

Rho-Kinase Inhibitors for the Management of Metabolic Syndrome

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Metabolic syndrome is one of the main risk factors of the formation of Myocardial Infarction, Stroke, and Heart Failure, which are the main cause of disability and patient death worldwide. Estimates 17.9 million people died from CVDs in 2016 (31% of all deaths). Epidemiological researches identified genetic and non-genetic risk factors for formation atherosclerotic disease, which are targets for therapeutic intervention. To date, no specific therapies have been approved for treating the metabolic syndrome. The risk factors of Atherogenesis such as excessive calorie intake, low physical activity, obesity and insulin resistance are the main causes of endothelial dysfunction associated with down-regulation of eNOS/NO pathway and up-regulation of RhoA/Rho-kinase pathway, forming a vicious circle of metabolic disorders. RhoA, and the RhoA/Rho-kinase pathway plays an important role in various physiological cellular functions, such as vascular smooth muscle contraction, cell adhesion, motility and cytokinesis. Rho-kinase is also one of the central mediators of inflammation, proliferation, fibrosis and apoptosis through activation of MEK/ERK, NF- κ B and p38MAP kinase pathways. Moreover, some clinical trials identified that Rho-kinase increase phosphorylation of insulin receptor substrate-1 (IRS-1) and leads to formation of insulin resistance. Additionally, the latest clinical studies results indicate that the long-term inhibition of Rho-kinase in vivo exerts several beneficial effects on insulin resistance, such as suppression of inflammation, reduction in cytokines production and improvement of endothelial functions. Therefore Rho-kinase can be considered as a target for the therapeutic intervention to manage metabolic syndrome. However, since the detailed mechanism(s) of the relation between Rho-kinase and metabolic disorders has not been elucidated, we intend to address this important issue in the future study.

Conclusion & Significance: The inhibition of 3-ketoacyl-CoA thiolase as well as prevention of IRS-1 phosphorylation by Rho-Kinase inhibitors may have off-target effects on metabolic syndrome.

Keywords: Rho-kinase, 3-ketoacyl-CoA thiolase, Metabolic Syndrome, Atherosclerosis.

Biography

Ana Archvadze is a member of Member of European Association for Clinical Pharmacology and Therapeutics (EACPT). Over 12 years experience as a Trainer/Teacher of Medical Sciences; Over 11 years experience in health and Social project/program development, execution, monitoring and completion; Over 7 years experience in International Project Management working for the World Bank Financed Health projects; Over 11 years experience in procurement of drugs/vaccines, equipment/furniture, medical services; Familiar with local and international procurement regulations; Over 10 years of experience in supervision of the contract performance with medical institutions, pharmaceutical firms, governmental and non-governmental organizations; Over 7 years of experience in health insurance (budgeting, financing, monitoring and evaluation of State Medical Insurance Programs); Over 7 years of experience in provision of medical services; Over 5 years experience in an assessment of training needs; design and elaboration of training programs, provision of trainings for emergency care medical staff and for healthcare services providers.

