Original Article

Effects of Acute Potassium Chloride Administration on Ventricular Dysrhythmias after Myocardial Infarction in a Rat Model of Ischemia/Reperfusion

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Abstract

Background: *Acute myocardial infarction is an important cause of morbidity. This study aimed to investigate the effects of the administration of potassium chloride (KCl) on reperfusion-induced injuries in a rat model of myocardial ischemia/reperfusion.*

Methods: *Thirty-six male Wistar rats, weighing 200 to 250 g, were randomly assigned to 3 experimental groups: control, K1 (10 µg/kg of KCl), and K2 (20 µg/kg of KCl). Twenty minutes before ischemia, a single dose of 10 and 20 µg/kg of KCl was intraperitoneally administered in the K1 and K2 groups, respectively. The coronary artery was occluded for 30 minutes (ischemia); thereafter, it was opened for 60 minutes (reperfusion) to measure hemodynamic parameters and ventricular arrhythmias. Blood sampling was performed after the reperfusion period to determine the serum levels of lactate dehydrogenase, troponin I, creatine kinase (CK)-MB, malondialdehyde, and pro-oxidant-antioxidant balance.*

Results: *Serological parameters significantly decreased in the potassium groups compared with the control group. In particular, the decline was more pronounced for the serum levels of lactate dehydrogenase (1180.25±69.48 vs 1556.67±77.02 U/L; P=0.011), troponin I (21.98±0.61 vs 28.76±1.65 ng/mL; P=0.020), and pro-oxidant-antioxidant balance (15.51±0.72 vs 20.63±1.42 HK; P=0.041) in the K2 group compared with the K1 group. Moreover, the administration of 20 µg/kg of KCl significantly decreased the incidence of ventricular tachycardias and fibrillations compared with the control group (P=0.002). Additionally, no considerable differences were observed between the control group and the groups with 10 µg/kg and 20 µg/kg of KCl regarding the number of ventricular ectopic beats.*

Conclusion: *The administration of KCl before ischemia could reduce ventricular arrhythmias and reperfusion-induced injuries by reducing oxidative stress.*

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Keywords: *Potassium chloride; Ischemia; Reperfusion injury; Myocardial reperfusion injury; Arrhythmias, cardiac; Oxidative stress*

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Introduction

Acute myocardial infarction (MI) is one of the main causes of death and disability in the world.[1] Following MI, a large number of structural and functional changes inside the myocardium may occur due to the obstruction of the coronary blood flow, which finally may cause irreversible injuries to the heart, hence the significance of treatment protocols aimed at reducing myocardial ischemic injuries.[2] Reperfusion, defined as the rapid restoration of the coronary blood flow, is one of the standard methods for alleviating MI-induced injuries.[1, 2] Although the reperfusion of the ischemic heart is more effective in the reduction of the infarct size, the beneficial effects of this approach would be limited due to cardiomyocyte death, which happens in the first few minutes after the provision of oxygen for hypoxic tissues and potentiates excessive injuries known as "myocardial reperfusion injuries".[1, 2] Such injuries may lead to the further production of reactive oxygen species (ROS), causing oxidative stress, apoptosis, and necrosis due to, at least in part, mitochondrial dysfunction.[3] Reperfusion-induced injuries can be prevented by applying some mechanical or pharmacological interventions prior to sustained lethal myocardial ischemic events.[4] Nonetheless, the commonly used antiarrhythmic approaches such as electrical cardioversion may result in minor myocardial injuries or dysfunction, which explains why antiarrhythmic agents should be considered.[5]

Hypokalemia promotes the incidence of ventricular and atrial arrhythmias by distinct mechanisms in cardiomyocytes, especially by inducing progressive Ca^{2+} overload in ventricular cells, as well as in a subpopulation of atrial cells,[6] which finally may affect the contraction of the heart and lead to decreased blood supply through the coronary arteries and produce lethal arrhythmias.[4] Massive calcium influx into hypoxic and necrotic areas caused by reperfusion can activate phospholipase-A, which breaks down the normal phospholipids of the mitochondrial membrane and consequently results in mitochondrial dysfunction and oxidative stress.[7] Elevated serum levels of K^+ may alleviate reperfusion-associated injuries by preserving mitochondrial function and may exert an antiapoptotic effect against post-ischemic myocardial injuries.[8, 9] This point is further supported by an anecdotal case report of an inguinal hernia repair operation on a 3-year-old boy as early as 1961, which demonstrated that the direct infusion of potassium (K) into the heart chamber decreased ventricular fibrillations.[10] Furthermore, some studies have reported the clinical significance of extra KCl doses on the strength of its antiarrhythmic effects during cardiac surgery for the treatment of post-declamping ventricular arrhythmias.[11-14] Collectively, such evidence indicates that the prior stimulation of the K channels in the process of preconditioning confers cardioprotection against ischemic insults. Therefore, given the important role of K in the pathophysiology of arrhythmias, we aimed to investigate the potential effects of the administration of potassium chloride (KCl) on reperfusion-induced injuries and ventricular arrhythmias in a rat model of myocardial ischemia/reperfusion (I/R).

Methods

This experimental study was approved by the Institutional Animal Care and Use Committee (IACUC) at Shahid Beheshti University of Medical Sciences, Iran (IR.SBMU.MSP.REC.1399.722), and it complied with the Guide for the Care of Use of Laboratory Animals published by the United States National Institute of Health (NIH Publication no. 85-23, revised 2011). All the procedures were performed in sterile conditions by the same surgical team.

Thirty-six male Wistar rats, weighing 200 to 250 g, were prepared from a breeding colony and kept for 2 weeks before the experiment with free access to commercial food and tap water at 20 to 25 °C and 12:12 hour light-darkness cycle. The rats were randomly divided into 3 groups, each composed of 12 rats: control, K1 (10 µg/kg of KCl), and K2 (20 µg/kg of KCl). Twenty minutes before the induction of ischemia, a single dose of 10 and 20 µg/kg of KCl (Pasteur Institute, 1228054808, Tehran, Iran) was administered intraperitoneally in the K1 and K2 groups, respectively.

Anesthesia was induced intraperitoneally with 50 mg/kg of thiopental (Exir, Tehran, Iran); then, electrocardiography (ECG) was recorded after thoracotomy and ventilation using a rodent ventilator with a tidal volume of 2 to 3 mL and a respiratory rate of 60 breaths per minute (Harvard Rodent Ventilator [model 683], Holliston, MA, USA). Afterward, hemodynamic parameters were monitored by cannulating the right carotid artery. The pulse wave of the artery was recorded before and during I/R periods and then 1 minute after the reperfusion period. MI was induced in all the experimental subjects by the ligation of the left anterior descending artery using a 6-0 silk suture for 30 minutes. Reperfusion was then performed for 60 minutes by loosening the suture. Successful ligation was confirmed by ECG changes consisting of ST-elevation. Post-reperfusion blood samples were collected for serological studies. Finally, the animals were submitted to euthanasia after the reperfusion period. An investigator, who was blinded to the groups' identity, performed all the measurements in this study.

In our previous study (no data published as yet), we subjected a group of animals to sham surgery in the same way as described for MI induction except for the ligation of the coronary artery, and our results concerning serological parameters such as lactate dehydrogenase (LDH), troponin I, and CK (creatine kinase)-MB in this group showed no increase compared with these parameters in the I/R group. Moreover, we observed no incidence of arrhythmias in these

animals after the sham surgery. Thus, we did not consider another sham group for the purposes of the present study.

Isolated sera were analyzed for the measurement of LDH (Pars Azmoon, Iran), high-sensitive cardiac troponin I (Siemens, Belgium), and CK-MB (Siemens, Belgium) levels via the colorimetric method in accordance with the manufacturer's instructions.

For the evaluation of oxidative stress, malondialdehyde (MDA) levels in the sera were assessed by thiobarbituric acid reactive substances (TBARS) assay using an ELISA kit (ZellBio, Germany) based on the manufacturer's instructions.

For the measurement of the levels of oxidants and antioxidants simultaneously in a single test, a pro-oxidant-antioxidant balance (PAB) assay was employed. PAB values were expressed in arbitrary HK units. While a low PAB value indicates an increased antioxidant level, a high PAB value represents a decreased antioxidant level.[2]

As was previously described, ventricular arrhythmias induced by ischemia were determined according to the Lambeth Conventions.[3]

The results are expressed as the mean±the standard deviation (SD). The statistical comparison between all the groups for parametric variables, including ventricular arrhythmias and serological parameters, was performed by 1-way ANOVA and a subsequent Tukey test as needed. Comparison of hemodynamic parameters during the baseline, ischemia, and reperfusion periods between the groups was done by 2-way ANOVA, followed by the Tukey test. The arrhythmia scores were analyzed using the Kruskal–Wallis test (nonparametric test), and the incidence of ventricular tachycardias (VTs) and ventricular fibrillations (VFs) was analyzed using the Fisher exact test. The analyses were performed with the SPSS software (version 20; SPSS Inc, Chicago, IL, USA), and a P value less than 0.05 was statistically considered a significant difference.

Results

The hemodynamic data of the studied groups are shown in Table 1. Our statistical analyses revealed no significant differences between the experimental groups with respect to all hemodynamic parameters. Moreover, no differences were observed between the baseline, ischemia, and reperfusion periods within each group regarding heart rate, systolic blood pressure, and diastolic blood pressure.

As is shown in Table 2, CK-MB levels in the 10 µg/kg KCl group (437.84±19.58 U/L; P=0.043) and the 20 µg/kg KCl group (368.84±19.92 U/L; P<0.001) significantly decreased compared with the control group (530.84±35.59 U/L). There was also no significant difference between the K1 and K2 groups concerning the serum levels of CK-MB.

The serum level of LDH significantly decreased in the 10 µg/kg KCl group (1556.67±77.02 U/L; P<0.001) and the 20

Table 1. Hemodynamic parameters in the studied groups*

Variable/Group	Control	K1: 10 µg/kg of potassium chloride	K2: 20 µg/kg of potassium chloride
HRB (beats/min)	303.08±12.95	310.00±10.67	310.25±6.78
HRI (beats/min)	306.10±3.26	301.00±5.91	303.44±5.89
HRR (beats/min)	310.25±8.01	302.75±14.93	308.33±5.24
SBPB (mmHg)	129.91±5.29	129.58±5.29	130.75±4.90
SBPI (mmHg)	124.16±7.48	127.58±3.65	125.83±6.71
SBPR (mmHg)	93.41±6.17	92.08±7.86	87.58±6.43
DBPB (mmHg)	82.58±3.05	78.58±5.05	79.25±6.42
DBPI (mmHg)	77.08±6.18	79.16±2.16	74.41±7.36
DBPR (mmHg)	58.83±3.40	58.83±3.95	59.75±2.30

*Data are presented as mean±SD.
HRB, Heart rate basic; HRI, Heart rate of ischemia time; HRR, Heart rate of reperfusion period; SBPB, Systolic blood pressure basic; SBPI, Systolic blood pressure of ischemia time; SBPR, Systolic blood pressure of reperfusion period; DBPB, Diastolic blood pressure basic; DBPI, Diastolic blood pressure of ischemia time; DBPR, Diastolic blood pressure of reperfusion period

Table 2. Serological parameters in the studied groups*

Variable/Group	Control	K1: 10 µg/kg of potassium chloride	K2: 20 µg/kg of potassium chloride
CK-MB Concentration (U/L)	530.84±35.59	437.84±19.58	368.84±19.92
LDH Concentration (U/L)	2229.14±104.21	1556.67±77.02	1180.26±69.48
Troponin I Concentration (ng/mL)	34.37±1.42	28.76±1.65	21.98±0.61
MDA Concentration (nmol/mL)	4.75±1.05	4.04±0.12	3.65±0.11
PAB Concentration (arbitrary HK units)	26.20±1.88	20.63±1.42	15.51±0.72

*Data are presented as mean±SD.
CK-MB, Creatine kinase-MB; LDH, Lactate dehydrogenase; MDA, Malondialdehyde; PAB, Pro-oxidant-antioxidant balance

μg/kg KCl group (1180.26±69.48 U/L; P<0.001) compared with the control group (2229.14±104.21 U/L) (Table 2). In addition, a significant decrease in the serum level of LDH was seen in the 20 μg/kg KCl group in comparison with the 10 μg/kg KCl group (P=0.011).

The obtained data pertaining to the serum level of troponin I revealed that it significantly fell in the 10 μg/kg KCl group (28.76±1.65 ng/mL) and the 20 μg/kg KCl group (28.76±1.65 ng/mL) compared with the control group (34.37±1.42 ng/mL; P=0.013 and P<0.001, respectively) (Table 2). Additionally, this decrease was more pronounced in the K2 group compared with the K1 group (P=0.020).

The obtained data apropos of MDA activity showed that MDA levels significantly decreased in the 10 μg/kg KCl group (4.04±0.12 nmol/mL; P=0.047) and the 20 μg/kg KCl group (3.65±0.11 nmol/mL; P=0.001) by comparison with the control group (4.75±1.05 nmol/mL) (Table 2). There was also no statistical difference between the K1 and K2 groups concerning the serum levels of MDA.

The results of the PAB assay on the serum concentrations of PAB are presented in Table 2, which shows that they significantly declined in the 10 μg/kg KCl group (20.63±1.42 HK; P=0.025) and the 20 μg/kg KCl group (15.51±0.72 HK; P<0.001) compared with the control group (26.2±1.88 HK). In addition, a significant decrease was observed in the serum levels of PAB in the K2 group compared with the K1 group (P=0.041).

All arrhythmic events occurred during the reperfusion period and terminated spontaneously with no requirement for cardioversion. Our analysis of the ischemia-induced ventricular arrhythmias yielded no statistical differences between all the experimental groups in terms of the number of ventricular ectopic beats (Figure 1). Moreover, our results showed that the administration of 20 μg/kg of KCl significantly decreased the incidence of VTs compared with the control group (P=0.002) (Figure 2). Still, there was no significant difference in the occurrence of VTs between the K1 and K2 groups. Finally, VFs occurred in 4 rats: 1 animal in the low-dose (10 μg/kg) KCl group (1/12) and 3 animals in the control group (3/12) following the induction of MI, and none of them was sustained.

Our nonparametric analysis showed that the score of arrhythmias in the 20 μg/kg KCl group was considerably lower than that of the control group (P=0.016), and the 10 μg/kg KCl group was not statistically different from the control and K2 groups in terms of the arrhythmia score (Figure 3).

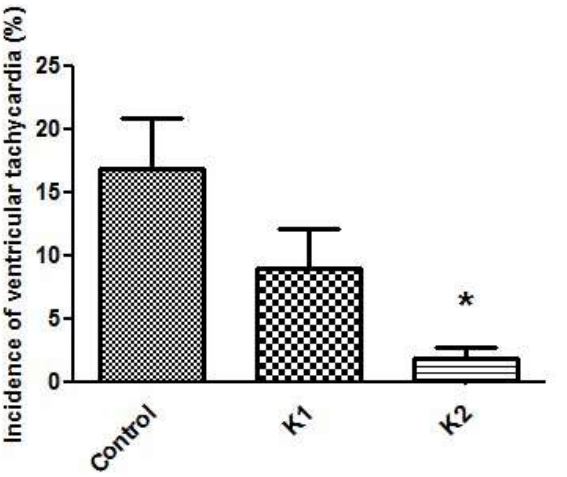

Figure 2. The figure presents the incidence of ventricular tachycardia (%) during ischemia/reperfusion using the Fisher exact test (n=12/group).
K1, 10 μg/kg potassium chloride group; K2, 20 μg/kg potassium chloride group
*P<0.05 compared with the control group

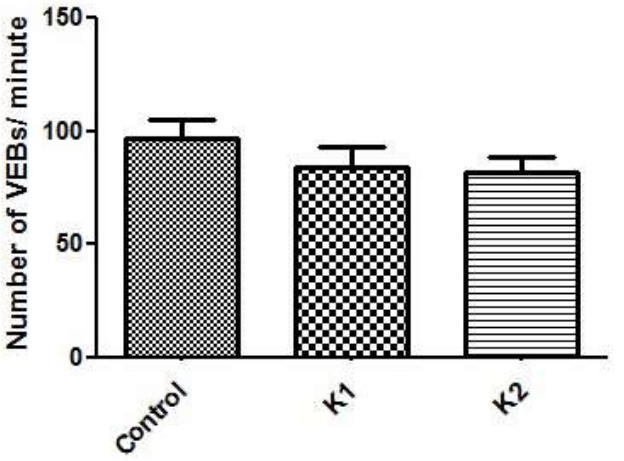

Figure 1. The figure presents the number of ventricular ectopic beat episodes (VEBs/min) during ischemia/reperfusion using 1-way ANOVA (n=12/group).
K1, 10 μg/kg potassium chloride group; K2, 20 μg/kg potassium chloride group
VEBs, Ventricular ectopic beats

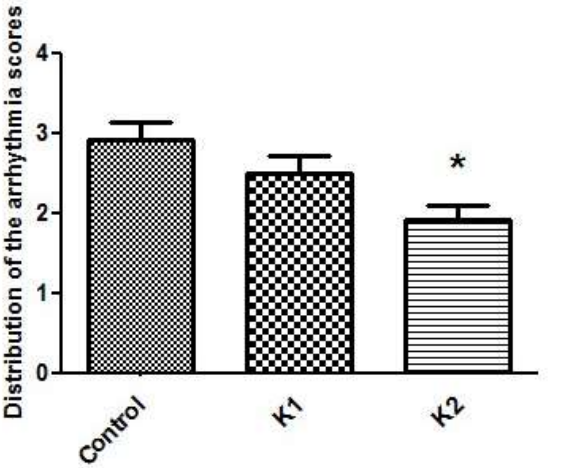

Figure 3. The figure illustrates the distribution of arrhythmia scores during ischemia/reperfusion using the Kruskal–Wallis test (n=12/group).
K1, 10 μg/kg potassium chloride group; K2, 20 μg/kg potassium chloride group
*P<0.05 compared with the control group

Discussion

Ischemic preconditioning through repeated short episodes of ischemia is a phenomenon that renders the myocardium more resistant to the loss of blood supply and protects it against subsequent and more severe insults. However, I/R injuries sometimes occur following the reestablishment of blood flow to previously ischemic tissues, and they are accompanied by further damage to cardiomyocytes, contractile dysfunction of the heart, and ventricular arrhythmias.[4] It is of great importance to prevent these phenomena by interventions applied before and/or at the time of I/R. During the reperfusion phase, the augmented activity of the NA^+/K^+ pump creates a sympathomimetic stimulation, leading to the acute and rapid exchange of the K ion.[15] The decrease in the extracellular K level at this stage results in VFs and triggers arrhythmias,[16] which are created by a reduction in cardiac repolarization reserve and an increase in Ca^{2+} accumulation within cardiomyocytes, manifested by premature depolarizations (ie, early or delayed afterdepolarizations).[17] ROS accumulates in response to K deprivation, and pre-treatment of tissues with K channel openers can promote the recovery of mitochondrial function through increased ATP-sensitive mitochondrial K^+ transport and consequently modulate the mitochondrial production of ROS.[18] With this in mind, in the present study, we evaluated the effects of acute KCl administration on ventricular dysrhythmias after MI in a rat model of I/R and the potential effects of the intraperitoneal administration of KCl (10 and 20 µg/kg) to control reperfusion-induced injuries in a rat model of I/R.

Given that ECG has a lower sensitivity to detect ST-segment elevation and new Q-waves after cardiac ischemia, the diagnosis of acute MI by evaluating cardiac enzymes is superior to ECG.[19] Following myocardial injuries, the disruption of the integrity of normal cardiac myocyte membranes may result in the release of a wide variety of biologically active intracellular proteins such as troponin, CK-MB, and LDH, which could be considered cardiac markers (diagnostic markers) of myocardial tissue damage and augment the accuracy of MI diagnosis.[20] Thus, in the current study, with the hypothesis that KCl may decrease the serum levels of enzyme markers, including CK-MB and LDH, we showed that the intraperitoneal administration of 10 and 20 µg/kg of KCl could considerably alleviate the serum concentrations of these two markers. However, due to the lack of the tissue specificity of LDH and CK-MB, it is now generally accepted that the diagnosis of myocardial injuries by evaluating these two enzyme markers is not of great value unless we additionally evaluate more sensitive and specific markers of cardiac injuries such as cardiac troponins. Troponins, which are associated with tropomyosins, regulate the interaction between myosins and actin filaments for muscle contraction and are regarded as indicators of primary arrhythmias after MI.[21] Persistent and mild elevations of troponin levels constitute a common finding in cardiac fibrillations.[22] Accordingly, we assessed the serum concentrations of troponins in all the experimental groups and showed that the intraperitoneal injection of 10 µg/kg and 20 µg/kg of KCl significantly decreased the serum levels of troponin I in the K1 and K2 groups compared with the control group. Hypokalemia is reported to cause myocyte destruction and the leakage of troponin, CK-MB, and LDH from the damaged membranes into the circulation.[23] Hypokalemia-induced myopathy and massive CK elevation as the first presentation of Conn's syndrome may occur due to hypertension.[24] Zhang et al[9] in 2004 reported that the administration of glucose-insulin-K combination attenuated the accumulation of LDH and CK in rabbits subjected to myocardial injuries. Another study revealed that the activation of ATP-sensitive K channels protected cardiac myocytes against apoptosis.[25] Based on these findings, we can deduce that the pre-MI injection of KCl could prevent further damage to cardiomyocytes and enhance the activity of troponin I, CK-MB, and LDH after I/R.

Although there was no statistical difference in the serum concentrations of CK-MB between the K1 and K2 groups in the present study, our results established a significant reduction in LDH and troponin I serum levels in animals that received a higher dosage of KCl (20 µg/kg) than the K1 (10 µg/kg) group. Since concurrent skeletal muscle injuries may occur at the time of MI induction and greater amounts of CK-MB could be released from skeletal muscles than cardiac muscles, it is believed that the analysis of the serum CK-MB as a sole biomarker for the detection of cardiac injuries is inappropriate, and it is essential that other biomarkers of MI such as troponin and LDH be evaluated to assess the extent or severity of myocardial injuries in animal models.[26] In further support of this notion, our results revealed that higher amounts of troponin and LDH could be released from cardiomyocytes after the ligation of the left anterior descending coronary artery, which may be affected by KCl dose-dependently. In other words, a higher dosage of KCl is associated with a greater decrease in troponin and the possible leakage of LDH.

Oxidative stress, which is caused by an imbalance between ROS production and impaired antioxidant defense, has a pivotal role in the initiation and expansion of I/R-induced myocardial injuries.[2, 19] After prolonged ischemia, due to oxygen and nutrient deprivation, the permeability of the inner mitochondrial membrane is increased, leading to the dysfunction of the electron transport chain, intracellular Ca^{2+} overload, and mitochondrial swelling. The damage to mitochondria is accompanied by a massive burst of ROS production during reperfusion, which exceeds the antioxidative capacity of the cells and exerts detrimental effects on cardiomyocytes.[27] In this regard, a reduced antioxidant response associated with the increased level of

pro-oxidants has been observed in patients with acute MI.[28] Although it has not been indicated which compartment of cardiomyocytes is the ultimate end-effector of ischemic preconditioning, some studies have suggested that mitochondria can be considered the main signaling pathway in this process. Mitochondrial KATP channel (Adenosine triphosphate-sensitive K^+ channels) opening using ischemic preconditioning may not only inhibit mitochondrial Ca^{2+} overload, followed by the excessive generation of ROS, but also attenuate myocardial reperfusion-induced injuries.[27] We have previously shown that the blockage of mitochondrial KATP channels might abolish the protective effects of cardiac preconditioning.[29] In this context, the present study demonstrated that pre-ischemic treatment with KCl significantly attenuated the increased levels of PAB and MDA induced by I/R, suggesting that K might exert cardioprotective effects through the reduced activity of ROS. In further support of these results, Li et al[8] in 2018 indicated that higher serum levels of K caused by KCl administration were coupled with an increase in ATP production, as well as alleviated oxidative stress. These findings indicate, to some extent, that elevated K^+ outside mitochondria can increase the recovery of the mitochondrial proton gradient and attenuate pro-oxidant markers. The current study also revealed that the level of PAB in the high-dose KCl (20 µg/kg) group was markedly decreased compared with the low-dose KCl (10 µg/kg) group. In patients with acute coronary syndromes, antioxidant activity for scavenging myocardial-free radicals can be increased by the administration of a solution of glucose-insulin-K,[30] indicating that the restoration of intracellular K (ie, K^+ outside mitochondria) by elevated serum levels of K after the injection of KCl could promote the activity of antioxidant enzymes, especially with the administration of high-dose KCl.

Increased heart rate and ventricular ectopic beats are known to be involved in the initiation of a variety of cardiac arrhythmias.[29, 31] Nevertheless, in the present study, we found no significant differences in hemodynamic parameters and the number of ventricular ectopic beats between the control, K1, and K2 groups, and it appears that susceptibility to the occurrence of VTs and VFs in our study was not associated with heart rate and ventricular ectopic beats. Although some studies have shown that heart rate and blood pressure changes may not influence the incidence of arrhythmias, further investigation is needed to explain why hemodynamic parameters did not change significantly while troponin and VTs showed considerable differences. Ventricular tachyarrhythmias, which commonly occur early during ischemia, can lead to VFs and may significantly increase the mortality rate after MI.[32] Myocardial ischemia causes dysfunction in KATP channels, followed by prolonged effective refractory periods, in the ischemic zone, which may sensitize the myocardium for the initiation of ventricular arrhythmias. Of note, reperfusion can amplify the heterogeneity of membrane potentials caused by ischemia without restoring the refractory period after MI and lead to lethal ventricular arrhythmias.[33] Therefore, it would be desirable to attenuate these arrhythmias by ischemic preconditioning-induced antiarrhythmic strategies. Herein, we found that the administration of 20 µg/kg of KCl significantly decreased the incidence of VTs and VFs compared with the control group, suggesting that K might restore enzymatic activity in the electron transport chain and provide protection against ventricular arrhythmias.

Finally, in our preliminary experiment, different doses of KCl (ie, 10, 20, 30, 40, and 50 µg/kg) were injected intraperitoneally into male Wistar rats, and the serum concentration of K was evaluated 10 minutes after the KCl administration. Our results revealed that all the animals at the beginning of the study were normokalemic and serum K^+ had significantly increased in the rats that received the KCl solution compared with the normal saline group. Additionally, no statistically significant differences were observed between the KCl groups concerning these increased serum levels of K. Moreover, hemodynamic stability was not affected by the administration of the KCl solution at 10 and 20 µg/kg doses; nonetheless, a further increase in the dose of the KCl solution (ie, 30, 40, and 50 µg/kg) led to cardiac arrhythmias and hemodynamic instability. Therefore, in the current study, we used KCl solutions at concentrations of 10 and 20 µg/kg based on the notion that KCl might confer better protection against reperfusion-induced ventricular arrhythmias.

Despite its strengths, the present study suffers from the following limitations. Firstly, our findings would have been augmented had we assessed baseline serological parameters and the serum levels of inflammatory mediators such as C-reactive protein. Secondly, in the initial steps of our experiment, we believed that an evaluation of serological parameters would be sufficient; however, another evaluation, for instance, a histological assessment of the infarct size was needed to determine whether KCl would prevent I/R injuries by limiting the infarct size. Consequently, we will consider it in our future studies.

Conclusion

Our findings suggested that the pre-ischemia administration of KCl at 10 and 20 µg/kg doses could attenuate increased levels of troponin, LDH, and CK-MB, as well as oxidative stress markers, after ischemia/reperfusion, which would finally alleviate reperfusion-induced injuries. In particular, our results showed that high-dose KCl (20 µg/kg), compared with low-dose KCl (10 µg/kg), might considerably minimize the incidence of VTs and VFs through a further reduction of LDH, troponin I, and pro-oxidant-antioxidant balance.

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