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Original article

To study comparison between Vitamin- E Levels and heart rate in Depressive Subjects of Pravara Rural Hospital of Western Maharashtra

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Abstracts:

Background: Depression is one of the common psychiatric disorders that cause change of mood, loss of interest, disturbances in sleep or appetite, low physical energy and poor ability to concentrate. By the year 2020 depression will be the second major cause of disability and disease worldwide after cardiovascular disease.

Material and Methods: The present observational case control study was conducted in the Department of Physiology for a period of three years duration.. A total of 83 depressive patients diagnosed by Psychiatrist and a total of 100 normal individuals without any psychiatric disorders were taken as controls were included in the study. Non-probability purposive sampling method was adopted for selection of subjects. Comparison between the non-enzymatic antioxidants Levels in Depressive Subjects in Pravara Rural Hospital was studied.

Results: The vitamin-E Levels showed a significant decrease in depressive patients as compared to control subjects. A significant difference was observed in the mean values heart rate in depressive patients as compared to control subjects (Unpaired‘t’ test, *p* value < 0.05).

Conclusion: The present study concludes that utility vitamin-E and heart rate plays an important role in monitoring management of depressive patients.

Key Words: Vitamin-E, heart rate, depressive patients

Introduction:

Psychiatric disorders are important contributors to the disease burden and disability globally. Abnormalities in serotonin and dopamine, affects the enzymes in the catabolic pathway such as monoamine oxidase. Disturbances in the antioxidant defense mechanism plays an important role in neuropsychiatric disorders.[1] Depression is marked by inflammatory processes, increased pro-inflammatory cytokines, decrease in the number of neurons, mitochondrial dysfunction and disruption in hypothalamic-pituitary-adrenal axis. A slight change in antioxidant defense mechanisms and oxidative stress is detrimental to neurons. The molecular mechanism represents one of the factors in the etiology of depression and anxiety disorders.[2] Depression is associated with oxidative stress it was decided to study non-enzymatic antioxidant like vitamin-E levels in depressive subjects and compare them with normal

controls.Considering the association of autonomic dysfunction with its effect on morbidity and mortality this study was carried out to assess resting heart rate in depression and compare them with control group.

Material and methods:

The present observational case control study was conducted in the Department of Physiology in collaboration with Department of Psychiatry, Rural Medical College and Hospital, Pravara Institute of Medical Sciences (DU).The study protocol was approved by Institutional Ethics Committee (IEC) , Loni, for the period of three years. Written informed consent was obtained from all participants. The Non-probability purposive sampling method was used for those satisfying the inclusion criteria**.**

Inclusion criteria:

Control (Group I) the inclusion criteria was the controls were free from depression with males in the age group 20-55 years and they were willing to participate in the study whereas the exclusion criteria was no history of consumption of psychotropic substances and patients suffering from other co-morbidities (HTN, COPD, Asthma, Diabetes) were excluded from the study.

For selection of depression cases (Group II) the inclusion criteria was the depression cases were diagnosed by psychiatrist & rated on the basis of Hamilton's depression scale with males in the age group 20-55 years and they were willing to participate in the study whereas the exclusion criteria was history of consumption of psychotropic substances and patients suffering from other co-morbidities (HTN, COPD, Asthma, Diabetes) were excluded from the study. First a written consent was obtained from all subjects. The blood sample was collected in plain bulb from each case & control from cubital vein with all aseptic precautions. Serum was separated by centrifugation at 3000 rpm for 10 minutes.

Antioxidants test conducted in cases and controls

Sr. no	Antioxidants	Normal values	Methods
1	Vitamin- E	5.5 -17 µg/ml.	Baker H and Frank O (1969-172)[3]

"CANWIN" Cardiac Autonomic Neuropathy Analyzer: Cardiac Autonomic Neuropathy Analyzer was used to assess resting heart rate. It is a fully automatic windows based instrument which gives graphical interpretation and keeps subject's data. As it is automatic, recordings, readings and calculation becomes possible.

Estimation of vitamin – E (α -Tocopherol):

Method: Baker H and Frank O (1969-172)[76]

Principle:

Serum tocopherol was measured by its ability to cause reduction of ferric to ferrous ions which then form a red complex with α, α dipyridil. Tocopherols and carotenes are first extracted into xylene and the absorbance is read at 460 nm to measure the carotenes. A correction for the carotenes is made after adding ferric chloride and reading at 520nm.

Reagents:

1) Absolute alcohol, aldehydes free (Ethanol).
2) Xylene
3) ά ά dipyridil,1.20 g/l in n- propanol
4) Ferric chloride solution 1.20 g FeCL3, 6H2O/l in ethanol. Keep in brown bottle.
5) Standard solution of DL- ά tocopherol, 10 mg/l in ethanol.

Technique:

Into three coppered centrifuge tubes measure 1.5 ml serum, standard or water (Blank) respectively. To the test and blank add 1.5 ml ethanol and to the standard 1.5ml water. Add 1.5 ml xylene to each tube, stopper, and mix well and centrifuge. Transfer 1.0 ml of each xylene layer into a clean stoppered tube, carefully excluding any protein or ethanol. Add 1.0 ml dipyridil reagent to each tube, stopper and mix. Pipette 1.5 ml 0f the mixture into colorimeter cuvettes and read the absorbance (A_{460}) of the test and standard against the blank at 460 nm. Then in turn beginning with the blank add 0.33 ml ferric chloride solution, mix, and after exactly 1.5 min read test and standard against the blank at 520 nm.

Calculation:

$$\text{Serum tocopherol mg/l} = \frac{\text{(Read of unknown at 520 nm – Read at 460 nm)}}{\text{Read of standard at 520 nm}}$$

Since standard contains 10 mg/l

Table No.1.1: Comparison of Vitamin-E in group I and group II

Antioxidants	Control (Group I) n=100 Mean ± SD	Range	Depression cases (Group II) n = 83 Mean ± SD		Range	P value
Vitamin-E (mg/dl)						
Category I (26)	11.27 ±1.21	10.55 -9.9	Category I (11)	9.92±1.1	10.4 -9.45	0.00
Category II (38)	10.99 ±1.03	10.55 -9.9	Category II (39)	10.4 ±1.3	10.25 -9.45	0.04
Category III (36)	11.44 ±1.20	10.25 -9.4	Category III (33)	10.21 ±1.3	10.2 -9.45	0.01

In table 1.1, shows the estimated mean values of the vitamin-E which is significantly low in depression patients (Group II) as compared to control group (Group I) (Unpaired 't' test, p value<0.05)

In table 1.2, the parasympathetic functions such as resting heart rate/min are shown.
The resting heart rate/min was significantly increased in depression cases as compared to control (Unpaired't' test, p value < 0.05).

Table No. 1.2: Comparison of resting heart rate/min in group I and group II

Parasympathetic functions	Control (Group I) n=100 Mean ± SD	Range	Depression cases (Group II) n = 83 Mean ± SD		Range	P value
Resting heart rate/min						
Category I (26)	76.15 ±5.84	65–88	Category I (11)	81.09 ±6.36	72–90	0.00
Category II (38)	73.58 ±6.24	62–83	Category II (39)	80.59 ±6.87	63–94	0.04
Category III (36)	76.97 ±7.51	60-96	Category III (33)	80.55 ±8.23	60–96	0.03

Table No 1.3: Comparrison between Vitamin-E and resting heart rate in group I and group II

	Control (Group I)		Depression cases (Group II)	
Sr. no	**Type of Antioxidant**	**r (p)***	**Type of Antioxidant**	**r (p)***
1	Vitamin-E	0.1 (0.23)	Vitamin-E	0.0 (0.59)
*Note: r = Correlation coefficient, Value in bracket indicate= p value (Unpaired't' test, p value < 0.05)				

Discussion:

Studies have reported that there is a definite autonomic imbalance in patients suffering from depression. On this basis, in the present study, levels of Vitamin-E and resting heart rate in patients of depression were compared with healthy normal controls. In total, 183 males were included in the present study consisting of 100 healthy normal controls and 83 patients suffering from depression. They belong to age group 20-55 years and were further subdivided into category I (20-30 years), category II (31 – 40 years) and category III (41 -55 years). In the present study only male patients were included because female patients not supportive and denied to participate.The

estimated mean values of the vitamins-E was significantly low in depression patients (Group II) as compared to control group (Group I) (Unpaired 't' test, *p* value<0.05) (Table No.1.2).There are various studies evaluating vitamin-E in depression.

D'Souza B, *et al* (2003) reported decreased levels of antioxidant Vitamin-E in schizophrenic patients, which may cause oxy-radical mediated injury of central nervous system in schizophrenia. Adjunctive treatment Vitamin-E at the initial stages of illness further prevent oxidative injury, thereby improve and preventing further possible worsening of associated neurological and behavioral deficits in schizophrenia.[4] Gautam M *et al* (2012), observed reduced levels of vitamin- E in both depression and generalized anxiety disorder (GAD) subjects as compared to normal healthy subjects. After antioxidant vitamins (Vitamin- E) were administered for six weeks, a significant increase in their levels were observed by the authors in patients suffering from generalized anxiety disorder (GAD) and depression.[5]

Dadheech G *et al* (2006), reported increased oxidative stress but the condition lead to decrease in the antioxidants vitamins like vitamin-E in patients of Schizophrenia (SCZ).[6] Bajpai A et al (2014), concluded that oxidative damage leads to increased oxidative stress. The antioxidant defence system of the body counteracts the stress which leads to alteration in the levels of the antioxidants. This conclusively establishes the major role of oxidative stress and antioxidant vitamins in depression.[7] However, study by Liu T *et al* (2015) reported no change in the vitamin-E levels in depression; therefore this study shows contradictory results pertaining to vitamin- E.[8] The results indicate a statistical significance correlation as observed between antioxidants like Vitamin-E and resting heart rate (RHR) in control subjects (group I). Similar results are obtained between Vitamin-E and resting heart rate in control subjects (n =100) (Unpaired't' test *p* value <0.05) (Table no. 1.4)

The study of heart rate is an important to assess the parasympathetic functions. Researchers have studied resting heart rate, heart rate variability to assess the parasympathetic functions of patients suffering from depression. In the present study we found significant increase in resting heart rate in depression cases . Similar results were observed by other studies results . Carney R, *et al* (1999) suggested that depression is associated with the altered autonomic activity.[9] Alvares G *et al* (2016) in their study reported reduced heart rate in the patients suffering from psychiatric disorders. Further, they also studied effect of psychotropic medication on heart rate .They observed that ANS dysfunction is a characteristic feature in otherwise healthy patients with major psychiatric disorder, with the largest effects observed in patients with psychotic disorders and psychotropic medications.[10]

Ehrenthal J *et al* (2010), in their study compared cardiovascular reactivity to anger recall and mental arithmetic tasks in 25 patients with severe depression without heart disease and 25 non-depressed subjects. The depressed patients exhibited the overall decreased in heart rate.[11] Jahan C *et al* (2014) had found decreased heart rate ($p< 0.001$) in depressive patients as compared to healthy controls. The authors suggested lower parasympathetic and higher sympathetic drive as well as higher low to high frequency (LH/HF) ratio as an index of sympathovagal imbalance in major depressive 21disorder (MDD) patients.[12] Wang Y *et al* (2013) had recently suggested that depression is related with dysfunction of the cardiac autonomic nervous system; also the severity of depression is directly proportional to the severity of dysfunction. It appears that patients with depression are susceptible to

premature atrial and/or ventricular disease.[13] By studying, heart rate the role of parasympathetic nervous system in the physiology of depressive patients is known. Thus present study gives a clear idea regarding status of antioxidant defense system, level of oxidative stress status and the role of autonomic nervous system, in patients suffering from depression as compared to healthy controls.

Conclusion:

The present study concludes that utility of Vitamin-E Levels and resting heart rate plays an important role in diagnosis, treatment and monitoring of depressive patients.

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