Effect of Saxagliptin and Vardenafil on cardiac dysfunction and Atrial Natriuretic Peptide gene expression in chronic Isoproterenol - treated rats

Thesis

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ABSTRACT

The aim of the present work is to clarify the potential effect of Saxagliptin and Vardenafil on cardiac dysfunction and Atrial Natriuretic Peptide gene expression in chronic Isoproterenol - treated rats .

Cardiac dysfunction was induced in male albino rats by injecting isoproterenol subcutaneously daily for 15 days as follows: doses of 30, 20, and 10 mg/kg were given on days 1, 2, and 3, respectively, followed by 5 mg/kg on days 4 to day 15. Rats were divided into four main groups; control groups (control group, saxagliptin group and vardenafil group), isoproterenol group, saxagliptin pretreated group and vardenafil pretreated group. Saxagliptin 10 mg/kg and vardenafil 10mg/kg were administered orally with isoproterenol daily for 15 days to study their effects on electrocardiogram data (heart rate, QT interval and R wave amplitude), cardiac contractility, atrial natriuretic peptide and tumor necrosis factor α gene expression and histopathological analysis of cardiac tissue was also performed.

The present study revealed that isoproterenol led to significant increase in HR, QT and Rwave amplitude by 31.5% , 51.2%, and 82% respectively.

The present study proved that Saxagliptin treatment decreased HR, QT and R wave amplitude by 26%, 36.2% and 51.3% respectively and vardenafil treatment decreased HR, QT and R wave amplitude by 25.1%, 34.3% and 55.6% respectively compared to isoproterenol group.

Repeated administration of isoproterenol significantly decreased cardiac contractility by 63.62%.Saxagliptin treatment increased cardiac contractility

by 53.9% while vardenafil treatment increased cardiac contractility by 125%.

Isoproterenol increased ANP and TNFα by 1006% and 1674% respectively. Saxagliptin treatmentdecreased ANP and TNFαgene expression by 67.2% and 72.6% respectively, while vardenafil treatment decreased ANP and TNFα gene expression by63.7% and 66.4% respectively.

Histopathological examination by light microscopy using hematoxylin and eosin revealed that isoproterenol led to scattered swollen cardiac muscle fibres with granular pale cytoplasm with perinuclear vacuolations. Interstitium showed focal areas of oedema, congested capillaries and mononuclear inflammatory cellular infiltrate. There were large thick patches of subendocardial and interstitial fibrosis by masson trichrome stain. Pretreatment with saxagliptin or vardenafil led to improvement of isoproterenol-induced histopathological changes. Cardiomyocytes were arranged in interlacing bundles with normal histological pattern and there was no fibrosis by masson trichrome stain.

The results of the present study implicate that treatment with saxagliptin and vardenafil may prevent isoproterenol induced cardiac dysfunction.

Key words: Isoproterenol, cardiac dysfunction, ANP and TNFα gene expression, saxagliptin and vardenafil.