±3.197	15.650 ±3.167	16.050 ±2.762
Serum albumin (g/L)	3.910 ±0.384	4.020 ±0.353	3.890 ±0.342
Serum BUN (mg/dL)	12.750 ±2.712	13.700 ±2.618	13.550 ±2.481
Creatinine (mg)	0.675 ±0.195	0.720 ±0.153	0.785 ±0.176

Table (2): Comparison between different groups regarding serum oxytocin

Groups	**Serum oxytocin level (µg/ml)**	**ANOVA**	
	Mean ± SD	**F**	**P-value**
Group1	231.850±45.828	27.326	<0.001*
Group2	38.450±5.343		
Group3	93.550±22.456		
TUKEY'S Test			
I&II	I&III	II&III	
<0.001*	<0.001*	0.111	

Table (3): Correlation between serum oxytocin and different variants

	Serum oxytocin level	
	R	**P-value**
Age (year)	-0.184	0.255
AST (U/L)	-0.065	0.691
ALT (U/L)	-0.071	0.662
Serum albumin (g/L)	-0.111	0.496
Serum BUN (mg/dL)	-0.101	0.535
Creatinine (mg)	0.034	0.833

DISCUSSION
Oxytocin has a major role in initiating labour, also it is a treatment for postpartum hemorrhage. Oxytocin may be a new promising line of treatment for social anxiety disorders and schizophrenia [6].

According to our study serum oxytocin level was higher in manic patients than depressed and control groups, which agrees with **Turan *et al.*** [7] who stated that serum oxytocin was significantly higher in patients with manic attacks of bipolar disease and lower in those with depressive attacks in comparison with control. **Daban *et al.*** [8] found an association between oxytocin and effective disorders. Oxytocin (OT) is involved in the regulation of the hypothalamus-pituitary-adrenal (HPA) axis, which has been found to be overactive in bipolar disorders. Plasmatic and CSF neuropeptide levels were significantly altered in affective disorders (BD and MDD) being significantly low in depression and higher during manic attacks.

Glucocorticoids inhibit oxytocin neurons. So anxiolytic and antistress effects of oxytocin are attenuated, preventing action of this important controller, and so lack of central oxytocin is associated with depression [9]. **Eser** [10] found higher serum oxytocin in depressed and manic bipolar disorder patients, with no significant difference between the two groups, in a research that included 67 bipolar disorder patients: 22 in manic episode, 21 in depressive episode, and 24 in remission at the outset. **Ozsoy *et al.*** [11] investigated serum oxytocin levels in individuals with depression, as well as the impact of gender and antidepressant medication on these levels, in their study.

Serum oxytocin levels were measured in 40 inpatients (30 women, 10 men) who met the DSM-IV criteria for major depressive disorder (n=29) or bipolar affective disorder depressive episode (n=11), as well as 32 healthy controls, before and after treatment with antidepressants or electroconvulsive therapy (ECT) (20 women, 12 men). The patients' serum oxytocin levels were lower both before and after treatment when compared to the controls. Antidepressant medication or ECT had no effect on serum oxytocin levels. The female patients had significantly lower oxytocin levels than the control females, but the male patients and male controls exhibited no differences. There was no change in serum oxytocin levels between unipolar and bipolar depressed patients, according to the researchers. Their findings reveal that depression causes a decrease in oxytocin levels, as well as a gender difference in oxytocin levels. Antidepressant medications also appear to have no effect on oxytocin levels in the blood[(11)].

Charlotte [(12)] investigated the impact of selective serotonin reuptake inhibitors on plasma oxytocin and cortisol levels in patients with serious depression. The study included 20 individuals who were sampled twice: once when they were untreated during a current depressive episode and again after 12 weeks of SSRI medication. The samples were taken at the same time of day for each patient. All of the participants in this trial responded to treatment. There were no significant variations in oxytocin or cortisol concentrations before and after SSRI treatment, and no significant correlations between oxytocin and cortisol were found.

In conclusion, our study found that there was significant change in serum oxytocin in patients with bipolar disorders being significantly high during manic attack and decreasing during depression, these results suggest a possible role of oxytocin in management of patients with such psychiatric disorder. Oxytocin function impairments may contribute to neurological and behavioral deficits and as a result to development of impairments. These impairments may be prominent in neuropsychiatric disorders such as mania, depression and schizophrenia. Oxytocin administration may represent a novel treatment paradigm in these disorders.

CONCLUSION

Our study found that there is significant change in serum oxytocin in patients with bipolar disorders being significantly high during manic attack and decreasing during depression. These results suggest a possible role of oxytocin in management of patients with such psychiatric disorder.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.

REFERENCES

1. **Murphy D, Si-Hoe S, Brenner S *et al.* (2008):** molecular genetics of the hypothalamo-neurohypophysial system. Bioassays, 20:741- 749.
2. **Kirsch P, Esslinger C, Chen Q *et al.* (2005):** Oxytocin modulates neural circuitry for social cognition and fear in humans. J Neuroscience, 25 (49): 11489–11493.
3. **Boyd H, Weissman M (2008):** The epidemiology of affective disorders: A reexamination and future directions. Arch Gen Psychiat., 38: 1039-1046.
4. **Bell A, Erikson E, Carter S (2014):** Beyond labor: the role of natural and synthetic oxytocin in the transition to motherhood. J Midwifery Womens Health, 59: 35-42.
5. **American Psychiatric Association (2013):** Diagnostic and Statistical Manual of Mental Disorders (Fifth ed.). Arlington, VA: American Psychiatric Publishing. Pp: 5–25. https://doi.org/10.1176/appi.books.9780890425596
6. **Leknes S, Wessberg J, Ellingsen D *et al.* (2012):** Oxytocin enhances pupil dilation and sensitivity to 'hidden' emotional expressions. Soc Cogn Affect Neurosci., 8: 741–9.
7. **Turan T, Uysal C, Asdemir A *et al.* (2013):** Oxytocin as a trait marker for bipolar disorders. Psychoneuroendocrinology, 38 (12): 1-7.
8. **Daban C, Vieta E, Mackin P *et al.* (2007):** Hypothalamic–pituitary– adrenal axis and bipolar disorder. Psychiatry Clinical North America, 28: 469–480.
9. **Malcher-Lopes R, Di S, Marcheselli V *et al.* (2010):** Opposing crosstalk between leptin and glucocorticoids rapidly modulates synaptic excitation via endocannabinoid release. J Neuroscicence, 26: 6643–6650.
10. **Eser S (2013):** Search for biological/genetic markers in a long-term epidemiological and morbid risk study of affective disorders. Psychiatry Research, 18: 425-445.
11. **Ozsoy S, Esel E, Kula M (2009):** Serum oxytocin levels in patients with depression and the effects of gender and antidepressant treatment. Psychiatry Research, 169 (3): 249-252.
12. **Charlotte A (2009):** The extracellular signal-regulated kinase pathway: an emerging promising target for mood stabilizers. Curren Opinion in Psychiatry, 19: 313– 323.