

Original Research Article

Effect of taurine pretreatment on ECG changes in isoproterenol induced myocardial infarction in male albino rats

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Abstract: The incidence of myocardial infarction was found to be high among people of Indian origin who are living abroad. Disease of coronary artery is almost always due to atheroma and its complications. It is predicted that heart disease and stroke will become one of the leading causes of death and disability worldwide by the year 2020. The Materials And Methods were All Wistar strain male albino rats weighing 150 – 200g were selected for the study. Group- 1 (Control group) Rats received a standard diet for a period of 30 days. Group – 2 (taurine treated group) Rats were orally administered with taurine 100mg/kg body weight / day dissolved in distilled water by intragastric intubation for 30 days. Group- 3 (Isoproterenol treated) Rats 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 + taurine) Rats were pretreated with taurine 100mg /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. ECG was recorded before injecting Isoproterenol and 24hrs after the injection of Isoproterenol for both the groups of wistar male rats. In Results ECG shows decrease in heart rate, decrease in duration of QRS complex, decrease in duration of QT interval, increase in amplitude of R wave G4 (Isoproterenol + taurine) rats as compared to G 3(Isoproterenol treated) rats. Taurine may provide cardio protection under conditions of I-R, by virtue of its antioxidant properties, and may prevent oxidant-mediated damage of the cardio myocytes membrane and subsequent intracellular Ca²⁺ overload. In Conclusion The case-control inter heart and inter stroke studies reported that hypertension, lipid abnormalities, smoking, obesity, diabetes, sedentary lifestyle, low fruit and vegetable intake, and psychosocial stress are as important in India as in other populations of the world. Individual studies have reported that there are substantial regional variations in risk factors in India.

Keywords: Taurine, Isoproterenol, Myocardial Infarction

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. It is often assumed that myocardial infarction is a disease of affluent, industrialized countries. Taurine (2-amino ethane sulfonic acid) is a conditionally essential amino acid which is not utilized in protein synthesis. It is found free or in simple peptides. It was first discovered as a component of ox bile in 1827 [1]. The significance of taurine in human nutrition was identified, when it was discovered that formula fed, pre-term infants were not able to sustain normal plasma or urinary taurine levels. Signs of taurine deficiency have

also been detected in children on long term, total parenteral nutrition in patients with blind loop syndrome .Taurine comprises over 50 % of the total free amino acid pool of the heart [2]. It has positive inotropic action on cardiac tissue. Cardiac effects of taurine are due to its ability to protect the heart from effects of either excessive or inadequate calcium (Ca²⁺) levels. Taurine may both directly or indirectly helps to regulate intracellular Ca²⁺ level by modulating the activity of voltage dependent Ca²⁺ channels and by regulation of Na⁺ channels. Taurine also acts on many other ion channels and transporters [3]. Therefore its action can be quite nonspecific. When adequate amount of taurine is present, calcium induced myocardial damage is significantly reduced, perhaps by interaction between taurine and membrane proteins Taurine

function as a membrane stabilizer and has capacity to prevent suppression of membrane bound NaK ATPase. Taurine protects the heart from neutrophil induced reperfusion injury and oxidative stress. Because respiratory burst activity of neutrophils is also significantly reduced in presence of taurine, perhaps taurine's protective effect is mediated by its anti-oxidative properties. Taurine could reverse EKG abnormalities such as ST segment changes and T wave inversion and Extra systole in animals in the chemically induced arrhythmias [4].

MATERIALS AND METHODS:

All Wistar strain male albino rats weighing 150 – 200g were selected for the study. The animals were allowed a standard diet and water ad libitum and reared in Central Animal House, RMMC, and Annamalai University. All animal experimental procedures were approved by the Institutional Animal Ethical Committee (IAEC), vide proposal NO.457, Annamalai University, Chidambaram, Tamil Nadu, India, as well as by the committee for the purpose of Control and Supervision of Experiments on

Animals(CPCSEA).Registration NO.160/1999/CP CSEA, Government of India before starting the experiment.

Exclusion Criteria

- A) Wistar strain female albino rats.
- B) Wistar strain male albino rats weighing below 150 and above 200g.
- C) Diseased animals, Instrument CARDIART for recording ECG.

Myocardial infarction was induced in experimental animals by subcutaneous injection of Isoproterenol 100mg / kg body weight / day for 2 consecutive days. At the end of experimental period i.e. 24 hrs after the last injection of Isoproterenol the experimental animal were sacrificed. ECG was recorded before injecting Isoproterenol and 24hrs after the injection of Isoproterenol for both the groups of wistar male rats.

DATA ANALYSIS AND INTERPRETATION

Table 1: Comparison of HR in control and taurine treated group of rats expressed as beats/min

Groups	Control Group (N=6)	Experimental Group (N=6)	Student t - test	
			t-Value	P-Value
Taurine	396.17 + 25.48	389.17 + 40.42 ^a	0.434	0.68 (NS)
ISO	396.17 + 25.48	536.00+80.63 ^b	3.580	0.01 (S) **
ISO+T	396.17 + 25.48	403.00+31.08 ^c	0.399	0.70 (NS)

a- ISO, b - Taurine, c- ISO +T

** - Significant at P- value < 0.01 level, * - Significant at P- value < 0.05 level

Table 2: Comparison of PR interval in sec control and taurine treated group of rats

Groups	Control Group (N=6)	Experimental Group (N=6)	Student t – test	
			t-Value	P-Value
Taurine	0.305 + 0.017	0.321 + 0.035 ^a	1.22	0.27 (NS)
ISO	0.305 + 0.017	0.100 + 0.021 ^b	25.42	0.001 (S) ***
ISO+T	0.305 + 0.017	0.273 + 0.020 ^c	5.83	0.002 (S) ***

a- ISO, b - Taurine, - ISO +T

*** - Significant at P- value < 0.001 level

Table 3: Comparison of duration of QRS in sec in control and taurine treated group of rats

Groups	Control Group (N=6)	Experimental Group (N=6)	Student t - test	
			t-Value	P-Value
Taurine	0.060+0.021	0.046 +0.016 ^a	1.581	0.175 (NS)
ISO	0.060 + 0.021	0.130+ 0.030 ^b	3.955	0.011 (S) ***

a- ISO, b - Taurine, c- ISO +T

*** - Significant at P- value < 0.001 level

Table 4: Comparison of QT interval in sec in control and taurine treated group of rats

Groups	Control Group (N=6)	Experimental Group (N=6)	Student t - test	
			t-Value	P-Value
Taurine	0.186+0.074	0.200 +0.066 ^a	1.00	0.363 (NS)
ISO	0.186 + 0.074	0.353+ 0.030 ^b	7.67	0.001 (S) ***
ISO+T	0.186 + 0.074	0.146+ 0.032 ^c	1.46	0.203 (NS)

ECG changes in control and experimental group of rats

There was decrease in heart rate, decrease in duration of QRS complex, decrease in duration of QT interval, increase in duration of R wave G 4 rats as compared to G 3 rats. Taurine 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. It should be pointed out that during acute coronary events (unstable angina and myocardial infarction, often before the onset of ischemic damage), neutrophils are known to secrete proteolytic enzymes in latent forms, which are activated by hypochlorous acid (HOCl) generated by myeloperoxidase. Because taurine is a physiological antagonist of HOCl, supplementation with this agent protects the heart by diminishing the inflammatory response in cases of acute coronary artery disease. On the other hand, taurine interaction with HOCl produces taurine monochloramine, a less toxic and more stable oxidant that has been reported to activate a cell death pathway involving Bax protein and caspase-9 in lymphocytes. While there is no known similar effect in the cardiovascular system, such an interaction would be undesirable. The major function of taurine in leukocytes is to trap chlorinated oxidants (HOCl) and convert them into less toxic chloramines and taurine chloride production is found to result in decreased NO production thereby causing increase in Neutrophil count and decrease in Lymphocyte count [5].

DISCUSSION:

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 peroxidation 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 [6]. In addition the accumulation of polymorphonuclear cells (PMN cells), by their supplementary oxygen free radical production may initiate the reocclusion of damaged vessel, explaining why there is only a partial success of revascularization procedures. Taurine administered before or after ischaemia prevents infarction; being a potent free radical scavenging antioxidant, it reduced myocardial injury and provided significantly better functional recovery when given immediately after infarction [7]. Taurine at early reperfusion significantly reduces myocardial damage and preserves cardiac function in the isolated rat's heart. This study was conducted to show the protective effect of antioxidants taurine in myocardial infarction

in rats. Taurine may both directly or indirectly helps to regulate intracellular Ca²⁺ level by modulating the activity of voltage dependent Ca²⁺ channels and by regulation of Na⁺ channels. Taurine also acts on many other ion channels and transporters. Therefore its action can be quite nonspecific. When adequate amount of taurine is present, calcium induced myocardial damage is significantly reduced, perhaps by interaction between Taurine and membrane proteins [8]. Taurine protects the heart from neutrophil induced reperfusion injury and oxidative stress. Because respiratory burst activity of neutrophils is also significantly reduced in presence of taurine, perhaps taurine's protective effect is mediated by its anti-oxidative properties. Taurine could reverse EKG abnormalities such as ST segment changes and T wave inversion, prolonged QRS complex, QT interval and Extra systole in animals in the chemically induced arrhythmias. It has been demonstrated earlier that isoproterenol administration produces free radicals and via beta adrenoreceptor mechanism affects the cell metabolism such as that toxic free radicals formed producing myocardial cell necrosis. In accordance with these reports we have observed an increase in the levels of lipid peroxides in the heart tissue and serum during isoproterenol administration [9]. Taurine treatment significantly reduced the levels of LPO in both the heart and serum., taurine inhibited the auto-oxidation of adrenaline to adrenochrome at pH 7.8 where this auto-oxidation is O₂-independent and superoxide dismutase insensitive. We thus conclude that taurine acts as a potent, but non-specific, scavenger of free radicals that cause heart damage and protects against reperfusion-induced ventricular fibrillation [10]. Taurine protects cardiac cells from injury caused by ischemia probably by its membrane stabilizing effect as reported earlier. It has also been recently observed that taurine protects against Ca²⁺ paradox-induced cardiac injury by preventing Ca²⁺ overload in cardiomyocytes and cell death. Because the increase of intracellular Na⁺ is a critical step in cardiac damage due to Ca²⁺ paradox, taurine supplementation may reduce the intracellular Na⁺ concentration, and subsequently reduce Ca²⁺ overload by inhibition of the Na⁺-Ca²⁺ exchanger [11]. Taurine is an abundant β-amino acid that regulates several events that dramatically influence the development of ischemia-reperfusion injury. One of these events is the extrusion of taurine and Na⁺ from the cell via the taurine/Na⁺ symport. The loss of Na⁺ during the ischemia-reperfusion insult limits the amount of available Na⁺ for Na⁺/Ca²⁺ exchange, an important process in the development of Ca²⁺ overload and the activation of the mitochondrial permeability transition, a key process in ischemia-reperfusion mediated cell death [12]. Taurine also prevents excessive generation of reactive oxygen species by the respiratory chain, an event that also limits the activation of the MPT. Because taurine is an osmoregulator, changes in taurine concentration trigger "osmotic preconditioning," a

process that activates an Akt-dependent cytoprotective signaling pathway that inhibits MPT pore formation. These effects of taurine have clinical implications, as experimental evidence reveals potential promise of taurine therapy in preventing cardiac damage during bypass surgery, heart transplantation and myocardial infarction [13]. Moreover, severe loss of taurine from the heart during an ischemia-reperfusion insult may increase the risk of ventricular remodeling and development of heart failure. ECG of rats recorded reveals that Control rats showed a normal P wave and no Q waves were observed and every P wave was followed by a narrow QRS of normal contour. In isoproterenol administered rats a significant elevation in the ST segment and a higher heart rate was observed when compared to control [14]. ST segment elevation is a sign of myocardial infarction. Similar findings on isoproterenol induced myocardial infarction have been reported. Group 4 rats showed a normal ECG with P-QRS-T configuration except slight elevation in ST segment. Heart rate was maintained near normal. The maintenance of normal ECG pattern confirms the protective effect of taurine in preventing free radical mediated myocardial damage [15].

CONCLUSION:

The potential health benefits of taurine in cardiovascular disease are rapidly emerging. Although more research needs to be performed, numerous experimental and several clinical studies demonstrated that taurine helps the cardiovascular system through a variety of mechanisms including an improved lipid profile, modulation of $[Ca^{2+}]_i$, antioxidant effects and antagonism of Ang II action. Because oxidative stress is known to cause intracellular Ca^{2+} overload, it is likely that the modulation of $[Ca^{2+}]_i$ by taurine may be mediated through its antioxidant effects. Furthermore, because Ang II generates reactive oxygen species, it can be argued that the antagonism of Ang II actions by taurine may also be a consequence of its antioxidant effects. A recent report demonstrated that taurine can prevent endothelial cell dysfunction induced by high glucose and oxidized LDL. Thus, this action of taurine could be an important mechanism for providing benefits to the cardiovascular system during different pathophysiological conditions.

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