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A REVIEW OF ENDOTHELIAL FUNCTION IN ALTERED GRAVITY ENVIRONMENTS

Abstract

Background: Decades of ground-based and spaceflight research as well as clinical observations demonstrate that cardiovascular deconditioning happens with disuse. Some have also raised the possible existence of a syndrome of "endothelial dysfunction" which contributes to cardiovascular deconditioning. Although "organ systems" have been widely studied, few studies have analyzed the cellular aspects in the pathophysiology of spaceflight cardiovascular deconditioning from the perspective of changes in endothelial function. Objective: To review the literature related to endothelial function in altered gravity environments in order to determine the potential contribution of these cellular changes to spaceflight cardiovascular deconditioning with a focus on monolayer integrity, gene expression, inflammatory activation, metabolic function and physiologic function. Search Strategy: A pubmed search was performed of articles published between the January 1970 and February 2010 using the following keywords: "endothelial function", "endothelial cells", "nitric oxide", "microgravity", "hypogravity", "simulated microgravity", "spaceflight", "simulated microgravity". Selection Criteria: Articles written in English and French language that were hypothesis-driven and assessing monolayer integrity, gene expression, inflammatory activation, metabolic or physiologic function. Results: Twenty-five studies were identified that met the above criteriae. All studies evaluated endothelial function using either cell cultures (clinostat or random-positioning machine) or animal model (hindlimb suspension). Overall responses vary based on the bed of origin of the cell. Growth appears to be altered with shifting of cell cycle to G0-G1 phase and reduction in S phase and growth pattern as "aggregates" in multilayers. There appears to be remodelling of the cytoskeleton of cell with a decrease in actin. Cells displayed an enhanced permeability and increased expression of junctional complex proteins. Gene expression is altered with changes in nitric oxide synthase (NOS), the direction of the response varying based on the isotype and district of origin. Metabolic function displays basal increase in nitric oxide and prostaglandin secretion by the cell. Physiologic function also appears to be altered with an increase in vasorelaxation to nitroprusside. Conclusions: These findings demonstrate that changes in endothelial function could have an important impact on cardiovascular deconditioning through alteration in cell phenotype, gene expression, inflammatory activation and metabolic function. This may open new strategies to treat spaceflight cardiovascular deconditioning as well as terrestrial diseases where endothelial dysfunction is present. Spaceflight provides a unique model to study cardiovascular physiology in the context of disease states and deconditioning.