Original Research Paper

Volume-7 | Issue-10 | October-2017 | ISSN - 2249-555X | IF : 4.894 | IC Value : 79.96

Clinical Research

A STUDY ON THE INCIDENCE OF STRESS HAZARDS RELATIVE TO ALLOSTATIC LOAD AMONG HEALTHY VOLUNTEER IN INDIA

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ABSTRACT

Introduction: The objective of this study was to assess the stress hazards in respective to Allostatic load factors in Indian human volunteers. The benefits of establishing the relation of Allostatic load and vital body physiological functions would be helpful in measuring drug effectiveness.

Methods: The Perceived Stress Scale 10 (PSS 10) was used to measure the stress levels. The Allostatic load factors such as Epinephrine, Norepinephrine, Dopamine and Cortisol were measured from urine and serum samples. The physiological vitals like blood pressure (BP), heart rate (HR), respiratory rate (RR) and body temperature were also measured manually.

Results: The Allostatic load factors were found to be elevated with increased stress. The primary mediators of Allostatic; Epinephrine, Norepinephrine and Cortisol were elevated ($p<0.05$) with increased stress while Dopamine changes were little. The secondary mediators systolic blood pressure (134.17±5.15, $p<0.05$) and diastolic blood pressure (87.54±8.67, $p<0.05$) were high. The heart rate and respiratory rate were increased but body temperature had not altered.

Conclusion: The Allostatic load factors can be used as better predictors of altered physiological functions. This shall be extrapolated to rate of drug metabolism during stress exposure. The study recommends further studies with repeated samples to prove this hypothesis.

KEYWORDS : .Perceived Stress Scale 10 (PSS 10), Allostatic load, Cortisol, Moderate stress, High stress.

INTRODUCTION

Allostasis and Allostatic load are relatively new concepts, which were proposed to explain the physiological responses to stress like variations of hormones, temperature, blood pressure etc. Perhaps, Allostasis was used to represent the adaptation process of complex physiological systems to physical, psychosocial and environmental challenges [1, 2]. The more frequent or chronic challenges which produce Allostasis would dysregulate several major physiological systems, including the hypothalamic–pituitary–adrenal (HPA) axis, the sympathetic nervous system (SNS) and the immune system[3]. Allostatic load represents the interplay of different systems (inflammatory, neuroendocrine, and metabolic) and the markers may act as acute (primary mediators) or more long-term effects (secondary outcomes). Primary mediators representing an endocrine system, on the other hand, are more strongly associated with stress than secondary outcomes in cardiovascular or metabolic systems[4]. Assessment of Allostatic load would optimally incorporate information on 'resting' levels of Allostatic mediators as well as the physiological system in dynamics[5].

METHODOLOGY

Study design

This prospective interventional study was carried out in healthy male volunteers, non-smoker, non-alcoholics of age 20-60 years with normal body mass index (BMI) and waist-hip ratio (WHR). Subjects with known medical conditions, taking drugs for last 60 days were excluded. The informed consent was obtained from all study subjects. The study protocol was reviewed and approved by Institutional Review Board (IRB) of J.S.S. College of Pharmacy, Ooty, Tamil Nadu, India (Protocol id: JSSCP/DPP/IRB/008B/2013-14, Version 2) and this study was registered in Clinical Trial Registry of India (Reg. no: CTRI/2016/11/007464), New Delhi, India.

Assessment of stress

The stress was assessed by English and Tamil versions of PSS 10 from www.psy.cmu.edu/~scohen [6]. The permission was obtained from Dr Sheldon Cohen to use PSS 10 English version and from the author of Tamil language version Mr Santhalingam Sathish.

Assessment of Allostatic load and Cortisol

The subjects were followed under the prescribed study conditions for 48 hrs. The urine samples were collected that voided for 24 hours and the blood samples were collected at morning for serum Cortisol analysis. The cardiovascular and respiratory vital parameters were measured manually.

Assessment of physiological vital parameters

The physiological parameters such as blood pressure, heart rate, respiratory rate, body temperature and VO2max (maximum oxygen utilization) were measured manually.

Data interpretation and statistical analysis

According to the average score of PSS 10, the total subjects were divided in to two groups, high and moderate stress groups. Then, average scores of each parameter of Allostatic load and physiological vitals (secondary mediators) in moderate and high-stress groups were compared. The statistical analysis was done by using unpaired sample 't' test in SPSS 20 and significance was set at $p<0.05$.

RESULTS

A total of 24 subjects were successfully completed the study of which, 12 subjects each were put in to moderate and high stress groups based on the scores of PSS 10. The primary mediators of Allostatic load factors were elevated as showed in Fig 1; Epinephrine, Norepinephrine and Cortisol were elevated ($p<0.05$) with increased stress. Dopamine was little lowered in higher stress group as it was studied in previous researches; when stress increases, Dopamine would be dysregulated it could be either increased or decreased (Fig 1). The present study result showed when the content of stress increases through psychological, physical or environmental, Dopamine was decreased. The elevated Cortisol in both groups could better explain the intensity of stress exposed.

The physiological parameters, systolic and diastolic blood pressures, heart rate, respiratory rate and VO2max were considered to be the valid indicators for measuring the stress responses (Table 1). At resting position systolic blood pressure of high-stress group was 134.17±5.15 which was comparatively high than in moderate stress group 127.52±6.22. The resting diastolic blood pressure was higher; 84.58±7.21 and 87.54±8.67 respectively. Heart rate at resting state found higher in high-stress group respiratory rate was also high. Body Temperature was 98.62±0.19 in the high-stress group and 98.61±0.17

(Table 1) in moderate stress group in which the SD calculated showed the possible temperature fluctuations due to the cold climatic conditions in hill areas. The VO2max was lowered than normal in the high-stress group and normal in moderate stress group but this state was not considered under satisfactory oxygen level.

DISCUSSION

The Allostatic load often represented SNS and HPA responses to stress experienced or perceived by the human body. The present study had explained an approach to establish the Allostatic load dysregulation7 to basic physiological parameters[8] such as heart rate and blood pressure. Due to the methodological difficulties and some ethical aspects, noninvasive markers were preferred along with invasive markers for analysis in this study. Apart, perceived stress was also observed to initiate physiological[9] responses that cause Allostasis. The cardiovascular activity response to stress increases metabolic demands[10] by SNS and on this repeated and cumulative primary mediators of Allostatic load results in elevation of secondary mediators like blood pressure and heart rate further to increased cardiac output which would increase organ perfusion [11] of blood. In this condition, blood flow to kidneys would expect to be increased [12] while the elevated levels of circulating Catecholamines during stress exposure probably decreases hepatic blood flow in fact, low oxygenated blood flows through liver results in altered metabolism of drugs in the liver.

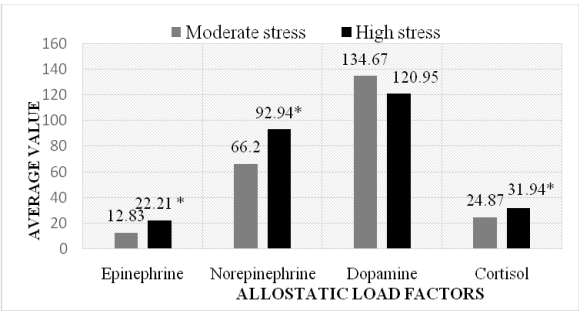
CONCLUSION

The Allostatic load can be used as a better predictor for alteration of human physiological functions. The relationship of primary mediators with secondary mediators (often called surrogate markers) would also be a better predictor of decrements in therapeutic outcome in association with or without drug pharmacokinetics. This approach can be used either with existing mainstream clinical practices as 'complementary' or in place of existing mainstream clinical practices as 'alternative' or with conventional treatments.

CONFLICTS OF INTEREST: The authors declare that they have no conflict of interest.

ACKNOWLEDGMENT: The authors thank all the participants involved in this study. They also thank Dr.Lalpathlab, New Delhi, India for the support in sample analysis.

Fig 1: The primary mediators of Allostatic load in stress groups. Values expressed as average.



*p<0.05, unpaired sample 't' test

Table 1: The secondary mediators of Allostatic load in stress groups. Values expressed as average ± SD.

Secondary Biomarkers	Moderate Stress Group (n-12)	High Stress Group (n-12)
Resting Systolic Blood pressure (mmHg)	127.52±6.22	134.17±5.15 *
Resting Diastolic Blood pressure (mmHg)	84.58±7.21	87.54±8.67*
Resting Heart rate (beats/min)	71.67±1.87	77.97±3.78*
Resting Respiratory rate (breaths/min)	22.42±1.67	24.42±1.5*
Resting Body Temperature (°F)	98.62±0.19	98.61±0.17
Resting VO2max (Vol. %)	45.31±3.05	29.19± 2.04*

*p<0.05, unpaired sample 't' test

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