INTRODUCTION

Several studies had indicated that type 2 diabetes, arterial hypertension, lipid disorders as well as visceral obesity are coronary risk factors which might belong to a syndrome which is caused by decreased insulin sensitivity with compensatory hyperinsulinemia, ***(Muller-Wieland, et al., 1998)***.

Endothelins ubiquitously produced 21 amino-acids peptides that were discovered as an endothelial product and may play important roles in cardiovascular physiology and pathophysiology. The main endothelin produced by endothelium is endothelin-1 (ET-1). The vasoconstrictor role of the endothelins may participate in blood pressure elevation and vascular hypertrophy in salt dependent models of hypertension, ***(Schiffrin, et al., 1997)***

The secretion of endothelin-1 was found to be stimulated by insulin both in experimental animal studies and in cultured human endothelial cells, ***(Ferri, et at., 1994).*** Furthermore, plasma endothelin-1 levels are increased in insulin treatment of diabetic and non-diabetic rats, ***(Takeda et at., 1991)*** and in non-insulin dependent diabetes mellitus (NIDDM), ***(Takahashi et at., 1990).***

Several independent predictors of the risk of atherosclerosis are known including plasma cholesterol, cigarette smoking, elevation of blood pressure as well as the 3 major elements of pathogenesis of atherosclerosis, involving modification of the endothelial function, changes in vascular tone, and clinical sequelae of hyperplasia of smooth muscle cells in the intima of the effected blood vessels, ***(Swedberg, 1998).***

Perfetto, et al., (1998) had demonstrated that circulating endothelin-1 levels are increased in patients with atherosclerosis and that those with NJDDM showed the highest endothelin-1 levels. These

observations strongly support a role of endothelin1 in the pathogenesis of atherosclerosis and also suggest that this peptide may be involved in the development of atherosclerotic lesions in the NIDDM patients. Chronic exposure to hyperinsulinemia, and hypertriglycedemia in the diabetic patients could account for the increased endothelin-1 levels found in these patients, ***(Perfetto, et at., 1998).***

The link between blood pressure and insulin sensitivity might be mainly related to concomitant obesity. Accordingly, obesity can be associated with an increased activity of the sympathetic nervous system, elevated plasma levels of vasoconstrictor endothelin-1, and decreased insulin-induced endothelium dependent vasodilatation. Furthermore, adipocytes can secrete vasogenic peptides, such as angiotensinogen, ***(Muller-Wieland, et at., 1998).***