EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 5
Issue: 4
771-774
Year: 2018

ROLE OF HERBAL ANTIOXIDANT HEMIDESMUS INDICUS IN TREATMENT OF ANXIETY DISORDER

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Article Received on 10/02/2018 **Article Revised on 02/03/2018** **Article Accepted on 22/03/2018**

ABSTRACT

Background: Plant derived medicines due to their less side effects, may have importance in future of medicinal system as 80% population is in favour of traditional medicine as per WHO, hence role of herbal antioxidant Hemidesmus indicus was studied in management of anxiety disorder. **Methods:** Newly diagnosed patients of mild to moderate anxiety disorder divided into two groups having forty patients in each group were enrolled. Group-I patients were given Tablet Clonazepam 0.5 mg orally daily for six months. Group-II patients were given Tablet Clonazepam 0.5 mg orally at night with Tablet Hemidesmus indicus 50 mg/kg in three divided doses for six months. Levels MDA, SOD and anxiety score was assessed at start of study and thereafter every month for six month. **Result:** Group-I patients showed significant increased MDA levels from 18.80 ± 0.37 to 27.97± 0.81, decreased SOD levels from 0.143± 0.004 to 0.111± 0.004 and decrease in anxiety score from 12.44± 1.24 to 2.55±0.72 after six months of treatment. In Group-II patient decrease in MDA levels from 18.81± 0.73 to 12.06±0.72 and increased SOD levels from 0.141± 0.005 to 0.185±0.004 after six months of treatment. Significant decrease in mean anxiety score from 12.54 ± 1.26 to 1.40 ± 0.68 was observed after first month onwards. **Conclusion:** Patients treated with Clonazepam show increase in oxidative stress though they were effective in reducing anxiety score. In Group-II patients, significant decreased oxidative stress and anxiety score was observed which may be because of antioxidant property of Hemidesmus indicus.

KEYWORDS: Anxiety disorder, oxidative stress, anxiety score, Clonazepam, Hemidesmus indicus.

INTRODUCTION

Anxiety is feeling of fear to threat which is a normal emotional response but when it is disproportionate to real situation and persistent it is pathological. Anxiety is a common symptoms of various stress related disorders such as generalized anxiety disorder, panic attack, post-traumatic stress disorder and obsessive compulsive disorder.[1] Prevalence rate of anxiety disorder in India is variable. As per the meta-analysis carried out by Ganguli prevalence rate of anxiety disorder is 16.5% and it is more in urban areas than rural areas because of lack of resources to carry epidemiological studies in rural areas and because of underreporting. It is also more common in females.[2] Anxiety disorder affect social and occupational responsibility of the individual because of worry, fatigue, lack of sleep and muscle tension.[3] Pathogenesis of anxiety disorder include interplay of hormones, biological factors, environmental factors.[4] It is found that anxiety disorders are associated with oxidative stress. Oxidative stress occurs when there is imbalance between cellular production of reactive oxygen species and counteracting antioxidant mechanism.[5]

Both animal and human studies have shown association of anxiety disorder with oxidative stress.[6] Brain is highly vulnerable to oxidative stress because it requires large quantity of oxygen and it has high levels of lipid which may undergo lipid peroxidation leading to production of reactive oxygen species. Desmurax et al found angiogenic behaviour in mice due to deficiency of vitamin E which may produce oxidative stress in brain.[7] G.Grases et al found low redox potential in individual with normal anxiety whereas high urinary redox potential in individuals with high anxiety states.[8] Anxiety disorders are of chronic nature and require treatment for long time. Benzodiazepines are commonly used for treatment of anxiety disorder because of its quick action. But their long term use is associated with dependence, withdrawal on discontinuation and impairment of cognition. Other drugs which are useful include selective serotonin reuptake inhibitors (SSRI), selective serotonin norepinephrine reuptake inhibitors (SNRI) and other drugs.[9] Though SSRI are drug of choice for treatment of anxiety disorder they may cause jitteriness, sexual side effects and suicidal tendency.[4]

Alternative medicines are also important in treatment of anxiety disorder. St. John's wort, nutritional vitamins due to their easy availability are used by patients of anxiety disorder. Kawa was used in treatment of anxiety disorder but because of hepatotoxicity it was banned.[9] Dietary polyphenols were found to exert anxiolytic action and decrease oxidative stress associated with it.[1] Various herbs such as Hemidesmus indicus, Saraca asoca, Butea monospermous found to have antioxidant action.[10] Hemidesmus indicus, known as Indian Sarasparilla in English belongs to Family Apocynaceae. It is a perennial, slender, twinning undershrub with woody and aromatic roots.[11]

Severity of anxiety disorder can be assessed by measuring symptoms of anxiety. There are various scales available to measure symptoms of anxiety such as State Trait Anxiety Scale (STAI), Beck anxiety Inventory (BAI). Beck anxiety inventory measures somatic symptoms of anxiety. It has 21 items to which patient responds on a 4 point Likert's scale either as self-report or on interviewer questionnaire.[12]

As anxiety disorders are associated with increased oxidative stress and requires treatment for long duration which may lead to adverse effects associated with drugs used for treatment. Scanty research is available depicting the role of herbal antioxidant in treatment of anxiety disorder. Hence present study was undertaken to study role of herbal antioxidant Hemidesmus indicus on outcome of anxiety disorder.

MATERIAL AND METHODS

In present study we included 80 newly diagnosed patients with mild to moderate anxiety disorder of either sex between the age groups 20-60 years with anxiety score 10 to 18. We excluded the patients with comorbid depression chronic illness such as hypertension, diabetes, patients receiving antianxiety drug and antioxidant therapy. These patients were divided into two groups containing 40 patients in each group.

Baseline anxiety score was measured by using Beck Anxiety Inventory. Baseline oxidative stress was measured by measuring serum malondialdehyde (MDA) levels by thiobarbituric acid method and superoxide (SOD) levels by inhibition of auto-oxidation of Pyrogallol.[13] After this Group I patients were given treatment with Tablet Clonazepam 0.5 mg orally daily at night for six month. Group II patients were treated with tab. Hemidesmus Indicus 50 mg/kg orally daily in three divided doses for six months. Anxiety score and Serum MDA, SOD levels were assessed every month till six month. Data was analysed by using descriptive statistics and student unpaired 't' test.

OBSERVATIONS

Table 1: Comparison of mean MDA, SOD and Anxiety Scores two groups by Student's unpaired't' test.

			Mean MDA				Mean SOD				Mean AS			
	Group	N	Mean	Std. Deviation	t-value	p-value	Mean	Std. Deviation	t-value	p-value	Mean	Std. Deviation	t-value	p-value
Pre Test	Group 1	38	18.80	0.37	0.09	0.92,NS	0.143	0.00489	1.54	0.12,NS	12.44	1.24	0.32	0.74, NS
	Group 2	37	18.81	0.73			0.141	0.00518			12.54	1.26		
1 month	Group 1	38	18.51	0.72	8.94	0.0001,S	0.140	0.00492	3.64	0.0001,S	11.21	1.06	3.69	0.0001,S
	Group 2	37	16.99	0.74			0.145	0.00651			9.83	2.02		
2 months	Group 1	38	19.52	0.82	19.65	0.0001,S	0.139	0.00539	15.44	0.0001,S	9.78	1.06	6.30	0.0001,S
	Group 2	37	15.90	0.77			0.157	0.00450			8.00	1.37		
3 months	Group 1	38	22.72	0.83	43.02	0.0001,S	0.135	0.00683	23.51	0.0001,S	7.60	1.17	4.07	0.0001,S
	Group 2	37	14.81	0.75			0.167	0.00450			6.51	1.14		
4 months	Group 1	38	24.27	0.83	61.33	0.0001,S	0.125	0.00557	39.12	0.0001,S	5.68	1.45	2.68	0.009,S
	Group 2	37	12.96	0.75			0.168	0.00393			4.91	0.95		
5 months	Group 1	38	25.86	0.84	74.31	0.0001,S	0.116	0.00534	55.25	0.0001,S	4.07	1.04	3.55	0.001,S
	Group 2	37	12.21	0.74			0.177	0.00417			3.24	0.98		
6 months	Group 1	38	27.97	0.81	89.34	0.0001,S	0.111	0.00437	68.83	0.0001,S	2.55	0.72	7.04	0.0001,S
	Group 2	37	12.06	0.72			0.185	0.00498			1.40	0.68		

RESULTS

Age and Sex Distribution

Mean age of patients in group I was 32.21±10.36 years, in group II was 36.56±10.41 years respectively. There was no statistically significant difference in the patients age group distributed in two groups. Group I had 17male and 21 female whereas in group II there were 15 males and 22 females.

Statistically non-significant difference was observed at pre-treatment assessment in levels of MDA. Mean MDA levels in group I was 18.80 ±0.37nmol/ml and in group II it was18.81 ± 0.73 nmol/ml. Increase in mean MDA levels was observed in group I from 18.80 ±0.37nmol/ml to 27.97±0.81 nmol/ml whereas there was progressive decrease in mean MDA levels in group II from 18.81 to 12.06 nmol/ml from 1st month onwards which was statistically significant as p=0.0001.

Mean SOD levels at baseline in group I and group II were 0.143±0.004U/gm. of Hb and 0.141 ± 0.005 U/gm. of Hb. respectively which was statistically not significant between the groups. From first month onwards there was progressive decrease in mean SOD levels in group I from 0.143±0.004U/gm. of Hb to 0.111 ± 0.004 U/gm. of Hb, whereas mean SOD levels increased progressively in

group II from 0.141 ± 0.005 U/gm. of Hb to 0.185 ±0.004 U/gm. of Hb respectively which was statistically significant.

Pre-treatment mean anxiety score in group I was 12.44±1.24 and in group II it was 12.54±1.26 which was statistically non-significant. There was progressive reduction in anxiety score in group I and group II from pre-treatment score to 2.55 ±0.72 and 1.40 ± 0.68 respectively till last month of treatment.

DISCUSSION

Present study was conducted at Acharya Vinoba Bhave Rural Hospital Sawangi (Meghe) Wardha. Total 80 patients of mild to moderate anxiety disorder were enrolled in present study. These patients were divided into two groups containing 40 patients in each group. There were five drop out, two from group I and three from group II. Total 75 patients were present in the study.

In present study there was increase in mean MDA levels in Group I due to increased lipid peroxidation which is a marker of oxidative stress. There was decrease in mean SOD levels and anxiety score from first month to last month of treatment.

El-Sokkary et al found decreased level of glutathione and decreased antioxidant activity of SOD and increased lipid peroxidation in rat liver as compared to control when diazepam was given for long time. Mendez – Cuesta, L.A et al in their study observed that when acute stress was produced in rats by immobilizing them, there was decrease in mitochondrial function, decrease in SOD activity and increase lipid peroxidation while administration of diazepam in single dose before initiating oxidative stress decreases lipid peroxidation. Nunez, M.J .et al studied effect of Alprazolam on acute stress in mice after 6 hours of immobilization. They found increased production of reactive oxygen species due to stress and when these mice were pre-treated with Alprazolam, it was partially effective in reducing oxidative stress.[6] These studies suggest different effect of different benzodiazepine on acute and chronic stress. Hence it requires further research to know the effect of benzodiazepine on acute and chronic stress.

In group II patients treated with Tablet Clonazepam and Tablet. Hemidesmus indicus for six months, there was decrease in mean MDA levels, increase in mean SOD levels and significant decrease in anxiety score from baseline to last assessment. Antioxidant action of methanolic extract of root bark of Hemidesmus Indicus was studied by Ravishankara et al in various in vivo and in vitro methods. They found that extract of Hemidesmus Indicus has intense action in scavenging superoxide radicals, moderate action in scavenging nitric oxide radical. They also found that Hemidesmus indicus has inhibitory effect on lipid peroxidation of liver homogenate and phenyl hydrazine induced haemolysis suggesting its membrane stabilizing activity. It is useful in treatment of treatment of various diseases because of its free radical scavenging action.[14] Sateesh Kumar et al evaluated iron chelating capacity of aqueous extract of Hemidesmus Indicus by using method of Benzle and strain. Iron chelating capacity of Hemidesmus indicus may be because of its polyphenol content that prevents the cell from free radical induced damage.[15] Doxorubicin is used in treatment of various malignancies but it may cause cardiotoxicity due to lipid peroxidation, damage to mitochondria, formation of free radicals and decrease Na+–K+ ATPase activity. It leads to decrease in levels of antioxidant enzymes such as SOD, CAT, GP and GSH. H. indicus root extract, due to its antioxidant properties significantly reduced the oxidative stress and thereby toxicity induced by doxorubicin. 70% methanolic extract of H. indicus root contains large amounts of flavonoids and phenolic compound which may be responsible for its free radical scavenging activity and high antioxidant action.[16]

Antioxidant activity of free and bound phenolic of Hemidesmus Indicus against oxidative damage was studied by Smitha Jayram et al. They found that free and bound phenol of Hemidesmus Indicus inhibits hydroxyl radical mediated lipid peroxidation. It also inhibits cleavage in DNA strand. Hemidesmus Indicus has a free radical scavenging action as it donate hydrogen from the phenolic hydroxyl group forms a stable compound and prevents further lipid peroxidation. Free and bound phenol are therefore free radical scavenger. They also found a strong positive correlation between total phenolic content and antioxidant activity of Hemidesmus Indicus.[17]

From these observation Hemidesmus indicus is effective in reducing oxidative and anxiety score when given along with antianxiety drug Clonazepam.

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