EFFECT OF SIX-MONTHS PRACTICE OF MEDITATION ON STRESS LEVEL IN CORONARY ARTERY DISEASE PATIENTS

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Abstracts: **Background and objectives:** Coronary artery disease (CAD) is the leading cause of morbidity and mortality worldwide. It has been recognized that stress, anxiety and depression are important in aetiology and progression of CAD. This study is to evaluate the role of Meditation in improving biochemical parameters like serum cortisol and ACTH in known CAD patients. **Method:** Sixty CAD patients are divided into two groups of which one group did Meditation and other did not. Serum cortisol and ACTH were measured before and at end of 6 months of study in both the groups. **Result:** At the end of study significant decrease was seen in patients who practiced Meditation as compared to other group. **Conclusion:** Meditation may modulate the physiological response to stress via neurohumoral activation, which may be a novel therapeutic target for the treatment of CAD.

Key Words: Coronary artery disease, Meditation, Adrenocorticotropic hormone, Cortisol, Electro chemiluminescence immunoassay.

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Introduction:

Coronary artery disease (CAD) is epidemic in world and the leading cause of death worldwide[1]. Previously thought to affect primarily high-income countries, CAD now leads to more death and disability in low- and middle-income countries[2], with rates that are increasing disproportionately compared to high-income countries. CAD affects people at younger ages in our country thereby having a greater economic impact.[3] Advances in therapy like angioplasty, stenting and by-pass surgery address effectively the problem of individual patients. However, they are very expensive and beyond the reach of the majority of patients in our country. Besides, these procedures are focused upon treating the manifestations of disease and not on the underlying cause of disease.

With increasing understanding of various risk factors as causative agents of CAD, lot of interest is generated in prevention of modifiable risk factors like tobacco smoking[4], high blood cholesterol[5], hypertension[6], physical inactivity[7], obesity[8] and diabetes mellitus.[6] It has been also recognized that stress, anxiety and depression are also important in aetiology and progression of CAD.[9] Cumulative exposure to chronic stressors may be a risk factor for CAD.[10] Individuals who are exposed to high levels of demands and low levels of control at work, to distressing marriages, and to low social support are more likely to have incident CAD than their less stressed counterparts.[10, 11, 12] Dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis is one of the pathways through which chronic stress may affect CAD risk. In healthy individuals, cortisol has a distinct diurnal pattern with the peak cortisol occurring in the early morning, declining throughout the day, and reaching a nadir around 2 or 3 AM.[13] Cortisol also exhibits sizable, short-term increases during the first hour after awakening and in response to a lunch meal or a threat-provoking stressor. Dysregulation can take the form of altered overall levels of cortisol or a smaller decline in cortisol throughout the day and evening, i.e., flatter slope.

The literature clearly supports that chronic stress in both animal and human studies alters the ability of the HPA axis to recover from challenges.[14] Elevated cortisol levels are associated with depressive symptoms[15], anxiety[16], caregiver stress[17], unemployment[18], and overall negative affect.[19] Elevated evening cortisol, resulting from a smaller cortisol decline throughout the day, is associated with unhappy marriages[20], low positive affect (men only[19]) and depressive symptoms, low network diversity, support, feelings of control, and low socioeconomic status.[21] Exposure to these

stressors results in a series of coordinated responses organized to enhance the probability of survival. These coordinated responses, often referred to as ''stress responses,'' are composed of alterations in behaviour, autonomic function and the secretion of multiple hormones including adrenocorticotropin hormone (ACTH) and cortisol. A higher level of morning cortisol has been observed among men with moderate to severe coronary atherosclerosis than those with no detectable disease.[22, 23]

The physiological underpinning of this link may involve excessive sympathetic nervous system activation.[24] Ornish et al[25] were the first to document the beneficial effects of lifestyle changes in reversing the coronary heart disease. Manchanda et al[26] in their study similarly showed encouraging results with their yoga lifestyle intervention. However, both these studies included only a small number of patients.

"Meditation" is a set of attentional practices leading to an altered state or trait of consciousness characterized by expanded awareness, greater presence, and a more integrated sense of self. Practice of concentrating focus on an imaginary point on forehead (between eyebrows), sound or object increase awareness of the present moment, reduce stress, promote relaxation, and enhance personal and spiritual growth. Meditation practice self-regulates the body and mind, thereby affecting mental events by engaging into a specific attentional set. These practices are a subset of other practices used to induce relaxation or altered states such as hypnosis, progressive relaxation and trance-induction techniques.[27] Meditation is a simple mental technique which has well documented benefits for health and wellbeing.[28, 29] It can be learned easily by anyone regardless of age, educational background, or culture. The technique is effortless and requires no belief or any change in lifestyle or diet.

During Meditation mental activity settles down in a natural way, while alertness is maintained and even enhanced. Scientific studies reveal that meditation produces a specific physiological response pattern that involves various biological systems. Mechanism most frequently suggested that meditation produces effects including metabolic,[30] autonomic, endocrine, neurological, cardiovascular and psychological responses on a multidimensional interactive basis. The objective of our study was to see the effect of six-months of meditation on stress level in CAD patients.

Material and Methods:

The study was conducted in Department of Physiology, Biochemistry and Cardiology, Maulana Azad Medical College and associated G. B. Pant Hospital from June 2011 to January 2012. The study group comprise of sixty angiographically proven (criteria: 50% or more obstruction in any coronary artery) coronary artery disease patients. They were equally divided into two groups, thirty each in Meditation and Control group, selected from Department of Cardiology, G. B. Pant Hospital, New Delhi. Randomization to Control and Meditation group was done with the help of chit method.

Inclusion criteria were 1) Age group 30-70 years of either sex, 2) Angiographically proven coronary artery disease, 3) non-smokers. Exclusion criteria were 1) Patients with a history of acute myocardial infarction in recent past (two months), 2) Patients with unstable angina pectoris, 3) Patients with clinical cardiac failure, those with ejection fraction of below 30% by echocardiography, 4) Patients who had undergone coronary angioplasty or by-pass surgery, 5)Patients with heart ailments other than CAD such as congenital heart disease, cardiac myopathies, etc., 6) Patients with endocrine disorders like thyrotoxicosis, 7) Patients with neurological or psychiatric disorders, 8) Patients who had participated in athletics/sports activity or routinely following yogic exercises.

The patients were equally divided in two groups, each group consisting of 30 patients. Randomisation to either group was done with the help of chit method. **Group I** consisted of Meditation group which contains CAD patients with medication and on prescribed meditation (concentrative meditation) and dietary modifications. **Group II** consisted of control group which contains CAD patients with medication and dietary modification. Ethical approval of study

protocal and consent from all the patients was obtained before the study.

Estimation of serum cortisol and ACTH was conducted in the Department of Bio-chemistry, Maulana Azad Medical College, New Delhi. 5 ml of fasting peripheral venous blood was collected in plain vials under aseptic conditions and estimation were done by electrochemiluminescence immunoassay (ECLIA) on Elecsys 2010 automated system using cobas e immunoassay analyzers kits.

Protocol for Meditation in Meditation group: Patients were called in group of 10 twice a week (Monday and Thursday) at 9 AM in the Department of Cardiology, G. B. Pant Hospital. They were instructed to come empty stomach, wearing clean, simple and loose clothing. They were made to sit comfortably on the floor and allowed to relax for about five minutes. This was to allay any apprehension associated with the class. To ensure free and fresh ventilation all the windows of the room were opened. The room's ambient temperature was maintained on all days between 16ºC-20ºC. The room was clean, noise-free and dim lighted. Meditation technique was demonstrated each day for first few days until they had learned the technique perfectly; subsequently they followed the procedure themselves. Special emphasis was laid on breathing technique practiced by each patient individually and the same was checked on each subsequent visit.

Meditation technique: **Concentration on body:** Sitting relaxed on the floor, patients were asked to focus attention on their body. Asked to put their attention at the area of forehead, and just sweep the body, feeling every part of body sensations, tensions. If they felt any tensions in their body, they were asked to just be aware of those tensions; don't try to resist or control those tensions and continue sweeping the body. **Concentration on breathing:** Patients were taught to allow their body to breath naturally, and focus their attention wherever they feel the sensation of the breath in the body. While inhaling, be aware, be conscious of inhaling; when exhaling, be aware, and be conscious of exhaling. Be with this movement of the breath; just come back to it as an anchor. **Distress to de-stress:** Patients were taught that whenever they experience tension, stress or anxiety, try to focus their attention on other things: perhaps the sounds they hear, the sensations in their body, the touch of their clothing, movements in their body, their heart beating, or the rise and fall of the abdomen during breathing. They were made to learn to be aware of other things that are happening while they are experiencing stress.

Forgiveness: Patients were taught to gently soften their thought towards themselves, accept themselves as they are, without any notion of what they should become. Making friends with whom they are - and really feel that friendship, that kindness. Then only they can extend that friendship, gentleness, softness even to those who have hurt, disappointed or frustrated them. Letting go of the hurts and wounds they have been carrying by learning to forgive, by learning to accept the common human-ness.

To ensure whether patients were doing meditation properly or not heart rate and blood pressure were recorded before (after 5 minutes of rest) and after doing meditation. Patients in meditation group were asked to maintain a Record Diary in which they entered days on which they did meditation and for how long. To ensure their compliance to program at home, they were subjected to stress management intake questionnaire (Appendix-V). Any patient not following instructions properly or doing meditation for less than 5 times in a week was not included in the study.

Follow-up: 1) All the patients were directed to fill up the requisite information with respect to the medication prescribed routinely as per performa given, 2) In the meditation group of patient they were instructed to routinely follow up the meditation process and to make the entries in the record diary, 3) Each patient in control group was instructed to report for follow up regularly at an interval of 15 days, 4) Each patient was instructed to immediately contact the investigator in case of any problem, 5) At the end of 6 months biochemical parameters were studied in both the group of patient.

Result:

Physical characteristics of two groups of patients are shown in Table 1. It can be seen that the

physical characteristics in the two groups of the patients showed no statistical difference in the age, height, weight and body surface area. Hence the two groups are statistically comparable to assess the effect of meditation on CAD patients.

Table 1:Mean±SD of baseline value of anthropometry in the two groups of patients.

		Mean	Std. Deviation	p value (gr. I compared with gr. II)
Age (years)	Group I	53.9	9.8	0.328 (NS)
	Group II	56.2	7.2	
Height (cms)	Group I	165.5	4.9	0.690 (NS)
	Group II	166.1	5.9	
Weight (kgs)	Group I	69.5	6.2	0.173 (NS)
	Group II	67.2	6.3	
BSA (m^2)	Group I	1.8	0.1	0.345 (NS)
	Group II	1.7	0.1	

Neurohormonal assay was done in both the groups of patients which included serum cortisol and ACTH and the result is shown in Table 2. Mean ± SD value of serum cortisol done in group I patients before and after study was 32.3±3.9µg/dl and 19.4±4.8µg/dl respectively. Mean ± SD value of serum ACTH in group I patients before and after study was 67.4±4.6ng/l and 48.9±6.6ng/l respectively. These differences were statistically highly significant (p<0.05).

Table 2: Mean ± SD value of neurohormonal assay in group I patients before and after study (n=30)

Parameters	Before study	After study	p value
Serum Cortisol (µg/dL)	32.3±3.9	19.4±4.8	0.000 (HS)
Serum ACTH (ng/L)	67.4±4.6	48.9±6.6	0.000 (HS)

p value: >0.05 not significant (NS); <0.05 significant (S); <0.01 highly significant (HS); ACTH=Adrenocorticotropic hormone

Mean ± SD value of serum cortisol in group II patients before and after study was 30.4±5.1µg/dl and 29.9±7.4µg/dl respectively. Mean ± SD value of serum ACTH in group II patients before and after study was 68.1±5.2ng/l and 68.5±10.7ng/l respectively. None of the parameters showed any statistically significant difference (p<0.05) (Table 3).

Table 3: Mean ± SD value of neurohormonal assay in group II patients before and after study (n=30)

Parameters	Before study	After study	p value
Serum Cortisol (µg/dL)	30.4±5.1	29.9±7.5	0.545 (NS)
Serum ACTH (ng/L)	68.1±5.2	68.5±10.7	0.771 (NS)

p value: >0.05 not significant (NS); <0.05 significant (S); <0.01 highly significant (HS); ACTH=Adrenocorticotropic hormone

Inter-group comparison of neuro-hormonal assay between two groups of patients at the end of study: After the end of study, mean ± SD values of serum cortisol and ACTH was markedly increased in group II patients as compared to group I patients

and the difference is statistically highly significant ($p<0.05$) (Table 4).

Table 4: Comparison of neurohormonal assay between the two groups of patients at the end of study

	Group	Mean	Std. Deviation	p value (gr. I compared with gr. II)
Serum Cortisol (µg/dL)	I	19.4	4.8	0.000 (HS)
	II	29.9	7.5	
Serum ACTH (ng/L)	I	48.9	6.6	0.000 (HS)
	II	68.5	10.7	

p value: >0.05 not significant (NS); <0.05 significant (S); <0.01 highly significant (HS)

Discussion:

Coronary artery disease (CAD) remains one of the major causes of morbidity and mortality in India. A number of risk factors have been identified to be strongly associated with CAD, stress and behaviour patterns are one of them. Hence the present study was chosen to study the effect of stress relieving technique i.e., meditation on biochemical parameters on coronary artery disease patients.

When one is exposed to a physical or psychological stressor, the brain initiates a stress response, from which a series of chemical reactions ensue. The stress response is a healthy defence mechanism and involves the release of hormones that have numerous biochemical and physiological effects. However, the continued release of these hormones under conditions of chronic stress can have detrimental effects on health. Indeed, the hormonal response associated with long-lasting stress increases the risk of many diseases, including heart disease, stroke, and angina. Stress hormones also trigger increases in blood pressure, heart rate, and respiration and raise the risk of heart attack.[31]

The present study was conducted in the Departments of Physiology, Biochemistry and Cardiology, Maulana Azad Medical College and associated G. B. Pant Hospital, New Delhi, on sixty CAD patients, age group between 30-70 years of either sex. These patients were randomly selected and were equally divided into two groups, each group consisting of thirty patients. Out of sixty patients fifty six (93.3%) were males and four (6.7%) were females.

At the end of study, there was significant decline in the levels of serum cortisol and ACTH as compared to their pre-test levels. These differences were highly statistically significant. Carlson et al[32] in their study demonstrated the beneficial effect on 8-week meditation program in decreasing salivary cortisol. Cortisol levels decreased systematically over the course of follow-up. Similar studies conducted by Witek-Janusek et al[33] and Marcus et al[34] showed similar effect of meditation in decreasing serum cortisol levels in subjects practising meditation. Infante et al[35] conducted similar study to see the effect of meditation on variation in hormone levels. They found decrease level of ACTH in subjects practising meditation as compared to those who were not, but cortisol levels were found to be similar in both the groups.

However from the various studies conducted, we can conclude that this effect of meditation is due to decrease in adreno-cortical activity which causes long term decrease in cortisol secretion.[36] Meditation also causes modification of anterior hypophyseal and hypothalamic activity. Meditating subjects seem to show increased hypophyseal sensitivity to the cortisol feedback mechanism. This is considered feasible, because the inhibition of ACTH secretion by this mechanism is known to be a sensitivity-level phenomenon.[37]

These results suggest that meditation may modulate the physiological response to stress via neurohumoral activation, which may be a novel therapeutic target for the treatment of CAD. Previous work by Reaven et al[38] and Brook and Julius[39] has suggested that sympathoadrenal system activation is linked with the CAD. Visceral obesity, insulin resistance, and diabetes are also associated with a proinflammatory state[40, 41] that is linked with elevated CAD risk.[42] The present study results expand this understanding and demonstrate that meditation, which is believed to

reduce sympathoadrenal system activation, beneficially alters the insulin resistance components of the metabolic syndrome and hence reduces CAD risk.

But there are also some studies that questioned the efficacy of meditation in improving various markers mentioned above. Infante et al[35] by their study suggested that meditation practitioners have similar cortisol levels and cortisol diurnal rhythms to those who did not practice meditation. A similar study by Cooper et al[43] found no convincing evidence that any of the stress-related hormones were suppressed in subjects performing the technique at rest. If anything, catecholamine levels were higher in meditators during the study. Furthermore, plasma free fatty acid concentrations, reflecting in part the lipolytic action of catecholamines and other stress hormones, showed a substantial elevation after the period of meditation was completed. However, there is a definite need for more directed scientific work to be carried out to elucidate the effects and the mechanism of such effects of meditation on the human body in health and disease. Considering the scientific evidence discussed thus far, it is fair to conclude that meditation can be beneficial in the primary and secondary prevention of cardiovascular disease and that it can play a primary or a complementary role in this regard.

Conclusion:

There is tremendous enthusiasm in cardiac rehabilitation circles to incorporate complementary forms of exercise therapy such as yoga, meditation to the mainstream practice of cardiac rehabilitation. Lack of infrastructure, expertise and funding seem to be the main hurdles in the implementation of such reform. Therefore more research needs to be carried out at leading rehabilitation centres into the benefits of complementary physical exercise modalities and a push for more funding is required once there is unequivocal evidence of the benefits of its incorporation into the mainstream post- and pre-event cardiac rehabilitation.

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