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Effect of Glutathione on Hematological Parameters in Isoproterenol Induced Myocardial Infarction in Rats

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ABSTRACT

Introduction: *Cardiovascular disease (CVD) is an important cause of mortality and morbidity in India. Analysis of Coronary heart disease by cross sectional and epidemiological studies performed over past 50 years reveals that (CVD) is increasing both in urban and rural areas. There is growing body of evidence for role of free radicals in mediating myocardial injury during myocardial ischemia and in particular during the phase of myocardial reoxygenation.* ***Aim of the study****: To study the protective effect of antioxidant Glutathione on hematological parameters in isoproterenol induced myocardial infarction in wistar male rats.* ***Materials and methods****: wistar male rats were randomly divided into four groups namely Control (G1),* ***Glutathione*** *(G2), Isoproterenol (G3) and Isoproterenol+****Glutathione****(G4).* ***Glutathione*** *treated group-received* ***Glutathione*** *(200mg/kg body wt) orally for 30 days. Myocardial infarction was induced in rats by isoproterenol administration (100mg/kg) subcutaneously (sc) at an interval of 24 hrs on 31st and 32nd day. Hematological changes were assessed from 24 hrs after the last dose of isoproterenol.* ***Results:*** *There was decrease in RBC count, WBC count, Platelet count, Hb%, Lymphocyte count, Eosinophil count and increase in Neutrophil count in G4 rats as compared to G3 rats* ***Glutathione*** *pre treatment preserved the changes to near normal.* ***Conclusion****:* ***Glutathione*** *may provide cardio protection under conditions of I-R, by virtue of its antioxidant properties, and may prevent oxidant-mediated damage of the cardiomyocyte membrane and subsequent intracellular Ca2+ overload.*

Key words*: Glutathione, Hematological Parameters, Isoproterenol*

INTRODUCTION

Cardiovascular diseases form the major health concern in recent years, causing severe illness and death throughout the world. About 16.7 million people around the globe die of myocardial infarction every year (WHO 2004) which this forms one third of global deaths[1]. At macro-level these regional variations in risk factors explain some of the regional differences in CVD mortality. Myocardial ischemia, reperfusion is the generation of oxygen derived free radicals from a variety of sources that include the mitochondrial electron transport chain biosynthesis of prostaglandins, enzyme Xanthine oxidase and circulating elements in the blood, with polymorph nuclear neutrophil assuming a primary focus of attention. Glutathione is typically used as a collective term to refer to the tripeptide- L gamma glutamyl–L-Cysteinyl–glycine in both its reduced and diametric forms[2]. Glutathione is an important part of body's antioxidant defense system. Due to its antioxidant properties, glutathione neutralizes damaging free radicals and peroxide molecules, recharges oxidized vitamin C.Glutathione is required for a variety of metabolic processes. In addition glutathione bolsters the structure of body proteins and assists in transport

of amino acid across cell membranes. It is involved in DNA synthesis and repair protein and prostaglandin synthesis, amino acid transport, prevention of oxidative cell damage and enzyme activation[3]. Glutathione supplementation improves human endothelial function and enhanced NO bioavailability with glutathione or related thiol substances supplementation suggests the potential role of this in the treatment and prevention of CAHD. Glutathione helps to protect cells and tissues against oxidants. Isoprenaline is sympathomimetic drug. It acts almost exclusively on adrenergic receptors. It has a powerful stimulating action on heart, increases cardiac output, excitability and rate. It also causes peripheral vasodilatation and produces fall in diastolic blood pressure and usually maintains or slightly increases systolic blood pressure. Isoprenaline should not be used after recent episodes of myocardial infarctions because it may increases the size of myocardial infarct by increasing heart rate and contractility. In addition it may exacerbate the ventricular ectopic activity that is commonly associated in the myocardial infarction[4].

MATERIALS AND METHODS

The sample for this study includes 48 wistar strain male albino rats of weight around 150-200 gm and fulfilling all the inclusion criteria, 24 rats were randomly selected for the study and they were divided into 4 Groups G1, G2, G3 and G4 with each group consisting of 6 animals each. Group- 1 (Control group) N=6Rats received a standard diet for a period of 30 days. Group – 2 (**Glutathione** treated group) N=6Rats were orally administered with **Glutathione** 200 mg/kg body weight / day dissolved in distilled water by intragastric intubation for 30 days Group- 3 (Isoproterenol treated) N=6Rats were injected with Isoproterenol 100mg/kg body weight /day subcutaneously for 2 consecutive days at an interval of 24 hrs. For induction of Myocardial Infarction. Group 4 (Isoproterenol + **Glutathione**) N=6Rats were pre-treated with **Glutathione** 100 mg /kg body weight orally for 30 days and Myocardial Infarction was induced with Isoproterenol at a dose of 100 mg / kg body weight at an interval of 24 hrs on 31st and 32nd day. At the end of experimental period i.e.24 hrs after the last injection of Isoproterenol the experimental animal were sacrificed. The blood samples were collected and stored in EDTA tubes and divided into two parts. One part was used for total blood cell count and other part was used to obtain plasma.

Estimation of blood parameters: Haemoglobin (Hob) concentration, Red blood cell (RBC) count, White blood cell (WBC) count, Neutrophil, Lymphocyte and Eosinophil percentages were estimated using an automatic haematological analyzer (Sysmex XS-1000IXS - 800 I automated haematology analyzer - Sysmex Corporation Kobe, Japan). The cells were counted based on the principle of electronic impedance[5].

Statistical analysis: The data was expressed as mean ± SD Statistical comparisons were performed by student's t-test. The results were considered as significant if the P values were 0.05 or less.

Table: 1 COMPLETE BLOOD COUNT IN CONTROL AND EXPERIMENTAL GROUP OF RATS

Blood Parameters	Control (GI) n=6	Glutathione (GII) n=6	Isoproterenol (GIII) n=6	Glutathione+ Isoproterenol (GIV) n=6	P value
RBC count×10^6 µc-^{1}	5.7 ± 0.06	4.8 ± 0.7	8.4 ± 0.6	7.71 ± 0.68*	0.000
WBC count× 103 µc-1	5.11 ± 0.7	3.8 ±0.7	8.9 ± 0.6	6.93 ± 0.7*	0.000
Platelet count×105 µc -1	879.5 ± 7.7	397.8±21.6	780 ± 6.4	659 ± 5.8*	0.000
HB g%	13.4 ± 0.6	9.3 ± 0.5	15.6 ± 06	13.2 ± 0.6*	0.000
Lymphocyte %	74.1 ± 4.7	74.0 ±7.9	79.1 ± 6.9	65.5 ± 5.8*	0.000
Neutrophil %	29.1 ± 6.7	29.3 ± 6.2	19.3 ± 2.7	32.6 ± 6.50*	0.000
Eosinophil %	2.0 ± 0.2	0.01 ± 0.0	0.03 ± 0.03	0.01 ± 0.08	0.000

Legend: 1 Data expressed as mean ± SD. The depicts comparison of GI, GII VS GII, & GIV with P value < 0.001.The table predicts the hematological parameters in normal and experimental group of rats. There was significant increase in RBC count, WBC count; HB % and decrease in platelet count and eosinophil count in GIII rats compared to GI rats. Glutathione pretreatment preserved the levels to near normal.

DISCUSSION

Despite understanding more about the etiology and pathophysiology of cardiovascular disease the burden of cardiovascular disease is likely to worsen rather than to improve over the next 20 years. In terms of global burden of disease in 1999, the World Health Organization (WHO) myocardial infarction in the sixth place and stroke in seventh place but by 2020 they will move to first and fourth place respectively. Free radicals play an important role in the pathogenesis of tissue damage in many different clinical disorders. Normally there is a balance between tissue oxidant and antioxidant activity. The latter is achieved by the antioxidant scavenger system which includes anti-oxidant enzymes (Super oxide dismutase, Catalase, Glutathione Peroxidase) and anti-oxidant vitamins C [6]. Early reperfusion by thrombolytic drug is now accepted as an effective treatment of acute myocardial infarction (AMI) both to restore coronary patency and to limit myocardial damage .However reperfusion may result in transient or permanent myocardial injury (reperfusion injury), assumed to be oxygen free radical mediated. Oxygen free radicals produce per oxidation of the membrane lipids with structural and functional changes. These mechanisms can explain some manifestations of the reperfusion injury such as myocardial stunning and reperfusion arrhythmias Evidence of increased oxygen free radical production was demonstrated by enhanced lipid per oxidation products[7]. Pharmacological reperfusion by infusion of Streptokinase (STK) resulted in elevated lipid per oxidation in peripheral blood measured by thiobarbuteric acid reactive substances (TBARS) in patients with coronary angiographically assed arterial patency. **Glutathione** administered before or after ischemia prevents infarction being a potent free radical scavenging antioxidant; it reduced myocardial injury and provided significantly better functional recovery when given immediately after infarction. **Glutathione** at early reperfusion significantly reduces myocardial damage and preserves cardiac function in the isolated rat's heart[8]. Evidence of increased oxygen free radical production was demonstrated by enhanced lipid per oxidation products. Pharmacological reperfusion by infusion of Streptokinase (STK) resulted in elevated lipid per oxidation in peripheral blood measured by thiobarbuteric acid reactive substances (TBARS) in patients with coronary angiographically assed arterial patency[9].

CONCLUSION

The main action of glutathione is that of protecting cells from oxidative stress and damage, mainly via its antioxidant properties. The magic of glutathione also lies in its sulfur compounds. Researchers report that people who have lower levels of glutathione have an increased risk of cardiovascular disease[10].

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