ISSN: 2278-778X
Research Article
www.ijbio.com

EVALUATION OF ANTIOXIDANT MECHANISM RELATIONSHIP WITH ADRENAL HORMONE INSUFFICIENCY IN THE TISSUES OF RAT

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Received for publication: November 15, 2012; **Accepted**: December 18, 2012.

Abstract: Changes in antioxidant metabolism in liver, heart, kidney and muscle tissues were observed on adrenalectomy. Uric acid levels were increased significantly in liver and kidney and it was depleted in muscle upon ADX. Ascorbic acid levels were depleted significantly in Liver and muscle and in contrast in heart and kidney they were significantly increased. Liver, heart and muscle showed a significant increase of glutathione content whereas in kidney it was significantly decreased. The present finding, in general, exhibit tissue specific alterations in free radical metabolism in conjunction with antioxidant defence mechanisms during adrenal hormone deficiency. It is also clear from the results that the mechanisms involved in selective activation / inhibition of different pathways seems to reflect multifaceted physiological adaptations as a compensatory measure during induced adrenalectomy.

Keywords: Adrenalectomy, Antioxidant metabolism, Ascorbic acid, Uric acid, Glutathione, Sham operated.

INTRODUCTION

Oxidative stress is a condition that is associated with an increased rate of cellular damage induced by oxygen and oxygen derived oxidants commonly known as reactive oxygen species (13). Free radical damage has been implicated in various disease states, ranging from arthritis and connective tissue disorders to carcinogenesis, aging, toxin exposure, physical injury and infection (5). Nature has evolved several enzymes and antioxidants which can work in a combined fashion to protect biological systems against oxidative damage and prevent disease occurrence.

Adrenal corticosteroid insufficiency due to adrenalectomy interferes with metabolic (9, 10). Cardiac (1,7,14) and Reproduction (3) and hematopoietic functions and modulates the development and maintenance of normal immunitory status, which in turn influences the inflammatory response (2). Adrenalectomy diminishes the glucidic metabolic response on irradiation (4). In the present study an attempt has been made to understand the metabolic modulations in liver and muscle tissues of male albino rat on adrenalectomy (ADX).

MATERIALS AND METHODS

Male, pathogen-free Wistar strain albino rats aged 3 months were obtained from Indian Institute of Sciences, Bangalore. They were housed and maintained in clean polypropylene cages, six in each, in a temperature controlled room (27° C) with photo-period of 12 hrs light and 12 hrs dark cycles. The rats were fed with standard laboratory chow (Hindustan Lever Ltd., Mumbai) and water *ad libitum.*

EXPERIMENTAL DESIGN

Rats were divided into two groups, each group consists of six individuals. First group of rats were called as sham operated (SO), the adrenal glands were kept intact and considered as control. The second group of rats were bilaterally adrenalectomized (ADX) by the dorsal approach in a single stage operation as described by (1).The rats were anaesthetized before surgery using ether. Adrenalectomized rats were given 0.9 % saline as drinking water and sham operated rats were given normal tap water.

The control and experimental rats were maintained for three weeks period. The three week period was chosen on the basis of preliminary data showing that three week period of adrenalectomy produced effects consistent with adrenal hormone insufficiency. After the three weeks of experimental period, the rats were sacrificed by cervical dislocation and the tissues like liver, heart, kidney and muscle were isolated, chilled immediately.

RESULTS

The data was presented in tables 1, 2, 3 & 4. The amount of uric acid was significantly increased in liver and kidney tissues of adrenalectomized rats. In contrast, muscle tissue showed depletion in uric acid content of adrenalectomized rat compared to sham operated. Ascorbic acid was increased in heart and kidney tissues in adrenalectomized rats when compared with sham operated rats. However ascorbic acid was decreased in liver and muscle tissues. The glutathione content was increased significantly in liver, heart and muscle of adrenalectomized rats in comparison with sham operated, but the same was depleted in kidney.

Table.1: Alterations in the levels of uric acid, ascorbic acid and glutathione in liver of both adrenalectomized and sham operated rats

Parameter	Sham operated	Adrenalectomized	Percent$ change
Uric acid µ moles / g wet wt of tissue	9.50 ± 0.74	12.37 ±1.00	+ 30.21 t = - 5.667 p = 0.001
Ascorbic acid mg / g wet wt of tissue	0.949 ± 0.073	0.835 ± 0.06	- 13.65 t = - 2.962 p = 0.015
Glutathione µ moles / g wet wt of tissue	5.37 ± 0.46	8.54 ± 0.63	+ 59.00 t = - 9.935 p = 0.001

Values are mean ± S.D of six individual observations. $ + or - indicate the percent increase or decrease over sham operated control respectively. "p" denotes the level of statistical significance.

Table.2: Alterations in the levels of uric acid, ascorbic acid and glutathione in heart of both adrenalectomized and sham operated rats

Parameter	Sham operated	Adrenalectomized	Percent $ change
Uric acid mg / g wet wt of tissue	8.48 ± 0.75	9.03 ± 0.89	+ 6.48 t = - 1.151 NS
Ascorbic acid mg / g wet wt of tissue	0.520 ± 0.03	0.557 ± 0.03	+ 7.11 t = - 2.197 p = 0.05
Glutathione µ moles / g wet wt of tissue	5.14 ±0.42	5.77 ± 0.44	+ 12.25 t = - 2.541 p = 0.02

Values are mean ± S.D of six individual observations. $ + or - indicate the percent increase or decrease over sham operated control respectively. "p" denotes the level of statistical significance. "NS" indicates non-significant change.

Table.3: Alterations in the levels of uric acid, ascorbic acid and glutathione in kidney of both adrenalectomized and sham operated rats

Parameter	Sham operated	Adrenalectomized	Percent$ change
Uric acid mg / g wet wt of tissue	7.37 ± 0.53	9.36 ± 0.75	+ 27.00 t = - 5.287 p = 0.002
Ascorbic acid mg / g wet wt of tissue	0.597 ± 0.06	0.699 ± 0.053	+ 17.08 t = - 3.283 p= 0.008
Glutathione µ moles / g wet wt of tissue	6.21 ± 0.45	5.46 ± 0.51	- 12.07 t = 2.667 p = 0.024

Values are mean ± S.D of six individual observations. $ + or - indicate the percent increase or decrease over sham operated control respectively. "p" denotes the level of statistical significance.

Table. 4: Alterations in the levels of uric acid, ascorbic acid and glutathione in muscle of both adrenalectomized and sham operated rats

Parameter	Sham operated	Adrenalectomized	Percent$ change
Uric acid mg / g wet wt of tissue	22.31 ± 0.92	18.95 ± 0.59	- 15.06 t = 6.845 p = 0.001
Ascorbic acid mg / g wet wt of tissue	0.461 ± 0.035	0.352 ± 0.026	- 23.64 t = 4.285 p = 0.013
Glutathione µ moles / g wet wt of tissue	2.66 ± 0.21	5.45 ± 0.48	+ 104.89 t = - 5.977 p = 0.002

Values are mean ± S.D of six individual observations. $ + or - indicate the percent increase or decrease over sham operated control respectively. "p" denotes the level of statistical significance.

DISCUSSION

The level of uric acid recorded considerable elevation in liver tissue of ADX rat when compared to the SO. This suggests that the formation of uric acid is more than its disposal in the liver tissue. The breakdown of nucleic acids is the main source of uric acid in tissues (17,11) and the same might have happened in the liver, thus causing elevation in uric acid levels. The level of ascorbic acid was lowered in the liver of ADX rat when compared to SO. Kipp and Rivers (6) also showed similar decrease in the liver of adrenalectomized animals. Adrenal gland i s the major source of ascorbate efflux into the circulation during oxygen deprivation, which supports for the depletion in liver.

Glutathione levels were elevated significantly in liver on adrenalectomy. In support to the present study, the elevated glutathione levels were observed in liver on adrenalectomy and treatment with 6-Hydroxydopamine (6-OH) combination (16).

In contrast to liver tissue, heart tissue showed significant elevation in ascorbic acid levels of ADX rat than SO. Adrenalectomy affects the degradation of ascorbic acid and its concentration in selected tissues, with a profound effect on the heart. Heart tissue also showed a significant increase in glutathione content of ADX rat over SO. Toleikis and Godin (16) reported similar increase upon adrenalectomy.

The level of uric acid was also raised in the kidney of ADX rat when compared to SO indicating the structural derangement in the kidney which might be responsible for the deposition of uric acid. Similar to this Devendra Naidu (3) reported atrophy and abnormality of seminiferous tubules in ADX rat. The concentration of ascorbic acid was significantly higher in the kidney of ADX rat. Changes in glutathione (GSH) metabolism might produce significant effects on kidney MT (metallothionein) levels.

The uric acid content was lowered in the muscle of ADX rat when compared to SO suggesting the impairment of nitrogenous wastes elimination. The reduced muscle RNA content (8) and reduced expression of retinoic acid receptors in the rat liver (12) are in support with the elevated metabolism of purines and pyrimidines which are main sources for the formation of uric acid (17,11).

Muscle tissue showed a significant increase in glutathione content of adrenalectomized rat than SO. Muscle contains thioltransferase which catalyzes the formation of glutathione-protein mixed disulfides. It is proposed that increased formation of oxidized glutathione and its interaction with muscle proteins may act as a signal for the initiation of proteolysis (15). The present study revealed the relationship exists between antioxidant status and adrenal hormone insufficiency in albino rats.

CONCLUSIONS

Uric acid showed an elevation in all the tissues studied except for muscle which indicates the potential role of uric acid in preventing the free radical injury.

The decrease of ascorbic acid in liver and muscle tissues are indicative of its utilization in countering the ascorbate radical production. Its increase in heart and kidney tissues shows a recovery of the impaired oxidative status and energy metabolism.

Elevation of glutathione content in in liver, heart and muscle tissues indicates the tissue capability of synthesizing more GSH upon ADX and the reduction in kidney indicate an increased susceptibility to oxidative damage.

REFERENCES

1. Bhaskar M, Stith RD, Brackett DJ, Wilson MF, Learner MR, Reddy YS, Changes in myocardial ATPase in chronically adrenalectomized rats with and without glucocorticoid replacement, Biochem.Med.Metabol, Bio, 1989, 42, 118-124.
2. Bishayi B, Ghosh S, Metabolic and immunological responses associated with *in vivo* glucocorticoid depletion by adrenalectomy in mature swiss albino rats, Life Sci, 2003, 73(24), 3159-74.
3. Devendra Naidu, Effect of adrenalectomy on testicular metabolism in albino rat, Ph.D thesis. 2000, S.V. University, Tirupati, India.
4. Groza P, Ghizari E, Butculescu I, Ciontescu L, Ciuntu L, Glucidic and lipidic metabolic changes in rats induced by irradiation and the effect of adrenalectomy, Physiologie, 1975, 12(1), 49-52.
5. Joyce DA, Oxygen radicals in disease, Adverse Drug Reaction, Bull, 1987, 127, 476-9.
6. Kipp DE, Rivers JM, The effect of bilateral adrenalectomy on metabolism and tissue distribution of ascorbic acid in the rat, Int J Vitam Nutr Res, 1987, 57(1), 91-7.
7. Lefer AM, Suttin, Cardio vascular effects of catecholamines in experimental adrenal insufficiency, Am J Physio, 1964, 206:1151-1155.
8. Liu CC, Yeh J, Qu B, Forsberg NE, Action of beta andrenergic agonist on muscle protein metabolism in intact adrenalectomized and dexamethasone supplemented adrenalectomized rats, Nutr Biochem, 1994, 5 (1): 43-49.
9. Madhuri E, Effect of adrenalectomy on the metabolism of male albino rat, M.Phil Dissertation, 1999, S.V. University, Tirupati.
10. Madhuri E, Effect of adrenalectomy on the metabolism of various tissues in male albino rat, Ph.D thesis, 2001, S.V. University, Tirupati.
11. Murray RK, Granner DK, Mayes PA, Rodwell VW, In: Harper's Biochemistry, 25th edition, Appleton and Lange publications, 2000, Starford, U.S.A.
12. Pallet V, Audouin-Chevallier I, Higueret D, Garcin H, Higueret P, Dexamethasone decreases the expression of retinoic acid receptors (RARs) in rat liver, J, Steroid Biochem Mol Biol,1996, 57(3- 4) 161-5.
13. Sikka SC, Rajasekaran M, Hellstorm WJ, Role of oxidative stress and antioxidants in male fertility, J Androl, 1995,16, 464-8.
14. Stith RD, Bhaskar M, Reddy YS, Brackett DJ, Learner, MR, Wilson, MF, Cardiovascular changes in chronically adrenalectomized conscious rats, Cir Shock, 1989, 28, 395-403.
15. Tischler ME, Fagan JM, Allen D, Relationship of the redox state to muscle protien degradation, Prog Clin Biol Res, 1985, 180, 363-72.
16. Toleikis PM, Godin DV, Alterations of antioxidant status following sympathectomy: Differential effects of modified plasma levels of adrenaline and noradrenaline, Mol cell Biochem, 1995, 152 (1), 39-49.
17. Vasudevan DM, Sree Kumari S, Pawan Kumar D, GopalaKrishna Bhat P, In: Text book of Biochemistry for medical students, Jaypee Brothers Medical publishers (P) Ltd 1996, New Delhi.

Source of support: Nil
Conflict of interest: None Declared