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Clinical and experimental study of the effect of angiotensin-converting enzyme inhibitors on the larynx

A thesis

submitted for partial fulfillment of the requirement of the Doctorate Degree (M.D.) in

Oto-Rhino-Laryngology

By

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بسم الله الرحمن الرحيم

" سبحانك لا علم لنا إلا ما علمتنا
إنك أنت السميع العليم "

سورة البقرة (٣٢)

صدق الله العظيم

To

My home & Family

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List of Abbreviations

ACE:	Angiotensin Converting Enzyme
ACEIs:	Angiotensin Converting Enzyme Inhibitors
CI-EI:	Complement I- Esterase Inactivator
F:	Female
Fig.:	Figure
H&E:	Haematoxylin & Eosin Stain
LP:	Lamina Propria
M:	Male
N.:	Number
PAS:	Periodic Acid Schiff
Tab.:	Table

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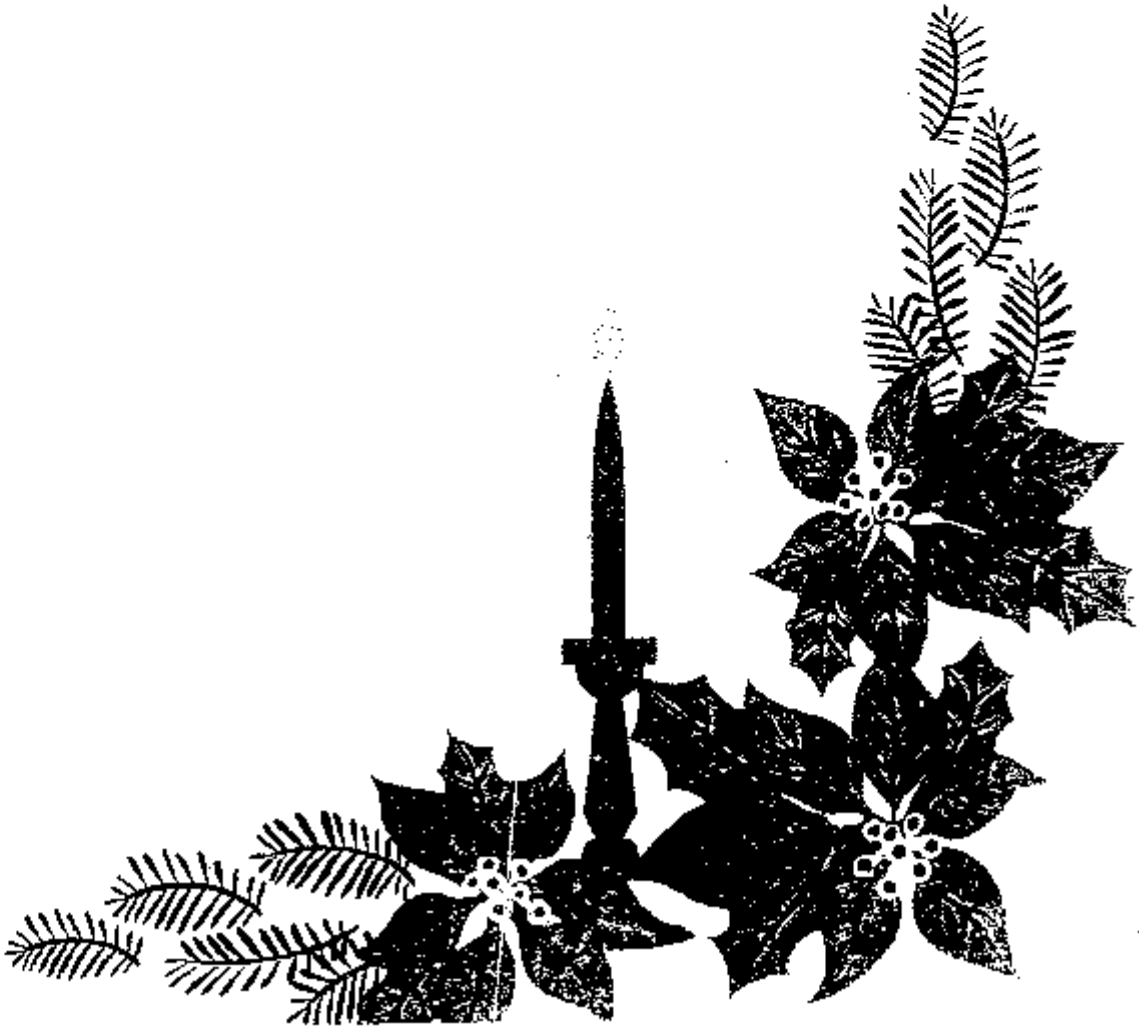
Introduction



Introduction

Angiotensin-converting enzyme inhibitors (ACEIs) have been widely used in the treatment of hypertension and congestive heart failure. They have been proven to improve heart function in congestive heart failure and are well tolerated, even by the elderly patients ***(Murphy et al., 1986).*** These drugs can cause several side-effects which are of specific relevance to otolaryngologists, cough, sore throat, and upper airway obstruction being the most notable ***(Cruickshank, 1995).***

One of its dangerous side-effects is development of upper airway obstruction, which can sometimes cause a life-threatening angioedema. The onset of the oedematous oropharyngeal swelling is often so fast that usually an intubation or tracheotomy is required to save the life of these patients ***(Gunkel et al.,1996).***

The oedematous reaction usually develops on the skin of the face, the extremities, the genital region, and in the mucosa and tissue of the upper aerodigestive tract (including the lips, tongue, palate, uvula, hypopharynx and larynx) ***(Cruickshank, 1995).***

The most dangerous localization was oedematous swelling of the hypopharynx and larynx, therefore can cause severe airway obstruction and even death due to suffocation. The first episode of adverse reaction usually occurs within the first few weeks of starting therapy. The adverse reaction can be expected to subside within hours of stopping the drug. ***(Gunkel et al., 1996)***

The mechanism responsible for the adverse reaction of angiotensin-converting enzyme inhibitors (ACEIs) in the upper airway obstruction is unclear. One of the main factors is the influence of vasoactive peptides, such as kinins on the metabolism. The kininase II enzyme, which is a major contributor to degradation of tissue bradykinin, is identical to angiotensin- converting enzyme and therefore inhibited by angiotensin converting enzyme inhibitors. It has also been shown that enzymatic reaction from angiotensin I to angiotensin II, which is promoted by the angiotensin converting enzyme, is blocked or decreased by the angiotensin-converting enzyme inhibitors. Therefore, the vasoconstrictive effect of angiotensin II is missing and can result hypotension, vasodilatation and interstitial oedema ***(Karger and Basel, 1992).***

On the other hand, angiotensin converting enzyme inhibitors have been shown to induce antibodies and auto-antibodies to various body tissue ***(Coleman et al., 1986).*** Edematous swelling of the upper aerodigestive tract resulting from taking (ACE) inhibitors is probably not an immune-mediated reaction, but as side effect, linked to the mode of action of the drug itself ***(Thompson andFrable,1993).***

Emergency physicians and otolaryngologists should play a key role in identifying patients with upper airway reaction associated with using of angiotensin-converting enzyme inhibitors ***(Cruickshank, 1995).***

Prevalence of cough induced by using angiotensin-converting enzyme inhibitors is high. The cough was usually, moderate or severe, paroxysmal and troublesome at night. It is often starts within a week of starting the therapy and usually subsides if the drug is withdrawn, but reccurs if the same or a different angiotensin-converting enzyme inhibitor is recommenced ***(Yesil et al., 1994).***

Various mechanism have been put forward to explain the cough involving bradykinin, substance P, and prostaglandins. Angiotensin-converting enzyme may be involved in the metabolism of kinins including bradykinin, so angiotensin converting enzyme inhibitors could result increased levels of these peptides ***(Cruickshank et al., 1995).***

This study, However, is concerned with effects of angiotensin-converting enzyme inhibitors on the larynx in human being with correlation to histological changes in the larynx of the experimental animals (rabbits) after ingestion of angiotensin-converting enzyme inhibitor (Captopril).