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The role of autophagy and death pathways in dose-dependent Isoproterenol-induced cardiotoxicity

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Isoproterenol (ISO) is a synthetic catecholamine bearing a non-selective β-adrenergic agonist property. In small dose it can be used in heart block, cardiac arrest. However chronic or high dose administration of ISO leads to the development of irreversible damage of the myocardial membrane and ultimately causes infarct-like necrosis in heart muscles. Our aims were to investigate the autophagy and cell death pathways including apoptosis and necrosis in isoproterenol-induced cardiac injury in a dose-dependent manner. Male Sprague-Dawley rats were treated for 24 hours with (1) vehicle (saline); (2) 0.005 mg/kg ISO; (3) 0.05 mg/kg ISO; (4) 01.005 mg/kg ISO, (5) 5 mg/kg ISO; and (6) 50 mg/kg ISO. Then animals were sacrificed and hearts were isolated and infarct size was measured. Serum levels of Troponin T (TrT), Lactate Dehydrogenase (LDH), Creatine Kinase Iso-Enzyme MB (CK-MB) enzyme were also measured. Heart tissue samples were examined with Tunel assay and Western blot was performed to evaluate the level of autophagic and apoptotic markers. Survival rate of animals was dose-dependently decreased. Serum markers and infarct size revealed the development of cardiactoxicity in ISO 5 and ISO 50 groups. Level of caspase-3, which is marker of apoptosis and results of TUNEL assay, which measure the DNA fragmentation, demonstrated that the level of apoptosis was dose-dependently increased. They reached the highest level in ISO 5 and it decreased in ISO 50. Furthermore, focusing of autophagic proteins (Beclin-1, LC3B-II and p62), we found that level of Beclin-1 was increased in dose-dependent manner, but significantly increased in ISO 50. However, level of LC3B-II and p62 showed the same manner, but the elevated level of p62 indicated that autophagy was impaired in ISO 5 and ISO 50 groups. Taken together these results suggest that in smaller dose of ISO autophagy may cope with the toxic effect of ISO; however, in higher dose apoptosis is initiated and in the highest dose necrosis occur.

Biography

Alexandra Gyongyosi is a Clinical Laboratory Scientist from Pharmacology Department, Faculty of Pharmacy, University of Debrecen, Hungary.

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