The Impact of the Drug Losartan on a Few Biochemical Indicators in Wistar Albino Male Rats with Isoproterenol-Induced Heart Infarction

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Abstract: Objective: Cardiovascular disease (CVD) remains a leading cause of death and disability worldwide. This study investigated the therapeutic and preventive effects of losartan on myocardial infarction in male albino rats.

Methods: Cardiac infarction was induced in 100 rats using subcutaneous isoproterenol (65 mg/kg/day) for five days. Rats were divided into two main groups: Group 1 received isoproterenol only, while Group 2 was subdivided into four subgroups, including a losartan-pretreated group (losartan for 55 days prior to isoproterenol). Biochemical markers, including troponin, CK-MB, angiotensin II, glutathione (GSH), and total protein, were measured.

Results: Isoproterenol significantly increased troponin, CK-MB, and angiotensin II ($p<0.001$) and decreased GSH and total protein compared to controls. Losartan treatment restored GSH and total protein levels close to normal and significantly reduced cardiac injury markers ($p<0.001$).

Conclusion: Losartan demonstrates both protective and therapeutic effects against myocardial infarction, improving biochemical markers and suggesting potential clinical relevance.

***Keywords*:** cardiovascular diseases, heart infraction, losartan, Isoproterenol

1. Introduction

The main cause of death worldwide is cardiovascular diseases (CVDs), which killed 17.9 million people in 2019, 32% of all fatalities. it is the main cause of death in industrialised and developing countries, and lifestyle changes have Over the past decades, events have increased [1]. Heart disease (CVD) is a group of cardiovascular disorders that cause acute phenomena such as heart attack and stroke by blocking the blood flow to the heart or brain. They are still the main cause of illness and mortality. Myocardial fibrosis (MF) is a common pathological result of heart damage, characterized by a gradual construction of external matrix (ECM) protein in the fibrilla collagen that contributes to CVD and heart failure. Fibrosis fibrous connective tissue, mostly collagen and fibronectin, is a pathological accumulation in the heart, a significant component of most heart disease [2]. Sudden cardiomyocyte loss adults

cause the most ventricular fibrotic rebuilding due to limited regenerative capacity in the heart. Acute heart attack causes a rapid reduction of cardiomyocytes, causing an inflammatory reaction with collagen marks [3] and replacement of death cardiovascular tissue. Biomarckers help to diagnose, analyze and provide pathological conditions to heart disease and their associated diseases, distinguish between heart disease, guide therapy and assess the risk of heart occurrence [4] Troponins, a group of regulatory proteins, are essential to the contractile machinery in in skeletal and heart muscle tissue, but not in smooth muscles. Actin and tropomyocin are essential for thin filaments in myofibrills and regulate muscle contraction through calcium-mediated mechanisms. troponin exclusively appears in serum during cardiac necrosis [5]. in individuals with acute coronary syndrome, cardiac troponins are sensitive and specific indications of minor heart muscle damage. Because of its unique, heart troponin or eye main cardiac marker [6]. After Acute heart attack, rapid reduction of cardiomyocytes causes an inflammatory reaction, replacing dead heart tissue with collagen scars. Many patopofiaological conditions can cause collagen to accumulate in the interstitial and perivascular regions without full infarction. also, creatinine kinase-muscle band (CK-MB) is only found in myocardial cells but also in skeletal muscle. increased CK-MB levels can correctly detect myocardial infarction, and a rapid drop can help detect a second heart attack. One of the cardiovascular system's most powerful endogenous antioxidants is glutathione (GSH). Disturbance of the GSH system, a potent antioxidant that prevents oxidative damage to cellular components and regulates mitochondrial metabolism, has been linked to myocardial damage in several studies [7]. Isoprenaline alters haemodynamics and biochemistry in Subdocardial Layer, epic myocardium, left ventricle, papillary muscle and interventricular septum. It is easy to inspire heart attack with isopreneelain. The distribution of drugs can occur in leather, intraparitoneal or intravenous methods [8, 9]. Losartan AT1 prevents receptors. According to research, Cardiac Ras is blocked by Essemedics. Angiotensin-converted enzyme inhibitors or blockage can improve the functional of the left ventricle, prevent changes in size and expand the life of people with high blood pressure, Heart failure, ischemic heart disease and diabetes mellitus. In lung fibrosis and other fibrotic disorders, Losron is antifibrootic [10]. On myocardial infarction in male albino rats, both therapeutically and preventatively.

2. Methods and Materials

2.1 Study samples

In this study, 100 adult male raster albino mice that weighed 200–250 grams (Ratus Norwegian) were used. He was provided by Laboratory Animal House at the Basra University College of

Veterinary Medicine. The animals were placed in plastic cages with a metal lid that included food and drinking areas. Each week the floor of Bergo was cleansed for two weeks, the animals were given free food and water to help them become used to their surroundings.

For five days, twenty male rats received a subcutaneous injection of 65 mg/kg/day isoproterenol in 1 ml of saline [11,12]. Ten days following the initial isoproterenol dose, cardiac troponin tests were conducted to look for myocardial infarction. The histology of myocardial infarction was examined using tissue sections from preserved hearts.

2.2 Study groups

In this study, animals were divided into two main groups, and each group was divided into several subgroups:

1. Group 1; Experimental induction of myocardial infarction: In this group, twenty (20) males were injected with 65 mg \ kg. B.w \ day isoproterenol for five days [11,12].

2. Group 2: This group consisted of forty -five Hannmus (48), who randomly divided into four (4) subgroups:

A. Sub Governor 1 Negative Control

The group consisted of eight male rats injected with leather with 1 ml of normal salt water.B. Subgroup 2: positive control included 24 male rats were injected 65 mg \ kg B.W \ _ with the day for five days and then held for ten days after that, subdivision randomly into three groups:

1. Group E: 8 Hannmus, all animals sacrificed, and later the blood was collected, and the hearts were formally preserved.

2. Group D30: 50 mg \ kg B.W \ Day Day Losartan was received orally for 30 days.

3. Group d60: received orally 50 mg \kg bw \day losartan for 60 days.

C. Subgroup 3: group b: 8 male rats Get 50 mg \ kg losartan oral for 55 days, then injected with 65 mg \ kg of isoproterenol for five days in fifty -five days (protective role of losartan).

D. Subgroup 4: group 8 male rats received orally 50 mg /kg b.w\day losartan for 60 days.

2.3 Blood collection

Each animal provided five (5 ml) blood samples following abdominal dissection and chloroform anesthesia. The greatest amount of blood was extracted from the heart by cardiac puncture using medical syringes. 3 ml of blood was placed in a tub of gel serum without anticoagulant to obtain enough serum. it was allowed for 10-15 minutes, then transferred to the centrifuge at 3000 rpm for 15 minutes to acquire the result. to measure biochemical characteristics, serum was frozen at -20 in clean, sterile tubes. and 2 ml of blood was

deposited in edta-containing test tubes for physiological parameter analysis.

2.4 Cardiac Troponin 1 (Rat Ct-1) Determination

Sandwich elisa (Wuhan fin biotech co., ltd -China) was used for troponin. after coating capture antibody on 96 healthy plates, biotin-conjugated detection antibodies, standards, test samples, and hrp streptavidin were added to the wells and washed with wash buffer. unbound conjugates were then washed away. tmb substrates visualised hrp enzymatic reaction. hrp catalysed tmb produced a blue product that turned yellow after adding an Acid resolution. The yellow density is proportional to the target volume of the sample trapped in the plate. read o.d absorbance at 450nm in a microplate reader to calculate target concentration.

2.5 Glutathione (GSH) determination

Competitive-elisa (Wuhan fin biotech co., ltd -China) detection was used in this kit. this kit's microtiter plate features target pre-coating, Sample or standard objectives compete with a fixed amount of the target on fasting phase soups biotinylated detection antibody sites specific to target excess conjugate during the reaction. plate is cleansed of unbound sample or standard. incubate HRP-HRP- Streptavidine (SABC) in each microplate well, then add TMB. We add substrate solution to each well. Enzyme-vegetarian reaction is stopped by adding sulfuric acid, and the color change is recorded at 450 nm.

2.6 Angiotensin 11 determination

Solid phase sandwich elisa kit (Wuhan fin biotech co., ltd -China). for the first reaction, samples and standards are put to a plate coated with a primary antibody. for the second reaction, hrp-conjugated secondary antibodies are added to the wells. after washing away the unbound secondary antibody, tmb is applied to the wells, and colour develops.

2.7 Total Protein determination

When copper salt is present in an alkaline solution, serum proteins combine to produce a violet-colored complex; the Color intensity is proportional protein content.

2.8 Serum Creatine Kinase Myocardial

Band (CK-MB) Determination CK-MB is based on an enzymatic ck determination accompanied by immunoinhibiting method [13]. Creatine kinase myocardial band concentration was carried out using ck-mb kit (Germany).

2.9 Statistical Analysis

The statistical analysis system was used to assess the effect of several elements, including hematological parameters in groups in the current study, including patients and controls. This study used T-test to compare the funds and found SD. The Piercene correlation coefficient was tested using a statistical package for social science (SPSS

v.26). In the current survey, the possibilities for P price are <0.001.

3. Results

3.1 Glutathione, Creatine Kinase

Enzyme, Troponin, Angiotensin, and Total Protein Levels in Different Experimental Groups

Serum glutathione levels were decreased ($p<0.001$) in experimental groups e (19.49 ± 2.27), d30 (29.12 ± 6.51), and d60 (33.48 ± 4.24), compared to control (34.82 ± 4.29). nonsignificant differences were found between group b (35.6 ± 4.09) and a (34.07 ± 3.48) compared to the control (Figure 1; Table 1) also serum cardiac troponin, angiotensin, and total protein levels significantly differed ($p<0.001$) in groups e (37.6 ± 6.28, 175.24 ± 9.06, and4 ± 1.04 respectively) and b (12.85 ± 4.67, 152.14 ± 9.16, and3.61 ± 1.05 respectively) compared to control, while there was no significant difference in groups d30 (3.16 ± 1.12, 137.79 ± 6.79, and 6.3) Figures 2 a, 2b and 2c) (Table 1). Serum creatine kinase enzyme levels significantly differed ($p<0.001$) in groups e (82.39 ± 4.73), d30 (27.59 ± 3.03), d60 (24.64 ± 3.31), and b (26.11 ± 3.87) compared to control, but not in group a (15.41 ± 2.6) (Figure 3) (Table 1).

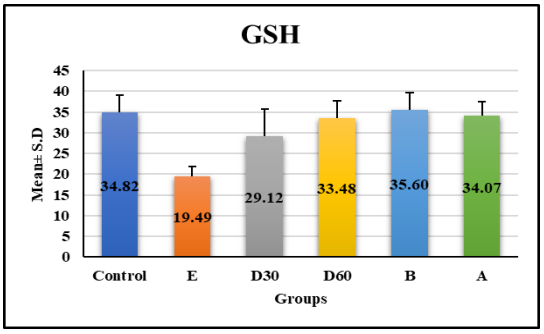

Fig. (1): Effect of isoprodanol injection and Losrton treatment at GSH levels in different experimental groups.

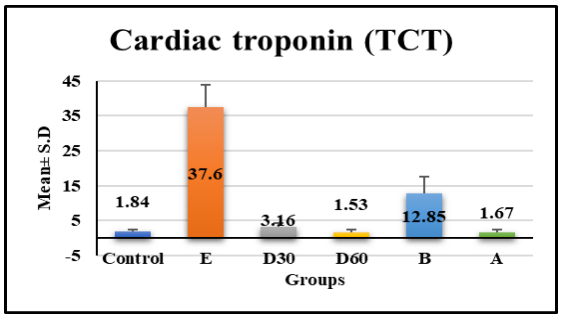

Fig. (2): Effect of Isoprosternol Injection and Losarton treatment on hearttroponin (TCT).

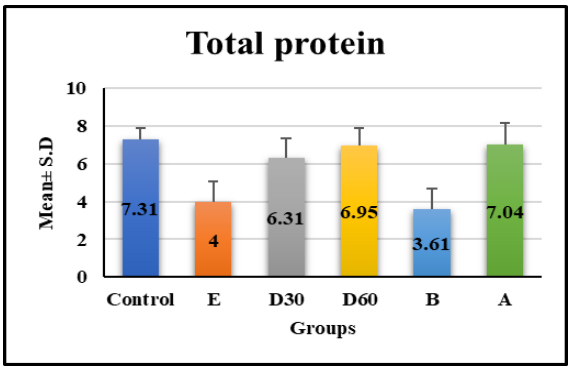

Fig. (3): Effect of Isoprosternol Injection and Losrton treatment on total proteins in different experimental groups**.**

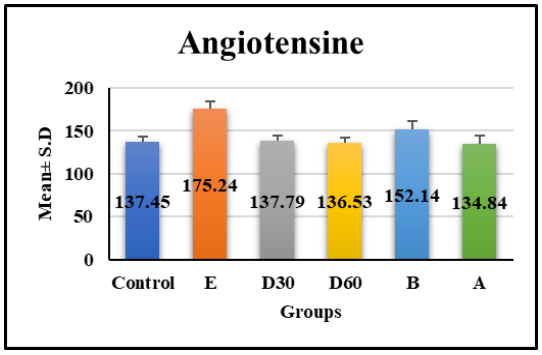

Fig. (4). Effect of Isoprosternol Injection and Losrton treatment on angiotensin 11 in different experimental groups.

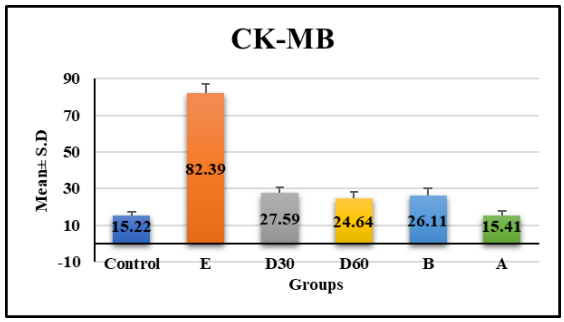

Fig. (5). Effect of Isoprosternol injection and Losrton treatment at CK-MB levels in different experimental groups.

3.2 Pearson Correlation coefficient between study parameters in different experimental groups

Table 2's correlation matrix displays substantial biomarker relationships. Compared to cardiac troponin (TCT) and Angiotensin, glutathione (GSH) correlates positively with total protein (r = 0.337*) and strongly negatively with CK-MB (r = -0.745**). TCT had positive associations with Angiotensin (r = 0.844*) and CK-MB (r = 0.941**) and negative correlations with total protein (r = -0.658**). Angiotensin and total protein are negatively correlated (r = -0.546* and -0.555*, respectively). various results reveal complex interactions between various biomarkers in the experimental context.

4. Discussion

A myocardial infarction (MI) is abrupt, toxic heart muscle injury. It may be the leading cause of death in developed and developing nations. [14], heart indicators are enzymes or chemicals released into circulation after cardiac tissue dies. Creatine kinase-MB and troponin I/T are the gold standard cardiac biomarkers, and serum or plasma testing may help during myocardial infarction. [15], worldwide, MI is causing epidemic morbidity and mortality. MI is myocardial necrosis. Due to a coronary blood supply-myocardial demand imbalance. [16]

The current study led to the second dose in the experimental induction of heart attack in a dose of isopranol (85 mg/kg). These conclusions [17-20] are struggling with people published by a heart attack, have also been seen as side effects of large doses of isoprandal, induced heart attack results. This outcome is consistent with studies [23,24] that employed a low dose of isoprenaline for an extended period of time. When there is injury to the heart muscle, troponin I and CK-MB are released into the plasma, and their levels increase. Cardiac troponin is a vital biomarker for evaluating heart issues and it is important to find out it early, risk classification, and the treatment of

heart-related conditions [25,26]. The study's results demonstrated that the level of troponin was Inspired compared to the control group is much higher in the Infarction Group (E) lower in the losartan treatment groups (D30, D60, and A) compared to the control group, while shown in Group B (isoprainalin injection + losrton treatment) a notable drop in troponin levels when compared to group E (heart infarction). This suggests that losartan treatment reduced troponin levels and brought them back to levels comparable to the control group; the longer the treatment period, the better the results. The troponin level in the 30-day losartan treatment (D30) was 3.16 ± 1.12. When compared to the induction group (E) (isoproterenol injection to induce the heart infraction: 37.6 ± 6.28), the result improved as the troponin level decreased in group B (protective role - Isoproterenol + Losartan: 12.85 ± 4.67). This was in contrast to the 60-day losartan treatment (D60): 1.53 ± 0.72. This suggests that losartan acts as a protective agent against induced myocardial infarction. This result is consistent with the findings [27-30] study demonstrated that oral administration of oleic acid improved cardiac injury such as the troponin level, suggesting its cardio-protective [31] demonstrated that injection of isoprenaline-induced heart infarction and the atorvastatin and quercetin have a protective role which decreases the troponin level in compression with heart infraction induction group. A nattokinase-containing Hard capsules have a heart-protecting effect against ISO-inspired Mi-Mus and improves the myocardial marker, [32,33], giving TQ together with losartan considerably decreased the oxidative and inflammatory alterations in heart tissue brought on by hypercholesterolaemia. In comparison to group E (isoproterenol injection to induce the injection of infraction: 82.39 ± 4.73), The current study revealed a significant reduction in CK-MB ($p<0.001$) in the Losarton treatment group (D30 Treatment for 30 days: 27.59 ± 3.03, D60 Treatment for 60 days: 24.64 ± 3.31, B (Protective role - Isoproterenol + Losartan: 26.11 ± 3.87). According to this, receiving an injection of isoproterenol raises the level of the CK-MB enzyme, which is one of the key markers Heart attacks. Losartan medication for varying lengths of time causes the level of this enzyme to drop. Enzyme Levels were higher than the level of the treatment group induction group, and the outcomes were enhanced by the extended losartan treatment duration. Losartan also protects against induced myocardial infarction, according to group B's data. This result contradicts [26,34]. However, in an experimental model of dox-inspired heart failure, the work by [35] demonstrated the cardioprotective activity of mebudipinein. BET-1 and other biochemical markers, including CK-MB, were decreased by mebudipine. Akmal and associates [36]. In a rat model of acute myocardial infarction, both are heartbeating in erythropoitin and renoprotective effects. Decreases in

erythropoietin an Isoproterenol cause a drop in biochemical measures like CK-MB. The current study showed that compared to the control group, the level of Glutation -enzyme (GSH)significantly decreased in group E (heart infarction caused by isoproterenol injection: 19.49 ± 2.27), and increased significantly in groups D30 (treatment by losartan for 30 days: 29.12 ± 6.51) and D60 (treatment by losartan for 60 days: 33.48 ± 4.24). Additionally, the rustle in group D60 was better than that of group D30. As a result, we concluded that the results improved with longer duration of Losartan medication, and group B (Protective role - Isoproterenol + Losartan: 35.6 ± 4.09) exhibited comparable results to the control group. This suggests that losartan protects against myocardial infarction that is caused; this conclusion is consistent with that of [37-39]. The pathophysiology of cardiovascular disorders heavily relies on the Renin-Angiotensin System (RAS). The kidney secretes renin, sometimes referred to as angiotensinogen, which causes angiotensin I (Ang I) peptide to be released. Ang I is changed into Ang II of angiotensin-converted enzyme (ACE), which isextensively expressed in the endothelial and epithelial cells of the heart, lungs, kidneys, and vasculature. One important vasoactive peptide that is necessary in both healthy and diseased situations is Ang II. In the cardiovascular system, Ang II and AT1R frequently combine to produce aldosterone secretion, proinflammatory and profibrotic reactions, and systemic vasoconstriction. Apooptosis, fan-induced pulmonary injury, increased pulmonary microcular permeability in air-sterilized epithelial cells, pregnancy cytocosin release and neutrophils and macrophae motacies improved in relation to pulmonary damage are all caused by activation of the ACE/Ang II/AT1R axis. In addition, the ACE/Ang II/AT1R axis triggers proinflammatory responses from both the innate and adaptive immune systems, leading to cardiovascular disease, autoimmune disorders, and inflammation. [40-42] In the current study, the angiotensin 11 enzyme level was significantly higher in group E (heart infarction caused by isoproterenol injection: 175.24 ± 9.06) than in the control group (137.45 ± 5.76), and it was significantly lower in the losartan treatment groups ($P<0.001$). D30: 30 days of treatment (137.79 ± 6.79), D60: 60 days of treatment (136.53 ± 5.76). This suggests that losartan has a significant therapeutic impact because it decreased the angiotensin enzyme levels and brought them nearly to their normal level. In addition, the study revealed that group B (Protective role - Isoproterenol + Losartan: 152.14 ± 9.16) had a lower level of angiotensin 11 than group E, which suggested that losartan might partially protect against myocardial infarction. In group A, however, angiotensin 11 levels were comparable to normal after treatment with just losartan. This result is consistent with the findings of [43,44]. An essential component of blood pressure regulation

is the renin-angiotensin system (RAS). In some cases, this steering system is impacted by a variety of harmful factors, mostly by over activating the RAS, which causes cardiovascular harm, such as coronary heart disease (CHD), which can cause persistent heart failure [45-47] clarified that losartan medication is also useful in reducing lipid profiles and oxidative stress, which helps to lessen problems related to hypertension.

According to the current study, isoproterenol significantly lowers serum total protein, and losartan treatment enhanced rustling, which is in line with [48]. Numerous factors can affect the total protein, which gives basic information about illness conditions in several organ systems [49]. According to the current study, all experimental groups' serum protein levels rose after receiving losartan. This outcome is consistent with [50] findings.

Table 1: Effect of isopranol injection and loss of treatment at some biomarcker levels in different experimental groups.

Parameters		Control	E	D30	D60	B	A	LSD0.(	p-value
GSH	Mean ± SD	34.82 ± 4.2	19.49 ± 2.27	29.12 ± 6.5	33.48 ± 4.24	35.6 ± 4.09	34.07 ± 3.48	15.97	<0.001
cardiac troponin (TCT)	Mean ± SD	1.84 ± 0.49	1.6 ± 0.28	3.16 ± 1.12	4.53 ± 0.72	2.85 ± 0.67	1.67 ± 0.78	2.17	<0.001
Angiotensin	Mean ± SD	137.45 ± 5.76	175.24 9.06	137.79 ± 6.79	136.53 ± 5.76	152.14 ± 9.16	134.84 ± 9.73	102.08	<0.001
Total protei	Mean ± SD	7.31 ± 0.58	4 ± 1.04	6.31 ± 1.01	6.95 ± 0.96	3.61 ± 1.05	7.04 ± 1.12	3.32	<0.001
CK-MB	Mean ± SD	15.22 ± 2.2	22.39 ± 4.73	27.59 ± 3.0	29.64 ± 3.31	26.11 ± 3.87	15.41 ± 2.6	17.87	<0.001

E: Heart infarction induced by isoprodanol injection, treatment for D -30: 30 days, D60: Treatment for 60 days, B: B: Protective role (Lsoprrnol+Losirton), A: Losrton.

S: Significant difference between groups (P-Meli <= 0.001)

NS: Non-realized difference between groups (P-Human> 0.001)

Table 2: Pearson correlation coefficient between parameters.

Parameters		GSH	Cardiac Troponin (TCT)	Angiotensin	Total protei	CK-MB
GSH	r	1	-.657**	-.565**	.337*	-.745**
	P		<0.001	<0.001	.019	<0.001
	r		1	.844**	-.658**	.941**

cardiac troponin (TCT)	P	<0.001	<0.001	<0.001
Angiotensin	r	1	-.546**	.816**
	P		<0.001	<0.001
Total protein	r		1	-.555**
	P			<0.001
CK-MB	r			1
	P			

* Correlation is important at 0.001 level (2-thing).

**r: Piercene Correlation coefficient, P: P-Man.

5. Conclusion

Important detection of the current study suggests that the relatively low and non-lethal dose of isoprano line may induce severe myocardial necrosis. And find that mice have the effect of losrton in the treatment of myocardial infarction inspired by isoprostranol. Also find that the administration of Losrton has significantly replaced biochemical parameters such as (GSH, total protein, angiotensin and CK-MB). Finally, the current study found that the duration of Losrton uses as a treatment for heart attack, its efficiency, where the longer the treatment is as long as the treatment, the higher the effectiveness of the drug.

Credit Author Contributions Statement:

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Ethical Approval

None.

Informed Consent

Not applicable.

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