Introduction

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Nitric oxide and endothelin are powerful vasoactive mediators involved in inflammation and regulation of vascular tone ***(Freedman, et al., 2000)***. Endothelial release of nitric oxide contributes to the regulation of vascular tone by inducing vascular relaxation. In addition, nitric oxide may inhibit the synthesis and hemodynamic effects of endothelin-1, a powerful endothelium-derived vasoconstrictor peptide that may stimulate nitric oxide production. However, whether nitric oxide and endothelin-1 physiologically interact, there regulation to vascular tone in humans has not been defined ***(Cardillo, et al., 2000)***.

Endothelin is a potent vasconstrictive polypeptide released by endothelial cells in response to various stimuli including vasoactive peptides such as angiotensin II, adrenaline, vasopressin and thrombocyte products like transforming beta growth factor and thrombin ***(Forslund and Metsarinne, 1992)***. In vascular smooth cells, endothelin binds to a specific receptors that activate phospholipase and leads to formation of inositol triphosphate diacylycerol ***(Luscher, 1991)***.

Intravenous administration of endothelin resulted in a dose dependent transient hypotension followed by a long lasting hypertension and inhibition of platelet aggregation ***(Herman, 1989)***.

On the other hand, the vascular endothelin is the site of formation of several powerful mediators. One of these is nitric oxide (NO), a chemically unstable radical formed by enzymatic conversion of L-arginine in the presence of molecular oxygen ***(Palmar et a., 1987)***. NO elicits relaxation of vascular smooth muscle cells by activating cytosolic guanylate cyclase. NO also counteracts platelet adhesion and aggregation

(Bolotina et al., 1994). The basal formation of NO maintains a moderate but significant vasodilation in the systemic resistance vessels. Beside this, several vasodilators (acetylcholine, bradykinine and histamine) operate by stimulating endothelial NO formation *(Wennmalm, 1994).*

A number of studies have shown that a variety of abnormalities in the function and biochemistry of the endothelium occur in diabetic animals *(Lorenzi & Cagliero, 1991 and Bar, 1992).* Endothelial cells increase synthesis of some prostaglandins, endothelin-1 and von Willebrand factor whereas production of prostacyclin is reduced *(Takda et al., 1991).* Conflicting results have been reported from previous studies concerning production of NO in diabetes. Increased NO production has been reported in diabetic animals *(Maree et al., 1996),* where the stable metabolites of NO (nitrite + nitrate) were measured in plasma and urine in diabetic and normal rats. On the other hand, a number of studies have shown that vascular relaxation in response to agents which release NO from the endothelium is impaired in diabetic animals and it was postulated that diabetes interferes with synthesis or release of NO by endothelial cells *(Vallance & Moncada, 1994).*

So, nitric oxide and endothelin now, considered a new system useful to understand and study the molecular mechanisms involved in many vascular alteration pathologies and in the aging process *(Donnini, et al., 2000).*