ORIGINAL ARTICLE

ANTI-MÜLLERIAN HORMONE LEVELS IN MALE PATIENTS SUFFERING FROM DEPRESSION

Sobia Waqas, Shazia Ali, Nasar Abbas Shamsi*, Humaira Fayyaz Khan, Waqas Hameed**

Department of Physiology, Islamic International Medical College, Rawalpindi, * Rawal Institute of Health Sciences, Islamabad, ** Pak International Medical College, Peshawar, Pakistan

Background: Anti-Müllerian Hormone (AMH) exerts a neuroprotective role by promoting neuroserpin expression through AMH dependent signalling pathway. The objective of this study was to determine the significance of serum Anti-Müllerian Hormone (AMH) levels in male patients suffering from depression. **Methods:** This case control study was carried out at the Department of Physiology and Multidisciplinary Research Laboratory, Islamic International Medical College, in collaboration with Armed Forces Institute of Mental Health, Military Hospital, Rawalpindi, from April 2016 to March 2018. A total of 96 males were divided into two groups. Group A (Control) consisted of 24 normal healthy males, and Group B (Cases) consisted of clinically diagnosed 72 male patients suffering from major depressive disorder. Serum AMH levels were evaluated in both the groups using ELISA method. Data was analysed using SPSS-22. **Results:** The serum AMH levels in Group B (8.54±0.62 ng/ml) were less than Group A (10.68±1.27), but the difference was not statistically significant. **Conclusion:** Patients suffering from depression have relatively low levels of serum AMH as compared to normal healthy adults but the difference is statistically not significant.

Keywords: anti-Müllerian Hormone (AMH), Depression, Neurogenesis, Neuroserpin

Pak J Physiol 2019;15(4):17−9

INTRODUCTION

Depression is a state of low mood and aversion to activity or apathy that can influence a person's thoughts, behaviour, and sentiments leading to social withdrawal from the society. Globally depression affects 10–20% of people[1], while in Pakistan an estimated 10–34% of the population suffers from depression[2]. Depression has many possible causes, including inconsistent mood regulation by the brain, genetic vulnerability, stressful life events, medications, medical problems and chemical imbalance.[3]

When the brain is insulted by various exogenous or endogenous factors including stress, depression, genetic aspects, neuroendocrine imbalances, environmental and behavioural influences[4], and the process of neurogenesis is affected. Formation of new neurons by neuron stem cells is referred to as the process of neurogenesis. This process occurs throughout the brain and reaches at its peak during perinatal period after which it remain strong and vigorous from childhood to adolescence in all areas of brain.[5–7] As the brain ages, the housing of neural stem cells become confined to distinct areas of the brain which now have the capacity to make new neurons throughout the adult life and this is known as adult neurogenesis. In adults, process of neurogenesis takes place in few areas. Hippocampus, amygdala, prefrontal cortex and sub-ventricular zone (SVZ) of the lateral ventricle are among those areas which are called as neurogenic regions of the adult brain. These newly generated neurons play a critical role in mood regulation in adult brain.[8] Neuronal dendrite branching, axonal lengthening and neural circuitry, all are down regulated in depression. Besides embryogenesis and folliculogenesis, Anti-Müllerian Hormone (AMH) exerts a neuroprotective role by promoting neuroserpin expression through AMH dependent signalling pathway.[9] The AMH acts through its receptor, anti-Müllerian hormone receptor type 2 (AMHR2), belonging to the transforming growth factor-β (TGF-β) superfamily. These receptors are distinctly localized to cortical and hippocampal areas which are regarded as neuroserpin rich areas of the brain.[10]

Neuroserpin is member of serpin family of serine protease inhibitor secreted from neurons. Increase in neuroserpin expression to a stimulus is modulated by AMH, a protein hormone produced from the Sertoli cells of testes. Neuroserpin expression recruits the transcription factors (Smads) which paly a cardinal role in the regulation of neural network formation. AMH dependent signalling pathway in the brain leads to an overexpression of neuroserpin which harmonizes the growth and survival of neurons. So balanced AMH levels appear to have an important role on physical and mental health of an adult individual and low levels of AMH can be one of the causative factors for depression.[11]

Studies are available in which AMH levels have been estimated in females suffering from depression. However, no data is available yet to evaluate the role of AMH in male patients suffering from depression. Literature study does not elucidate the role of AMH in regulation of neuroserpin in depression. In the current study, we investigated the levels of serum AMH (ng/ml) in depressed male patients.

MATERIAL AND METHODS

This case control study was conducted at Department of Physiology, Islamic International Medical College Rawalpindi in collaboration with Armed Forces Institute of Mental Health, Pak Emirates Military Hospital, Rawalpindi from 1st Nov 2016 to 28th Feb 2018. The Ethical Review Committee of Islamic International Medical College/Riphah International University approved this research project.

A total of 96 males aged 18–60 years were divided into 2 groups. Group A (control) comprised of 24 normal healthy males. Group B (cases) comprised of 72 diagnosed cases of depression by a consultant psychiatrist, on the basis of Siddiqui Shah Depression Scale[12], with a body mass index (BMI) of <30 and no physical deformity or chronic illness. These patients were receiving antidepressant treatment for an average of 1.5 years and were recruited from the Outpatient Department of Consultants' Clinic at Armed Forces Institute of Mental Health, Military Hospital, Rawalpindi. Patients undergoing Electroconvulsive therapy, taking drugs of abuse, alcohol users, and those suffering from chronic illness and obvious physical deformities were excluded from the study.

Age and Body Mass Index (BMI), and duration of illness of the participants were recorded. Blood samples were taken and serum was separated after centrifugation of samples at 3,000 rpm for 10 minutes and stored at -20 °C till further analysis by ELISA obtained from IMMUNOTECH, Beckman Coulter, Inc. USA, bearing catalogue No. A79765. The data was analysed using SPSS-22. Data was expressed as Mean±SEM and was analysed using students *t*-test, and $p \leq 0.05$ was regarded as significant.

RESULTS

The parameters of age and BMI (body mass index) of both the groups and duration of illness of Group B (1.60±0.17 years) are represented in Table-1. Mean±SEM of age of Group A showed no significant difference as compared to that of Group B. On comparing Mean±SEM of BMI of Group A and Group B, no significant difference was observed.

Serum AMH levels in Group A were 10.68±1.27 ng/ml and in Group B were 8.54±0.62 ng/ml. No significant difference was observed on comparison between both the groups.

Table-1: Age, BMI and duration of illness of Group A and B (Mean±SEM)

Parameters	Group A (Control) n=24	Group B (Cases) n=72
Age (Yrs)	34.12±1.49	35.19±1.18
BMI (Kg/m^2)	25.02±0.23	23.85±0.25
Duration of Illness (Yrs)	-	1.60±0.17
Serum AMH (ng/ml)	10.68±1.27	8.45±0.62*

*Non significant

DISCUSSION

In the current study serum AMH levels have been explored in males suffering from depression. However, no statistical difference of AMH levels is observed between controls and depressive patients. These results are similar to the study carried out by Jurczak *et al*[13], whose study showed no significant reduction in AMH levels in female patients of late reproductive age suffering from depression.

Altinkaya *et al*[14] have demonstrated that depression and anxiety are associated with low AMH levels. In the study they developed a correlation between depression, anxiety and ovarian reserve in infertile women. However, our study could not find an association of AMH levels with depression. This difference in outcome could be due to a gender difference as that study was carried out on women.[14] Furthermore, the females included in their study were all infertile and it has been shown that infertile women suffer from considerable emotional disturbances along with mood disorders and depression. Decreased AMH levels have been attributed to infertility as well and it is likely that the depression amongst these women was not due to low AMH levels, but rather infertility related emotional imbalance. Park *et al*[15] conducted a study on women suffering from polycystic ovarian syndrome (PCOS), which too supported the results of Altinkaya *et al*[14] in relating AMH levels with depression which is contrary to the results of our study.

Dong *et al*[16] have explored the correlation of psychological stress with AMH levels in infertile women. They concluded that stress and depression reduce the AMH levels in infertile females. This concept is further clarified by a study in which the authors have established the fact that upregulation of neuroserpin protein in brain is modulated by normal levels of AMH.[17] Therefore, depressed levels of AMH due to stress and anxiety would lead to a downregulation of neuroserpin in areas of brain concerned with emotions, thus generating a vicious cycle of depression.

Our study results have not shown any significant differences in serum AMH levels in depressive patients. One explanation to these results is that the patients included in the study were on antidepressant therapy for six or more months. Therefore, we speculate that improvement/normal AMH levels were due to the effect of treatment the patients were receiving.

CONCLUSION

Serum AMH level in cases was less than controls but the differences were not statistically significant. This could be due to the fact that all patients selected for this study were already receiving antidepressant treatment for more than six months.

STUDY LIMITATIONS

Newly diagnosed cases of depression should have been included in the study. Neuroserpin levels should have also been explored in the same subjects. These parameters could not be done considering the limitations of the budget to carry out the project.

RECOMMENDATIONS

Newly diagnosed cases of depression without any treatment may be included in further studies with MRI being carried out for analysis of hippocampal volumes. Levels of neuroserpin may also be estimated to evaluate the neurogenesis in brain. The effect of antidepressant treatment on AMH levels may also be explored.

REFERENCES

1. Depression [online]. Medline Plus 2012. Available from: http://www.nlm.nih.gov/medlineplus/depression.html
2. Altaf A, Khan M, Shah SR, Fatima K, Tunio SA, Hussain M, *et al*. Sociodemographic pattern of depression in urban settlement of Karachi, Pakistan. J Clin Diagn Res 2015;9(6):9–13.
3. von Känel R, Fardad N, Steurer N, Horak N, Hindermann E, Fischer F, *et al.* Vitamin D deficiency and depressive symptomatology in psychiatric patients hospitalized with a current depressive episode: A factor analytic study. PLoS One 2015;10(9):e0138550.
4. Mirza I, Jenkins R. Risk factors, prevalence, and treatment of anxiety and depressive disorders in Pakistan: Systematic review. BMJ 2004;328(7443):794–8.
5. Liu W, Ge T, Leng Y, Pan Z, Fan J, Yang W, *et al.* The role of neural plasticity in depression: From hippocampus to prefrontal cortex. Neural Plast 2017;6871089. doi: 10.1155/2017/6871089.
6. Hodes GE, Yang L, Van Kooy J, Santollo J, Shors TJ. Prozac during puberty: distinctive effects on neurogenesis as a function of age and sex. Neuroscience 2009;163(2):609–17.
7. He J, Crews FT. Neurogenesis decreases during brain maturation from adolescence to adulthood. Pharmacol Biochem Behav 2007;86(2):327–33.
8. Balu DT, Lucki I. Adult hippocampal neurogenesis: regulation, functional implications, and contribution to disease pathology. Neurosci Biobehav Rev 2009;33(3):232–52.
9. Woitke F, Ceanga M, Rudolph M, Niv F, Witte OW, Redecker C, *et al.* Adult hippocampal neurogenesis poststroke: More new granule cells but aberrant morphology and impaired spatial memory. PLoS One 2017;12(9):e0183463.
10. Noto R, Randazzo L, Raccosta S, Caccia S, Moriconi C, Miranda E, *et al*. The stability and activity of human neuroserpin are modulated by a salt bridge that stabilises the reactive centre loop. Sci Rep 2015;5:13666. doi: 10.1038/srep13666.
11. Cimino I, Casoni F, Liu X, Messina A, Parkash J, Jamin SP, *et al.* Novel role for anti-Müllerian hormone in the regulation of GnRH neuron excitability and hormone secretion. Nat Commun 2016;7:10055. doi: 10.1038/ncomms10055.
12. Siddiqui S, Shah SAA. Siddiqui-Shah Depression Scale (SSDS): Development and validation. Psychol Dev Soc 1997;9:245–62.
13. Jurczak A, Szkup M, Samochowiec A, Grzywacz A, Samochowiec J, Karakiewicz B, *et al*. An analysis of the influence of selected genetic and hormonal factors on the occurrence of depressive symptoms in late-reproductive-age women. Int J Environ Res Public Health 2015;12(4):3547–63.
14. Altinkaya SO, Nergiz Avcioglu S, Kucuk M, Yuksel H. Is there a relationship between ovarian reserve tests with depression and anxiety scales? Turkiye Klinikleri J Gynecol Obstet 2016;27(1):8–13.
15. Park CJ, Kim SM, Rhee JH, Kim JI. Emotional stress and associated factors in women with polycystic ovary syndrome. Fertil Steril 2014;102(3):e261.
16. Dong YZ, Zhou FJ, Sun YP. Psychological stress is related to a decrease of serum anti-müllerian hormone level in infertile women. Reprod Biol Endocrinol 2017;15(1):51.
17. Lebeurrier N, Launay S, Macrez R, Maubert E, Legros H, Leclerc A, *et al*. Anti-Müllerian-hormone-dependent regulation of the brain serine-protease inhibitor neuroserpin. J Cell Sci 2008;121(Pt 20):3357–65.

Address for Correspondence:

Dr. Sobia Waqas, Assistant Professor of Physiology, Islamic International Medical College, Rawalpindi, Pakistan.
Cell: +92-334-5505330
Email: sobwaq@hotmail.com

Received: 19 Dec 2019 **Reviewed: 28 Dec 2019** **Accepted: 29 Dec 2019**