Isoproterenol-induced cardiomyopathy and oxidative stress: a review of experimental models and insights

Mohammed Shaik Sahil[*1], Vindya N. S[2], Rupesh Kumar Mani[3]
[1]Mpharm, Department of Pharmacology, Al-Ameen College of pharmacy
[2]Assistant professor, Department of pharmacology, Al-Ameen College of pharmacy
[3]Hod, Department of Pharmacology, Al-Ameen College of pharmacy

**Corresponding Author: Mohammed Shaik Sahil*

Abstract:

Isoproterenol-induced cardiomyopathy is a valuable experimental model for studying various aspects of cardiovascular diseases. This model involves the administration of isoproterenol, a synthetic catecholamine and beta-adrenergic agonist, to induce cardiac stress and damage, thus mimicking conditions similar to human cardiomyopathy. The primary mechanism involves excessive stimulation of beta-adrenergic receptors, leading to increased heart rate, myocardial oxygen demand, and subsequent myocardial necrosis. This process is crucial for understanding pathophysiological changes observed in human heart diseases. The isoproterenol model has been extensively used to explore oxidative stress, inflammation, and apoptosis in the heart. Significant insights have been gained into molecular pathways of myocardial injury, such as the role of reactive oxygen species, inflammatory cytokines, and apoptotic signaling. These discoveries have enhanced the understanding of cardiomyopathies and other cardiovascular disorders. However, limitations exist. Isoproterenol-induced cardiomyopathy may not fully replicate all aspects of human heart diseases, and variations in dosage and administration protocols can lead to inconsistent results. The acute nature of induced damage may not accurately reflect the chronic progression of human cardiomyopathy. Future research directions include refining the model to better mimic chronic heart conditions, exploring genetic and molecular responses, and integrating this model with other experimental approaches to develop comprehensive treatment strategies. Despite its limitations, isoproterenol-induced cardiomyopathy remains a crucial tool for advancing knowledge and improving therapies for cardiovascular diseases.

Keywords:

Isoproterenol, cardiomyopathy, experimental model, cardiovascular diseases.

1. Introduction:

Amine beta-sympathomimetic the non-selective β-adrenergic agent isoproterenol, also known as isoprenaline, isopropyl analog of adrenaline, L-β-(3, 4-dihydroxyphenyl)-α-isopropylaminoethanol hydrochloride or "3,4-dihydroxy-alpha [(isopropylamino)methyl]benzyl alcohol." both Trace amine-associated receptor 1 and receptor agonist. Isoprenaline has no impact on alpha adrenoceptors but affects both beta 1 and beta 2 receptors. Isoprenaline exhibits favorable inotropic and chronotropic effects by interacting with beta one receptors on the heart. Acting on beta 2 adrenergic receptors and raising systolic blood pressure the main effect of the two is the vasodilatation of smooth muscles, which reduces mean arterial pressure. Isoprenaline causes the arteriolar smooth muscle to dilate, which lowers the lower diastolic blood pressure. Because of its simplicity and repeatability, the isoproterenol-induced model for myocardial infarction in rats is required as a widely accepted consistent screening approach to assess the efficacy of the cardioprotective medicines[1].

Globally, cardiovascular diseases (CVDs) remain the primary cause of morbidity and mortality. It is necessary to use appropriate experimental models that accurately replicate real-life illness settings in order to comprehend the biology of CVDs and create innovative treatment strategies. Because isoproterenol mimics the cardiac stress and dysfunction seen in a variety of cardiovascular illnesses, it is frequently used to induce cardiomyopathy in animal models. The etiology of MI has been linked to oxidative stress, which is defined as an imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses. The purpose of this review is to give a general overview of the mechanisms, applications, and learnings from experimental investigations related to the isoproterenol-induced cardiomyopathy model.

Oxidative stress is a crucial aspect of cardiovascular pathology during heart attacks, marked by an imbalance between reactive oxygen species (ROS) production and antioxidant defenses. When a heart attack occurs, the sudden cessation of blood flow to the heart muscle triggers a series of events, including inflammation activation and ROS generation. These reactive molecules, like superoxide radicals and hydrogen peroxide, cause damage to lipids, proteins, and DNA in cardiac cells, worsening tissue injury and advancing myocardial infarction. At the cellular level, oxidative stress impairs mitochondrial function, disrupts calcium balance, and promotes apoptosis, worsening myocardial damage. Furthermore, ROS can induce the release of pro-inflammatory cytokines and adhesion molecules, intensifying the inflammatory response and aggravating tissue damage.

Persistent oxidative stress leads to adverse cardiac remodeling, featuring fibrosis, hypertrophy, and diminished contractility, ultimately raising the risk of heart failure and other cardiovascular issues. Understanding oxidative stress's role in heart attacks has prompted research into various therapeutic approaches to mitigate its harmful effects. Antioxidants such as vitamin C, vitamin E, and coenzyme Q10 have been studied for their ability to counter ROS and reduce oxidative damage[7]. Additionally, targeting signaling pathways involved in ROS production and antioxidant defense mechanisms holds promise for novel therapeutic interventions to alleviate oxidative stress's impact on cardiac function post-heart attack[2].

Oxidative stress is a key player in heart attack pathophysiology, contributing to myocardial injury, inflammation, and adverse cardiac remodeling. Delving into the mechanisms of oxidative stress in heart attacks provides valuable insights into potential therapeutic targets for improving outcomes and lessening the burden of cardiovascular disease.

2. Mechanisms of isoproterenol-induced cardiomyopathy:

The principal mechanism by which isoproterenol works is by stimulating β-adrenergic receptors, which raises heart rate, oxygen consumption, and myocardial contractility. Prolonged beta-adrenergic stimulation, on the other hand, can cause oxidative stress by increasing the generation of reactive oxygen species (ROS) and compromising antioxidant systems, which can lead to cardiac damage. Extended high-dose isoproterenol exposure causes inflammation, oxidative stress, apoptosis, mitochondrial malfunction, and calcium excess, which all lead to cardiac damage, fibrosis, and dysfunction[3]. In experimental rats, acute administration of an elevated dose of isoproterenol results in cardiotoxicity. This may be caused by excessive beta-adrenergic receptor stimulation, which leads to catecholamine overload and cardiac malfunction. Catecholamine-induced isoproterenol Reduced oxygen consumption, functional hypoxia, and coronary insufficiency may result from mediated cell signaling, which can then induce myocardial ischemia and myocardial infarction[4].

The pathophysiological alterations seen in human cardiomyopathies are highly similar to these pathways, which makes the isoproterenol-induced model an invaluable resource for researching disease causes and assessing treatment options[11-13].

3. Applications and insights from experimental studies:

The isoproterenol-induced cardiomyopathy model has been used in experimental research to shed light on a number of cardiovascular disease-related topics, such as cardiac hypertrophy, arrhythmias, heart failure, and myocardial remodeling. The aforementioned studies have provided insight into the functions of oxidative stress, inflammation, autophagy, and neurohormonal activation in the advancement of disease. This has facilitated the creation of innovative treatment approaches that specifically target these pathways[5]. The isoproterenol model has also been useful in assessing the safety and effectiveness of gene-based therapies, stem cell therapy, and pharmaceutical medications for the treatment of cardiomyopathies[9].

4. Limitations and future directions:

Although useful, the isoproterenol-induced cardiomyopathy model has a number of drawbacks, such as species-specific variations, acute versus chronic effects, and individual animal variability in response. Upcoming studies ought to concentrate on enhancing experimental procedures, maximizing dosage schedules, and employing supplementary models to more accurately replicate human heart disease. Technological developments in genomic profiling, biomarker identification, and imaging modalities have the potential to accelerate the development of precision medicines for cardiovascular diseases and improve the translational value of preclinical research[10].

5. Discussion:

Inflammation, oxidative damage, and myocardial necrosis are the hallmarks of isoproterenol-induced MI. The administration of isoproterenol can cause myocardial injury due to many factors, such as ROS production, mitochondrial dysfunction, and activation of inflammatory pathways. One possible strategy for preventing or lessening isoproterenol-induced MI is to target oxidative stress pathways.

6. Conclusion:

To sum up, the model of isoproterenol-induced cardiomyopathy is a useful instrument for examining the etiology of cardiovascular disorders and assessing possible treatment approaches. This model has been used in experimental research to shed light on disease causes, myocardial remodeling, and potential treatment targets. To improve our knowledge and treatment of cardiovascular diseases, ongoing work is needed to improve experimental

procedures, confirm results in human cohorts, and integrate preclinical findings into clinical practice.The isoproterenol-induced cardiomyopathy model is important for cardiovascular research, and this review emphasizes how it might spur innovation and enhance patient outcomes in the cardiology sector.

7. References:

(1) Anandhi DV, Sowndarya R. Cardioprotective activity of Euphorbia hirta in isoproterenol induced myocardial infarction in rats. J Med Plants Stud. 2017; 5(3):335-7.

(2) Writing Committee Members, Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, Blankstein R, Boyd J, Bullock-Palmer RP, Conejo T. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Journal of the American College of Cardiology. 2021 Nov 30; 78(22):e187-285.

(3) Liu C, Huang Y. Chinese herbal medicine on cardiovascular diseases and the mechanisms of action. Frontiers in pharmacology. 2016 Dec 1; 7:230817.

(4) Bi FJ, Zhang H, Xu YJ, Hu J. Protective effect of catalpol on isoproterenol-induced myocardial injury in Wistar rats. African Journal of Biotechnology. 2012;11(38):9270-5

(5) Boarescu PM, Chirilă I, Bulboacă AE, Bocșan IC, Pop RM, Gheban D, Bolboacă SD. Effects of curcumin nanoparticles in isoproterenol-induced myocardial infarction. Oxidative medicine and cellular longevity. 2019 May 7; 2019.

(6) Nasa Y, Ichihara K, Yoshida R, Abiko Y. Positive inotropic and negative chronotropic effects of (-)-cis-diltiazem in rat isolated atria. British Journal of Pharmacology. 1992 Mar; 105(3):696.

(7) Meena B, Rajan LA, Anandan R. Protective effect of betaine on protein, glycoproteins and amino acids in isoprenaline-induced myocardial infarction in albino rats. Biomedicine & Preventive Nutrition. 2014 Jul 1; 4(3):403-9.

(8) Murugesan M, Manju V. Luteolin promotes mitochondrial protection during acute and chronic periods of isoproterenol induced myocardial infarction in rats. The Egyptian Heart Journal. 2013 Dec 1; 65(4):319-27.

(9) Mutneja E, Verma VK, Malik S, Narayanan SP, Sahu AK, Bhatia J, Arya DS. Cardioprotective effect of morin against oxidative stress and apoptotic damage in experimental model of isoproterenol induced myocardial necrosis in rats. Journal of

Hypertension. 2019 Jul 1; 37:e101.

(10) Nair PS, Devi CS. Efficacy of mangiferin on serum and heart tissue lipids in rats subjected to isoproterenol induced cardiotoxicity. Toxicology. 2006 Dec 7; 228(2-3):135-9.

(11) Ojha S, Goyal S, Sharma C, Arora S, Kumari S, Arya DS. Cardioprotective effect of lycopene against isoproterenol-induced myocardial infarction in rats. Human & experimental toxicology. 2013 May; 32(5):492-503.

(12) Panda S, Kar A, Biswas S. Preventive effect of Agnucastoside C against Isoproterenol-induced myocardial injury. Scientific reports. 2017 Nov 23; 7(1):16146.

(13) Pinelli A, Trivulzio S, Brenna S, Galmozzi G, Rossoni G. Pretreatment with tetrandrine has protective effects against isoproterenol-induced myocardial infarction in rabbits. In vivo. 2010 May 1; 24(3):265-70.