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Study the Anti-inflammatory Effect of Telmisartan and Valsartan in Airway Model of Female Rats: Comparative Study

A Thesis
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ABSTRACT

Background and Objective: Ongoing airway inflammation and associated airway remodeling are believed to play a role in the development of airway hyper responsiveness and airflow limitation. Many studies have suggested that angiotensin II and its receptors may be involved in the development of airway inflammation and remodeling. The aim of the present study is to investigate whether treatment of rats with the angiotensin II receptor blocker (telmisartan and valsartan) can treat inflammation of pulmonary system in rat model.

Methods: Twenty-four Wistar female rats were randomly divided into four groups (n=6 for each group); group A: Distilled Water-treated group (sensitized/non treated), group B: telmisartan-treated group (telmisartan 5mg/kg/day), group C: Valsartan-treated group (Valsartan 5mg/kg/day), and group D :Distilled water-treated group (control /non sensitized). Rats in groups A, B and C were sensitized by intraperitoneal injections of 1mg Ovalbumin, 100mg Aluminum hydroxide in 1ml of phosphate buffer saline at 1st day, and 100mg Ovalbumin , 100mg Aluminum hydroxide in 1ml of phosphate buffer saline at 4th day. At 8th day, the rats in the groups A, B and C were challenged by inhalation (using nebulizer) with 1% Ovalbumin (1gm Ovalbumin in 100ml phosphate buffer saline) for 30 minutes, while group D was challenged with inhaled phosphate buffer saline alone; then challenge by inhalation was continued daily for 7 days. Sixty minutes prior to the challenge, rats in the treated groups B and C were administered intragastric 5mg/kg of telmisartan and Valsartan respectively; while A and D groups were administered intragastric a

comparable volume of distilled water. Challenges took place in glass chamber (30cm × 30 cm × 30 cm) connected to piston-type nebulizer. The

animals were anesthetized by using sodium phenobarbitone (70 mg/kg) 24 h after the last challenge. Blood samples were collected from the heart. Then, the collected blood samples were centrifuged to separate the serum for measurement of Immunoglobulin E. After blood collection, the chest was opened, and the trachea with the heart–lung package was excised from the thorax, then the right lung was lavaged three times with 5ml of phosphate buffer saline solution and bronchoalveolar lavage fluid was collected, centrifuged to separate supernatant fluid for Interlukines-4 and tumor necrosis factor alpha measurement; Meanwhile, precipitated cells were collected for white blood cell and deferential cell count; Thereafter, the left lung was collected for histopathological examination.

Results: The result of the present study indicated that telmisartan in a dose (5 mg/kg) significantly suppress total white blood cell and deferential inflammatory cells count and reduce level of tumor necrosis factor alpha, Interleukin -4 in bronchoalveolar lavage fluid and serum Immunoglobulin E level. Telmisartan also significantly inhibit the increment in thickness of alveolar smooth muscle and trachea. In addition further the histopathological changes in rats' lungs were preserved toward normal ;meanwhile, valsartan in same dose had significant to reduce tumor necrosis factor alpha, Interleukin -4 and Immunoglobulin E levels only but it was not significantly reduced other parameter; As well as the histopathological changes were not maintained with normal architectures.

Conclusion: In the present study, telmisartan (5mg/kg) had a powerful effect in reducing inflammatory and remodeling parameters. On the other hand, valsartan had partial effect in this respect; the negative result of

valsartan might be due to insufficient dose (5mg/kg) and duration of treatment (7 days), as well as negative feedback effect of valsartan on renin secretion by blocking Angiotensin II subtype one receptor and lack of partial peroxisome activated receptor gamma activity.