IMPACT OF STRESS ON HISTOLOGY AND BIOCHEMICAL PARAMETERS OF LIVER AND KIDNEY OF MICE

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ABSTRACT

Epinephrine is a hormone and neurotransmitter. When produced in the body it increases heart rate, contracts blood vessels and dilates air passages and participates in the "fight or flight" response of the sympathetic nervous system. During stress concentration of epinephrine were increased many times. In present study epinephrine were administrated to mice @ 200nl/k.g.bw to induce stress in animal, which were dissected after 2 and 4 weeks. SGOT and Urea level in serum were increased in epinephrine administered group. Liver and kidney tissue were fixed for light microscopy and serum were collected for SGOT and urea assay. While administration of epinephrine frequent vacuolisation were observed. Elongated nucleus was also observed in hepatic cells. Degenerated hepatic vein were also observed. While in kidney dilated bowmen's capsule were observed. Frequent vacuolization were also observed in cortex region. Endothelial cells of PCT were observed in degenerated condition. Thus it is concluded from entire study that stress causes degeneration in hepatic cells, central vein, glomerulus, bowmens capsule, PCT and DCT which finally leading to both hepato-toxicity and nephro-toxicity.

INTRODUCTION

Stress is a response to physical, chemical, biological and emotional changes, consisting of a pattern of metabolic and behavioural reactions that helps in strengthening the organism[1]. Stress has been defined as "the pattern of physiological reactions that prepares an organism for action"[2]. The relationship between stressful life and health is well documented[3]. Among the many consequences of chronic stress, it was shown that it is associated with exacerbated stroke outcome in mice[4], with increased liver metastasis[5], increased susceptibility to endotoxic shock[6], and impaired antiviral immunity in wounded animals[7]. Not only is chronic stress unhealthy, also short-term stress episodes may damage some organs. Acute social stress insults, aggression between males to establish dominance, are a very common stressor in laboratory mice. Few studies addressed the consequences of such a behavior on organ integrity. Matte[8] reported a rise in plasma creatine kinase in regrouped male mice fighting for several hours; he could not reproduce such an increase, although he did observe a moderate increase in plasma lactate dehydrogenase and transaminase activities[9]. Since Bing and Poulsen[10] described that aggressive behavior in mice raises renin concentration in plasma, several laboratories have studied the influence of such behavior on other releasable submandibular salivary gland peptides.

Epinephrine is a hormone and neurotransmitter. When produced in the body it increases heart rate, contracts blood vessels and dilates air passages and participates in the "fight or flight" response of the sympathetic nervous system. It is a catecholamine, a sympathomimetic monoamine produced only by the adrenal glands from the amino acids phenylalanine and tyrosine. Japanese chemist Jokichi Takamine and his assistant Keizo Uenaka independently discovered adrenaline in 1900[11]. In 1901 Takamine successfully isolated and purified the hormone from the adrenal glands of sheep and oxen. Adrenaline was first synthesized by Friedrich Stolz and Henry Drysdale Dakin, independently, in 1904[12]. Thus the present work is designed to study impact of epinephrine induced stress on S.G.O.T., Urea and histology of liver and kidney of mice.

MATERIALS AND METHODS

1. Chemical: Epinephrine was used to prepare stress model.
2. Experimental model: Reared sexually matured 6-8 weeks old age group male and female Swiss Albino mice (Mus musculus) weighing 25-35gm b.w. in the animal house section of Mahavir Cancer Institute and Research Centre, Patna, were selected as an experimental model in the present study. The animals were housed at controlled environmental conditions 22±2°C, relative humidity.
50±10%, and 12h dark-light cycle. Animals were housed and allowed to free access to food and water. All experimental procedures were conducted as per the guidelines of CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals).

3. Methodology:

a) Experimental protocol: Selected pathogen-free mice were randomly divided into two groups (n=6 in each). One group served as control and epinephrine was administered intramuscularly to other groups at the dose of 200nl/kg b.w. respectively. Animals were sacrificed after two weeks and four weeks of treatment with epinephrine in each group.

b) Histopathological Studies: The liver and kidney was dissected out and fixed in 10% neutral formalin solution and the tissue was processed. The slides were stained with Haematoxyline and Eosin and examined morphometrically under Light Microscope.

c) Biochemical Assessment: With the separated serum S.G.O.T. and Urea analysis were performed with standard kit (Coral) to establish the effects of epinephrine induced stress.

RESULTS

In the present study SGOT of control mice was 24 IU/ml. After two weeks administration of epinephrine (200nl/kg b.w) it was 161 IU/ml and after four weeks administration of epinephrine (200nl/kg b.w) it was 166 IU/ml (Graph: 1). Urea level of control mice was 18 mg/dl. After two weeks administration of epinephrine (200nl/kg b.w) it was 31 mg/dl and after four weeks administration of epinephrine (200nl/kg b.w) it was 45 mg/dl (Graph: 2).

Liver of control group of mice show normal hepatic cells, hepatic veins are also normal, central vein are prominent (Figure: 1). While after two weeks administration of epinephrine degeneration were observed in hepatic cells. Many vacuolated spaces were observed, clustered nuclei were also observed (Figure: 2). While after four weeks of administration of epinephrine frequent vacuolisation were observed. Elongated nucleus was also observed in hepatic cells. Degenerated hepatic veins were also observed (Figure: 3). Degeneration of hepatic cells were observed with rudimentary cytoplasm and clustered nuclei. Degenerated nuclei were also observed with frequent vacuolisation (Figure: 4). In control group of mice kidney show normal glomerulus. Bowmen's capsule was also normal in structure. Proximal convoluted tubule (PCT) and distal convoluted tubule (DCT) were also observed in normal condition (Figure: 5). While after two weeks administration of epinephrine Clustered nuclei were observed in glomerulus with frequent degeneration of cytoplasm. Dilated bowmen's capsule were also observed (Figure: 6). While after four weeks of administration of epinephrine dilated bowmen's capsule were observed. Frequent vacuolization were also observed in cortex region. Endothelial cells of PCT were observed in degenerated condition (Figure: 7). Enlarged view of glomerulus show clustered nuclei and degenerated podocytes, degenerated cytoplasm were also observed in duct system (Figure: 8).
Acute and intense psychological stressors induce gastric ulceration and heart injury in rodents. Several acute stressors also alter liver structure. Thus, stressors are different as restraint and forced exercise induce formation of autophagic vacuoles among several ultrastructural modifications. This is associated with DNA oxidative damage, lipid peroxidation, protein oxidation, and ultimately, the loss of hepatocyte integrity, as indicated by the rise in plasma transaminase activities. All these alterations may be caused by catecholamines. Sustained elevation of plasma norepinephrine by means of miniosmotic pump implantation in peritoneal cavity causes hepatocyte injury and depresses liver function. In recent years, it became clear that liver injury, caused by stress, is the consequence of an inflammatory response. Both physical and psychological stressors elevate plasma IL-6 and increase hepatic IL-6 expression. In present study S.G.O.T level were increased to greater extent. Frequent vacuolisation were observed in hepatic cells. Elongated nucleus was also observed in hepatic cells. Degenerated hepatic vein were also observed. Degeneration of hepatic cells were observed with rudimentary cytoplasm and clustered nuclei causes improper function of liver.

Heat stress can negatively affect animal performance. Increase in body temperature and respiration rate are the most important signs of heat stress in farm animals. The increase in body temperature is associated with a marked reduction in food intake, the redistribution of blood flow and changes in endocrine functions, which can negatively affect the productive and reproductive performance of the animals. In present study urea level were gradually increased after increased duration. Dilated bowmen’s capsule was observed in epinephrine administered group. Frequent vacuolization were also observed in cortex region. Endothelial cells of PCT were observed in degenerated condition. Degenerated podocytes were also observed in duct system. This finally leads to improper filtration and reabsorption. This finally hampers urine formation. The blood electrolyte balance is also altered during heat stress result in abnormal filtration of urine in kidney. Additionally, environmental stress has been shown to cause an increase in the oxidative stress and an imbalance in the antioxidant status.

CONCLUSION

Thus it is concluded from above study that epinephrine induced stress causes increase in SGOT level and urea level in mice leading hepatotoxicity and nephrotoxicity. Stress also causes degeneration of nucleus in hepatic cells, cytoplasm were also degenerated which leads to hepatotoxicity. Glomerulus, bowmen’s capsule, PCT and DCT were also degenerated to greater extent causes abnormal filtration and reabsorption.

ACKNOWLEDGEMENT

The authors are grateful to Mahavir Cancer Institute and Research Centre, Patna for providing research facilities and we are also thankful to all research laboratory staff and animal house staff for their proper support during study.

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