Brain and Gastric AT1 Gene Expression Changes in Adult Male Albino Rats Induced by ChronicImmobilization Stress. The Possible Role of Angiotensin II Type 1 Receptor (AT1) Blockers

Abstract: Our study was conducted upon 60 male rats, they were divided into 6 equal groups, the first 3 groupswere left wandering in their cages, the last 3 groups were subjected to chronic immobilization stress for 60 minutesevery day for 10 consecutive days, 2 groups of non stressed group and 2 groups of stressed groups were givencandesartan in a dose of 1 mg and 2 mg / kg. On the tenth day Pyloric ligation were done to all groups for 4 hoursthen scarification were done with an over dose of anesthetic ether. The following parameters were measured:Measurement of AT1 gene expression in brain by polymerase chain reaction (PCR), Measurement of AT1gene expression in pylorus by polymerase chain reaction (PCR), Measurement of the following parameters inthe collected gastric juice (Titratable acidity. Pepsin activity.Mucous concentration).Ulcer index in gastricmucosa. The results showed that stress causes marked increase in AT1 gene expression in both brain and stomach.Also stress caused marked increase in titritable acidity, pepsin activity, gastric ulceration and decrease in mucousconcentration, with use of candesartan, gene expression had decreased dramatically in both brain and stomach, alsothere was a significant decrease in titritable acidity, pepsin activity, gastric ulceration and increase in mucousconcentration with use of candesartan. Stress induces acute gastric mucosa lesions by a variety of mechanisms,including psychological factors influencing individual vulnerability, stimulation of specific brain pathwaysregulating autonomic function, decreased blood flow to the mucosa, increase in muscular contractility, mast celldegranulation, leukocyte activation and increased free radical generation resulting in increased lipid peroxidationMaintenance of gastric blood flow is important to protect the mucosa from endogenous and exogenous damagingfactors, and Ang II, through AT1 receptor stimulation, increases vascular tone in resistance arteries including thoseof the gastric vasculature leading to decreased blood flow and ischemia. With the use of candesartan, known as apotent ARB, it was clear in the results of this study that it has a great protective role regarding gastric ulceration andstress response. The protection of gastric blood flow after administration of AT1 receptor antagonists is probablymediated by inhibition of receptors localized to the endothelium of arteries located in the gastric mucosa Lines ofevidence supporting the hypothesis of a major role of brain Ang II in stress include stress-induced increases incirculating and brain Ang II levels, high AT1 receptor expression in all areas involved in the stimulation of thehypothalamic-

pituitary-adrenal axis (HPA) activity, including the hypothalamic paraventricular nucleus (PVN), themedian eminence (ME) and the subfornical organ (SFO)). Sustained inhibition of peripheral and brain AT1 receptorsby peripheral administration of the AT1 receptor antagonist candesartan prevents not only the hormonal, but also thesympatho-adrenal response to immobilization stress). In addition, candesartan pretreatment prevents the activationof the brain sympathetic system during immobilization and produced anti-ulcer effect on gastric mucosa.

Keywords: AT1Gene, Albino, Chronic Immobilization, Angiotensin II.