INTRODUCTION

Adrenomedullin (AM) is a hypotensive peptide first isolated from human pheochromocytoma tissue eliciting a long-lasting vasorelaxant action. This 52-amino-acid peptide was observed to stimulate adenylyl cyclase activity in a platelet bioassay and shares a slight homology with the calcitonin gene-related peptide(CGRP),a potent hypotensive peptide ***(Kitamora et al., 1993a).***

AM levels are increased in hypertension and congestive heart failure, indicating that AM is acting as a counter-regulatory hormone to the hypertensive and volume-overloaded state ***[Hinson et al. (2000) and Hongshi et al. (2003).***

Infusion of AM into humans and rats with congestive heart failure has demonstrated beneficial effects of increased cardiac output, natriuresis and diuresis; decreased blood pressure and aldosterone; and increased renal blood flow ***(Nagaya et al., 2000).***

During normal pregnancy, important physiological adaptations occur in the mother that ensure an adequate blood supply to the fetus. Vascular resistance, mean arterial pressure, and sensitivity to endogenous constrictors are reduced, whereas cardiac output, heart rate, and blood volume are increased. This allows the maintenance of the placental vasculature in a state of near-maximal dilatation. Failure to achieve these adaptations may result in the reduced fetoplacental perfusion that develops during the disease states such as preeclampsia and intrauterine growth restriction. Because placenta lacks autonomic innervation, uteroplacental perfusion is regulated mainly by systemic blood pressure

changes through the action of both circulating and locally released vasoactive agents ***(Macara et al., 1993).***

Preeclampsia is a unique state occurring in pregnancy that is characterized by hypertension, proteinuria, abnormalities of endothelial function, reduced fetoplacental blood flow, and hypoxia that is cured by delivery of the placenta ***(Redman, 1993; and Hayman et al., 1999).***

Despite many abnormalities being described, there is as yet no clear cause of preeclampsia ***(Conrad and Benyo, 1997 and Page et al., 2000).*** Because of its vasodilatory properties, AM has been studied in pregnancy and preeclampsia as a potential pathogenic factor in this disease ***(Hongshi et al., 2003)***. AM is widely expressed in maternal and fetal tissues, including villous and extravillous trophoblasts, chorion, deciduas, and fetal membranes ***(Marinoni et al.,1998).***

Kobayashi et al. (2000) and Jerat et al. (2001), have shown a progressive increase in maternal plasma AM levels throughout pregnancy. In preeclampsia, early reports suggested that maternal AM levels were decreased, but subsequent larger studies found no difference from controls ***(Minegishi et al., 1999 and Makino et al., 1999)***. However ***Jerat et al. (2001)***, believe that this indicates a lack of compensatory increase in response to hypertensive state.

Di Iorio et al. (1998b), reported that although maternal AM concentrations did not significantly differ between preeclamptic and normal pregnant women, AM levels were increased in amniotic fluid and umbilical vein blood collected from preeclamptic pregnant women. In these patients, 48 hours after delivery, AM concentrations decreased

significantly at levels corresponding to those found postpartum in normal pregnancies. These findings confirmed local productions of adrenomedullin and suggested that it may modulate fetoplacental hemodynamics through a paracrine mechanism interacting with other vasoactive agents in physiological and pathological states during pregnancy, such as preeclampsia. They also reported that increased AM levels in preeclamptic pregnant women are not derived from the placenta. Alternatively increased AM concentrations in preeclampsia can be explained on the bases of an active secretion of this peptide by the fetus.

Hongshi et al. (2003), concluded that spontaneous placental syncytialization is impaired in preeclampsia and that AM production is markedly reduced in preeclampsia, possibly owing to an impaired epidermal growth factor (EGF) response. These abnormalities indicate poor placental production of AM as likely cause of a failed compensatory increase in maternal serum AM levels in preeclampsia.

Al-Ghafra et al. (2006b),suggested that fetal membranes, but not placental production of AM is increased in preeclampsia, AM may play an important role in the regulation of feto-placental hemodynamics and fetal physiology during preeclampsia.