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Original Article

Cardioprotective Effects of Mebudipine in a Rat Model of Doxorubicin-Induced Heart Failure

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What's Known

- Among calcium-channel blockers, dihydropyridines are extensively used due to their potent vasodilatory and weak cardiodepressant properties.
- Mebudipine is a newly synthesized dihydropyridine calcium-channel blocker that has significant negative chronotropic effects but without considerable negative inotropic properties.

What's New

- In an animal model, mebudipine reversed the increased plasma levels of biochemical markers, which act as the prognostic and diagnostic indicators of heart failure.
- Administration of mebudipine to animals with doxorubicin -induced heart failure palliated the clinical and biochemical signs of the disease.

Abstract

Background: Mebudipine, a dihydropyridine calcium-channel blocker (CCB), shows greater time- and voltage-dependent inhibitory effects than nifedipine. Its significant negative chronotropic effects without having considerable negative inotropic properties may make it a suitable candidate for the pharmacotherapy of heart failure (HF). This study aimed to investigate the possible beneficial action of mebudipine in a rat model of HF.

Methods: The present study carried out in the Department of Pharmacology at the Iran University of Medical Sciences during the years of 2009-2011. An experimental model of HF was induced in male Wistar rats using doxorubicin (DOX). The rats were divided into five groups with seven animals in each group: normal control group, DOX-induced HF control groups, and treatment groups. The animals were administered DOX for 15 days. A consistent deterioration occurred after a four-week rest period. The animals were then treated with intraperitoneal mebudipine (0.5 mg/kg) and intraperitoneal amlodipine (0.35 mg/kg), as well as an equal volume of distilled water for 15 days. The plasma levels of big endothelin-1 (BET-1), creatine kinase-myocardial band (CK-MB), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT), as well as the clinical status (heart rate and blood pressure), were assessed before and after treatment. Statistical analysis was performed with SPSS software using parametric and nonparametric ANOVA.

Results: Mebudipine and amlodipine reversed the increased plasma BET-1 values in the treated animals when compared with the HF control group (0.103 and 0.112 vs 0.231 pg/mL, respectively). The increased plasma levels of AST, ALT, CK-MB, and LDH were also reversed in the HF animals that received mebudipine or amlodipine.

Conclusion: The administration of mebudipine to HF animals, akin to amlodipine, palliated the clinical and biochemical signs of the disease in the present study.

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Keywords ● Mebudipine ● Amlodipine ● Endothelin-1 ● Heart failure ● Doxorubicin

Introduction

Heart failure (HF) is a chronic condition that results from any structural or functional cardiac disorders, leading to reduced cardiac output.[1, 2]