Noninvasive assessment of the effects of nicorandil on left ventricular volumes and function in reperfused myocardial infarction

Norbert Watzinger\textsuperscript{a,1}, Gunnar K. Lund\textsuperscript{a}, Charles B. Higgins\textsuperscript{a}, Mitsuaki Chujo\textsuperscript{b}, Maythem Saeed\textsuperscript{a,*}

\textsuperscript{a}Department of Radiology, University of California, San Francisco, 505 Parnassus Avenue, Room L-308, San Francisco, CA 94143-0628, USA
\textsuperscript{b}Chugai Pharmaceutical Co. Ltd., Tokyo, Japan

Received 2 April 2001; accepted 26 November 2001

Abstract

Objective: Nicorandil, a K-ATP channel opener with a nitrate-like effect, is a potent vasodilator and has favorable hemodynamic effects in heart failure patients. While its cardio-protective properties in the setting of acute ischemia are well known, the long-term effects of oral nicorandil therapy on post-infarction left ventricular (LV) dilatation have not been investigated. Methods: Myocardial infarction (MI) was induced in 30 Sprague–Dawley rats by 1 h of coronary artery occlusion followed by reperfusion. After matching for infarction size, animals were randomly assigned to nicorandil treatment (3 mg/kg/day) given in tap water or no treatment (control group). Treatment was started 2 days after MI and continued for 8 weeks. Contrast-enhanced and functional magnetic resonance imaging (MRI) were used to determine infarction size, LV volumes, mass, ejection fraction, and regional wall thickness. Results: Nicorandil significantly decreased end-systolic volumes (0.33±0.02 ml; \( P < 0.05 \)) and improved LV ejection fraction (37±2%; \( P < 0.01 \)) compared to control rats (0.43±0.04 ml and 28±2%, respectively) 8 weeks after MI. During the study period, the increase in LV mass (DLVM) was significantly greater in control (0.09±0.03 g) than in treated animals (0.02±0.02 g, \( P < 0.05 \)). Moreover, nicorandil improved systolic wall thickening of the rim of infarction (\( P < 0.001 \)) and remote non-infarcted regions (\( P < 0.01 \)). Conclusion: These results demonstrate that the long-term oral treatment with nicorandil started 2 days after MI attenuates left ventricular dilatation and improves cardiac function in rats with reperfused MI. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: K-ATP channel; Infarction; Heart failure; NMR

1. Introduction

The underlying mechanism leading to heart failure after myocardial infarction (MI) is represented by left ventricular (LV) remodeling, a process that is characterized by progressive LV dilatation and impairment of function. Remodeling is a time-dependent process involving both infarcted and non-infarcted myocardium [1,2]. It is mainly determined by the size [3], transmurality and location of MI as well as the patency of the infarct-related artery [4]. Slowing or reversing the remodeling process is the ultimate goal for medical therapy. A powerful therapeutic approach in attenuating LV remodeling is inhibition of the renin-angiotensin system. Angiotensin-converting enzyme (ACE) inhibitors have been shown to favorably influence parameters of LV remodeling and thereby improve symptoms and survival in patients with post-infarction heart failure [5,6]. Their efficacy has been at least partly attributed to their effects on cardiovascular hemodynamics resulting in a reduction of pre- and afterload.

Nicorandil, an adenosine triphosphate (ATP) sensitive potassium (K\(^+\)) channel opener with a nitrate-like effect, is clinically approved as an anti-anginal drug in Japan and Europe [7]. Nicorandil is a potent vasodilator that acts on both the coronary and the peripheral vascular bed. Hemodynamic studies in animals [8] and humans [9,10] have
demonstrated that nicorandil has similar hemodynamic properties as ACE-inhibitors, such as decreasing LV end-diastolic pressure and peripheral vascular resistance. Thus, this pharmacologic profile would predictably be of benefit in post-infarction LV dilatation.

While the beneficial effects of nicorandil in the setting of acute ischemia, such as reduction of infarction size [11,12] and preservation of microvascular integrity [13,14], are well documented, the effects of nicorandil on post-infarction LV dilatation have not been tested. Therefore, the purpose of this study was: (1) to investigate the long-term effects of oral nicorandil therapy on LV volumes and function in rats with 2-day-old infarction; and (2) to show the potential of MRI to noninvasively monitor the changes in LV volumes, mass, and wall thickness in rats subjected to reperfused MI. The effects of therapy were determined in animals with identical infarction sizes using a new necrosis-specific MR contrast medium.

2. Methods

2.1. Animal preparation

All experimental procedures received previous approval from the Committee on Animal Research at our institution and were performed in accordance with the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health [15]. Sprague–Dawley rats (Simonsen Labs, Gilroy, CA) were housed in an air-conditioned room with a 12-h light/dark cycle; they received a standard laboratory rat chow and tap water (with or without nicorandil). Prior to surgery and MRI sessions, rats were anesthetized with a mixture of ketamine (90 mg/kg) and xylazine (4.0 mg/kg) administered intraperitoneally. They were intubated and mechanically ventilated with room air using a small animal ventilator (Harvard rodent respirator, Harvard Apparatus, South Natick, MA).

In the current study, an established rat model of coronary occlusion/reperfusion was used to produce LV dilatation [16,17]. Experimental MI was induced by temporary ligation of the left anterior descending (LAD) artery. The LAD was occluded for 1 h by placing a snare loop around the vessel. Coronary ligation was considered successful when the anterior LV wall turned pale. After 1 h the snare loop was released but kept in place for later postmortem measurement of the area at risk. Reperfusion was confirmed by a myocardial blush over the ischemic pale zone after the release of the snare. Thereafter, the chest was closed in layers and the air was evacuated from the thoracic cavity.

2.2. MR imaging

Twelve hours prior to the first MRI session (2 days after MI) all animals received 0.05 mmol/kg Gd-mesoporphyrin intravenously via the tail vein. Gd-mesoporphyrin (Scher- ing AG, Berlin, Germany) is a gadolinium-porphyrin chelate that has high affinity for necrotic myocardium [18]. Gd-mesoporphyrin produces persistent enhancement in necrotic tissue up to 24 h after injection that matches precisely true infarction size on autopsy. The detailed physiochemical properties of Gd-mesoporphyrin have been previously described [19]. Gd-mesoporphyrin contrast-enhanced MRI was used to determine infarction size in the acute phase. For the assessment of LV volumes and function 8 weeks after MI, unenhanced MRI images were acquired.

Both MRI sessions (2 days and 8 weeks after MI) were conducted with a 2.0 T magnet (Omega CSI, Bruker Instruments, Fremont, CA). Each animal was placed in a supine position in a home-built birdcage resonator and was connected to an ECG monitor (AccuSync 6L, AMR Corporation, Milford, CT) that provided a trigger signal at the origin of R wave for ECG gating and heart rate monitoring. Multi-slice short-axis images were acquired encompassing the entire heart at end-diastole and end-systole using T1-weighted spin-echo imaging. Acquisition parameters were TR=450–600 ms; TE=12 ms; slice thickness=2 mm; number of acquisitions per step=4; field of view=50×50 mm; raw data matrix=256×128 zero-filled to 256×256; and voxel dimensions=0.04×0.04×2 mm. End-diastolic images were acquired at the origin of R wave and end-systolic images at 45% of the RR-interval [12,18].

2.3. Experimental protocol

Rats with identical infarction size were used in the current study to eliminate the effect of infarction size on the magnitude of LV dilatation at 8 weeks. After the completion of the first MRI, infarction size (% of total LV) was determined on contrast-enhanced images and rats were divided into two groups; namely control (n=15) and nicorandil-treated group (n=15). Treated animals received 3 mg/kg/day nicorandil (Chugai Pharmaceutical Co. Ltd., Tokyo, Japan) dissolved in tap water, while control animals received tap water solely. A fresh solution was prepared every 2 days. The average volume of solution ingested was 10 ml/100 g body weight/day (=3 mg/kg/day), which was in agreement with our prior experiments in rats [20].

2.4. Postmortem evaluation

After completion of the second MRI (8 weeks after MI) the LAD was re-occluded using the snare loop left in place at the initial operation and 0.2 ml phthalocyanine blue dye (Engelhard Corp., Louisville, KY) was injected into the tail vein. The dye imparts a blue color to normally perfused myocardium, but the territory supplied by the occluded artery remains unstained representing the area at risk. Animals were sacrificed thereafter by intravenous
injection of saturated KCl solution. The heart was excised and the LV was weighed after removal of the atria and the right ventricle. The LV was transversely sliced into 2-mm-thick slices corresponding to the MR images. Both upper and lower surfaces of the stained slices were scanned with a flatbed scanner (Silverscan IV, LaCie Limited, Hillsboro, OR). Each slice was then incubated in 2% of triphenyltetrazolium chloride (TTC) solution (Sigma Chemical Co., St. Louis, MO) to define infarcted myocardium. Subsequently, wet tissue samples were weighed, dried in a vacuum oven for 7 days, and re-weighed to calculate wet weight/dry weight ratio.

2.5. Data analysis

All images were transferred via Ethernet to a computer (Macintosh G3, Apple Computers, Cupertino, CA) and analyzed using the NIH Image software tool (NIH Image version 1.59, Bethesda, MD). By delineating endo- and epicardial contours on end-diastolic and end-systolic images and adding them together, LV volumes and mass were determined as previously described [21]. The LV mass was calculated as the sum of myocardial volume multiplied by the density of myocardial tissue (1.05 mg/ml).

The Gd-mesoporphyrin enhanced zone was delineated on end-diastolic images to determine the size of MI in the acute phase. The extent of the infarcted region defined by MRI as a percentage of the total LV was calculated as the sum of Gd-mesoporphyrin enhanced regions for all slices divided by the sum of LV cross-sectional areas from all slices.

On day 2 after infarction, absolute wall thickness and systolic wall thickening were measured on three contiguous mid-ventricular slices in the mesoporphyrin enhanced zone, the rim of the infarcted zone and in remote non-infarcted myocardium. Eight weeks after infarction, wall thickness was used to define infarction, rim of infarction and remote non-infarcted myocardium. Furthermore, unenhanced MR images were visually aligned with stained postmortem LV sections according to anatomical landmarks (i.e. papillary muscles, insertion of the right ventricle).

2.6. Statistical analysis

Data are expressed as mean±S.E.M. The unpaired t-test was used to compare between the two groups for normally distributed variables, while the Mann–Whitney rank-sum test was used for nonparametric data. Measurements within the groups were compared by applying the paired t-test for normally distributed variables and the Wilcoxon signed-rank test for nonparametric data. Differences in absolute wall thickness and wall thickening between three different myocardial regions were assessed with analysis of variance followed by the Student–Newman–Keuls post-hoc method. Linear regression was used to determine the correlation between LV mass measured at autopsy and with MRI. Differences were considered significant at P<0.05.

3. Results

All infarcted regions were located in the antero-lateral wall of the LV. The reperfused MI was visualized as a bright region on T1-weighted spin-echo images 12 h after the administration of Gd-mesoporphyrin (Fig. 1). Prior to treatment animals were divided into two groups based on the size of MI. Therefore, infarction size was identical in control (36±2% of total LV) and in nicorandil-treated rats (36±2%).

3.1. LV volumes and mass

At 2 days after MI, there were no significant differences in LV volumes and mass between control and nicorandil-treated animals (Table 1). At 8 weeks after MI, end-systolic volumes (ESV) were significantly smaller in nicorandil-treated (0.33±0.02 ml) compared to control rats (0.43±0.04 ml; P<0.05). End-diastolic volumes (EDV) did not differ between both groups, although there was a trend towards smaller volumes in the treated group (P=0.12). Long-term oral nicorandil therapy significantly improved LV ejection fraction (EF) compared to control animals (37±2% vs. 28±2%; P<0.01). Representative MR images obtained 8 weeks after MI clearly demonstrate the smaller LV chamber dimensions in treated animals (Fig. 2).

MI resulted in a significant increase in EDV and ESV accompanied by a decline in EF in both groups. However, the observed changes were less pronounced in the treated group. Additionally, stroke volume (SV) increased significantly in nicorandil-treated animals, but not in control rats (Table 1).

At day 2 after MI, LV mass (LVM) was similar in both groups. After 8 weeks, the absolute change in LVM was significantly greater in control animals (∆LVM 0.09±0.03 g) than that in treated rats (0.02±0.02 g, P<0.05). A significant increase in LVM was only observed in the control group (0.72±0.02 g to 0.81±0.03 g; P<0.01), but not in the treated group (0.71±0.02 g to 0.73±0.01 g; P=NS). There was an excellent correlation between MRI and postmortem LVM measurements (Y = 0.07 + 0.92X; r = 0.98; P<0.001), indicating that MRI provides an accurate measurement of myocardial mass in this small animal model (Fig. 3). Wet weight/dry weight ratios were similar in both groups (4.6±0.1 in control vs. 4.7±0.1 in treated rats; P=NS), suggesting that the increase in LVM in control rats was not related to myocardial edema.

3.2. Absolute wall thickness and systolic wall thickening

The absolute values for wall thickness and wall thicken-
Fig. 1. Representative multi-slice mesoporphyrin enhanced short-axis MR images during diastole (top row) and systole (bottom row) in a control animal. The contrast-enhanced area (arrows) represents infarcted myocardium.

infarcted myocardium increased significantly in control rats (1.88 ± 0.05 mm to 2.02 ± 0.03 mm; \( P < 0.05 \)), while little change was observed in nicorandil-treated animals (1.86 ± 0.05 mm to 1.87 ± 0.02 mm; \( P = \text{NS} \)). Moreover, nicorandil therapy improved systolic wall thickening in rim of infarction (\( P < 0.001 \)) and remote non-infarcted myocardium (\( P < 0.01 \)) (Fig. 4). Compared to remote areas wall thinning and persistent regional dysfunction were observed in infarcted regions 8 weeks after MI (\( P < 0.05 \) for both groups). The rim of infarction was characterized by moderate functional impairment and increased diastolic wall thickness compared to remote myocardium (\( P < 0.05 \) for both groups).

4. Discussion

The major findings of the current study were: (1) long-term oral nicorandil therapy started 2 days after infarction attenuated LV dilatation by reducing ESV, preserving LV function and diminishing the increase in LV mass and (2) MRI provided a noninvasive method to assess the structural and functional changes after acute myocardial infarction and to monitor the effects of therapeutic interventions.

4.1. Effects of nicorandil

Several regimens of therapy (before, during coronary occlusion and reperfusion) have been employed to determine the effect of nicorandil in the setting of acute ischemia. Animal \([12,22]\) and human \([13,14]\) studies have

Table 1

<table>
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<tr>
<th></th>
<th>Control (n = 15)</th>
<th>Nicorandil (n = 15)</th>
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<tbody>
<tr>
<td><strong>Acute phase</strong></td>
<td></td>
<td></td>
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<tr>
<td>HR (bpm)</td>
<td>273 ± 11</td>
<td>257 ± 4</td>
<td>NS</td>
</tr>
<tr>
<td>BW (g)</td>
<td>253 ± 5</td>
<td>237 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>0.31 ± 0.01</td>
<td>0.29 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>0.18 ± 0.01</td>
<td>0.16 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>0.14 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>EF (%)</td>
<td>43 ± 3</td>
<td>45 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>0.72 ± 0.02</td>
<td>0.71 ± 0.02</td>
<td>NS</td>
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<tr>
<td><strong>Chronic phase</strong></td>
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<tr>
<td>HR (bpm)</td>
<td>225 ± 6</td>
<td>232 ± 4*</td>
<td>NS</td>
</tr>
<tr>
<td>BW (g)</td>
<td>290 ± 4</td>
<td>279 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>0.60 ± 0.04</td>
<td>0.52 ± 0.02*</td>
<td>NS</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>0.43 ± 0.04*</td>
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<tr>
<td>SV (ml)</td>
<td>0.17 ± 0.02</td>
<td>0.19 ± 0.01*</td>
<td>NS</td>
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<tr>
<td>EF (%)</td>
<td>28 ± 2</td>
<td>37 ± 2*</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>0.81 ± 0.03*</td>
<td>0.73 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>ΔLVM (g)</td>
<td>0.09 ± 0.03</td>
<td>0.02 ± 0.02</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LVM autopsy (g)</td>
<td>0.79 ± 0.03</td>
<td>0.73 ± 0.02</td>
<td>NS</td>
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</table>

*\( P < 0.05 \), ** \( P < 0.001 \) vs. acute phase. HR, heart rate; BW, body weight; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; LVM, left ventricular mass; ΔLVM, absolute change in LVM; NS, not significant.
Fig. 2. Representative functional short-axis images during diastole (top row) and systole (bottom row) in (a) a control and (b) nicorandil-treated animal 8 weeks after infarction. Note the differences in LV volumes, particularly end-systolic volumes, in the treated compared to the control rat.

demonstrated that nicorandil reduces infarction size and improves the recovery of postischemic contractile dysfunction, when administered intravenously during occlusion or reperfusion. Several mechanisms were proposed to be responsible for these cardioprotective effects of nicorandil including: (1) reduction in pre- and afterload [9]; (2) improvement of myocardial perfusion [9,23]; (3) pharmacologic preconditioning [24]; (4) prevention of Ca\(^{2+}\) overload by opening K\(_{\text{ATP}}\) channels [25]; and (5) free radical scavenger and neutrophil-modulating properties [22,26].

While the mechanisms of nicorandil to protect myocardium during acute ischemic injury are well-documented, little is known about its effects in infarction-induced LV
dilatation. Hemodynamic measurements in healthy volunteers [9] and patients with impaired ejection fraction [10,27] demonstrated that nicorandil decreases peripheral vascular resistance and LV end-diastolic pressure, but increases stroke volume and myocardial perfusion. These effects were ascribed to a coronary vasodilating effect combined with a balanced peripheral action on veins and arteries, which leads to decreases in both pre- and afterload, respectively. Although the mechanism of action of nicorandil was not the scope of this investigation, it is conceivable that this hemodynamic profile may be the cause of protection found in the current study.

Clinical parameters currently used to determine the magnitude of the structural and functional changes after MI include the measurement of LV volumes, mass, and function [28]. It has been demonstrated that the extent of these changes is associated with short- and long-term prognosis in patients with infarction-induced heart failure. Particularly, LV-ESV [29] and EF [30] have been reported to be major determinants of survival in the post-MI population. Therefore, increasing efforts have been directed to the pharmacologic attenuation of LV dilatation after acute myocardial infarction. Several clinical trials have shown that ACE-inhibitors [5,6] and more recently β-blockers [31] are effective in slowing or reversing the deleterious process of LV remodeling. In this animal model of 8-weeks old infarction, we observed that nicorandil exerted similar effects by reducing LV-ESV and preserving LV function. These preliminary results demonstrate for the first time that LV dilatation can be slowed and may be prevented by oral nicorandil therapy started 2 days after infarction. Longer term studies in larger animals are needed to address the issue of whether nicorandil delays or prevents LV dilatation.

During the study period diastolic wall thickness of remote non-infarcted myocardium increased significantly in control animals, while nicorandil therapy attenuated the hypertrophic response in these regions. Several cellular mechanisms, such as activation of the mitogen-activated protein kinase (MAPK) cascades (extracellular signal-regulated protein kinase, p38-MAPK and c-Jun N-terminal kinase) and/or involvement of pathways modifying Ca\(^{2+}\) handling, have been proposed as possible transduction mechanisms between hypertrophic stimuli and protein synthesis [32]. It may be possible that nicorandil has a direct molecular effect in this regard by preventing in-

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Infarct Control</th>
<th>Infarct Nicorandil</th>
<th>Rim Control</th>
<th>Rim Nicorandil</th>
<th>Remote Control</th>
<th>Remote Nicorandil</th>
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<tbody>
<tr>
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<tr>
<td>Diastole (mm)</td>
<td>2.62±0.04</td>
<td>2.63±0.07</td>
<td>2.29±0.09</td>
<td>2.27±0.05</td>
<td>1.88±0.05</td>
<td>1.86±0.05</td>
</tr>
<tr>
<td>Systole (mm)</td>
<td>2.77±0.04</td>
<td>2.81±0.07</td>
<td>2.73±0.05</td>
<td>2.72±0.06</td>
<td>2.49±0.07</td>
<td>2.50±0.07</td>
</tr>
<tr>
<td>Wall thickening (%)</td>
<td>6±1</td>
<td>7±1</td>
<td>19±1</td>
<td>20±1</td>
<td>33±1</td>
<td>34±2</td>
</tr>
<tr>
<td><strong>Chronic phase</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Diastole (mm)</td>
<td>1.38±0.06</td>
<td>1.37±0.04</td>
<td>2.15±0.04</td>
<td>2.14±0.02</td>
<td>2.02±0.03</td>
<td>1.87±0.02</td>
</tr>
<tr>
<td>Systole (mm)</td>
<td>1.46±0.06</td>
<td>1.46±0.06</td>
<td>2.46±0.05</td>
<td>2.54±0.02</td>
<td>2.52±0.05</td>
<td>2.42±0.04</td>
</tr>
<tr>
<td>Wall thickening (%)</td>
<td>6±1</td>
<td>6±2</td>
<td>15±1</td>
<td>19±1</td>
<td>25±1</td>
<td>30±1</td>
</tr>
</tbody>
</table>

\*P<0.05 vs. acute phase, \(1\)P<0.05 vs. remote myocardium, \(2\)P<0.05 vs. control.
tracellular Ca\(^{2+}\) loading [25] or by interfering with one of the signal transduction pathways. Further research should address these points.

4.2. Noninvasive assessment with MRI

Several imaging modalities, such as echocardiography, radionuclide imaging, and computed tomography have been used to determine cardiac morphology and function. However, for repeated measurements a highly accurate and reproducible single imaging technique is mandatory. Cardiac MRI allows reliable quantification of volumes and function in the morphologically abnormal LV with high reproducibility and low interstudy variability [21]. Compared with echocardiography [33], MRI does not rely on assumptions about chamber shape and geometry which is of particular importance in hearts deformed by asymmetric dilation. Thus, cardiac MRI is ideally suited to assess LV volumes and function after MI and to document the response to therapies [34–36].

Animal [37] and human studies [3,38] have indicated that infarction size is one of the major determinants of LV remodeling. Non-specific standard extracellular MR contrast media have been employed extensively for sizing and characterizing myocardial injuries [39,40]. More recently, several reports [17–19,41,42] have indicated that necrosis-specific MR contrast media, represented by Gd-mesoporphyrin, provide a more accurate measurement of acute MI. Thus, this new MR contrast medium was used in the current study instead of non-specific extracellular agents. The potential of this protocol lies in the complementary use of contrast-enhanced and functional MR imaging to provide identical infarction size and to noninvasively monitor the effects of therapeutic strategies designed to attenuate LV dilatation.

4.3. Study limitations

It should be noted that the exact mechanism of protection exerted by nicorandil cannot be elucidated by the current capability of MRI. The objective of the current study was to use MRI as a noninvasive tool for detecting possible differences in LV volumes and function between nicorandil-treated and control animals. Other hemodynamic parameters, such as LV pressures, dP/dt and arterial blood pressure, were not measured because of the limitations of the MRI environment. Thus, based on our study it is not possible to determine whether the effects of nicorandil are due to hemodynamic changes and/or a direct effect on the myocardium.

Secondly, the plasma and tissue levels of nicorandil were not examined in this study. However, the issue of the distribution and transformation of nicorandil in rat myocardium after oral administration has been previously addressed [43]. Sakai et al. [43] found that nicorandil given orally to rats is preferentially distributed into mitochondria of the heart. It has also been shown that the magnitude of the nicorandil effect (i.e. reduction of infarction size) is positively correlated with the applied dosage and the plasma concentration of the drug [44].

Thirdly, it must be recognized that any animal model may not fully represent the complex clinical situation in patients. Moreover, it remains to be shown whether the observed effect of nicorandil will be additive to the salutary effects of ACE-inhibition and \(\beta\)-blockade in the setting of LV remodeling. Therefore, more studies with longer treatment periods are warranted to prove whether nicorandil has any effect on morbidity and mortality in experimental and clinical heart failure. Further research is awaited to address these very important points.

5. Conclusion

Our results indicate that oral long-term treatment with nicorandil started 2 days after infarction attenuates LV dilatation in a rat model of reperfused MI. Cardiac MRI is a valuable noninvasive method to study the structural and functional changes after acute MI and to monitor the effects of new therapies designed to reduce LV dilatation.

Acknowledgements

NW. was a Research Fellow supported by a Postdoctoral Research Exchange Grant from the Max-Kade Foundation, Inc., New York, USA. This study was supported by a gift from Chugai Pharmaceutical Co. Ltd., Tokyo, Japan.

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