BRONCHIAL HYPERREACTIVITY IN OLD PATIENTS WITH BACTERIAL CHEST INFECTION

THESIS
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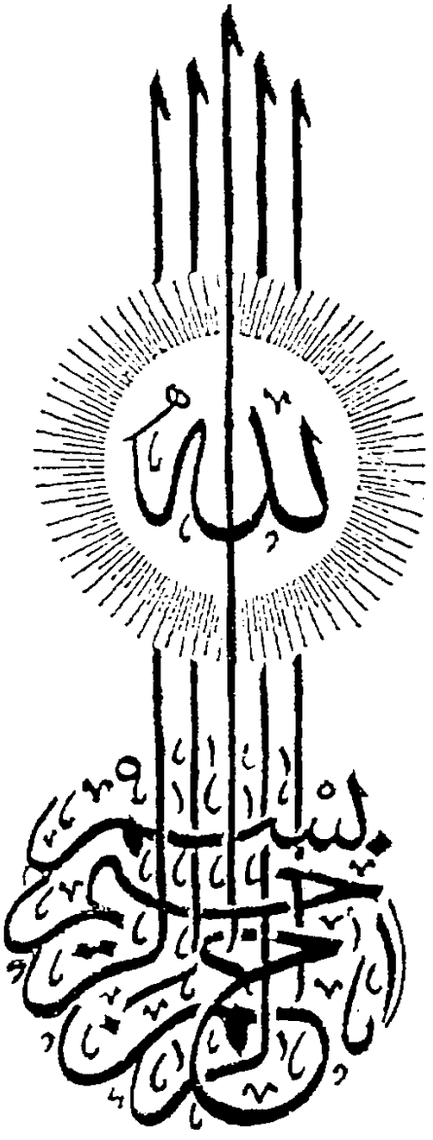

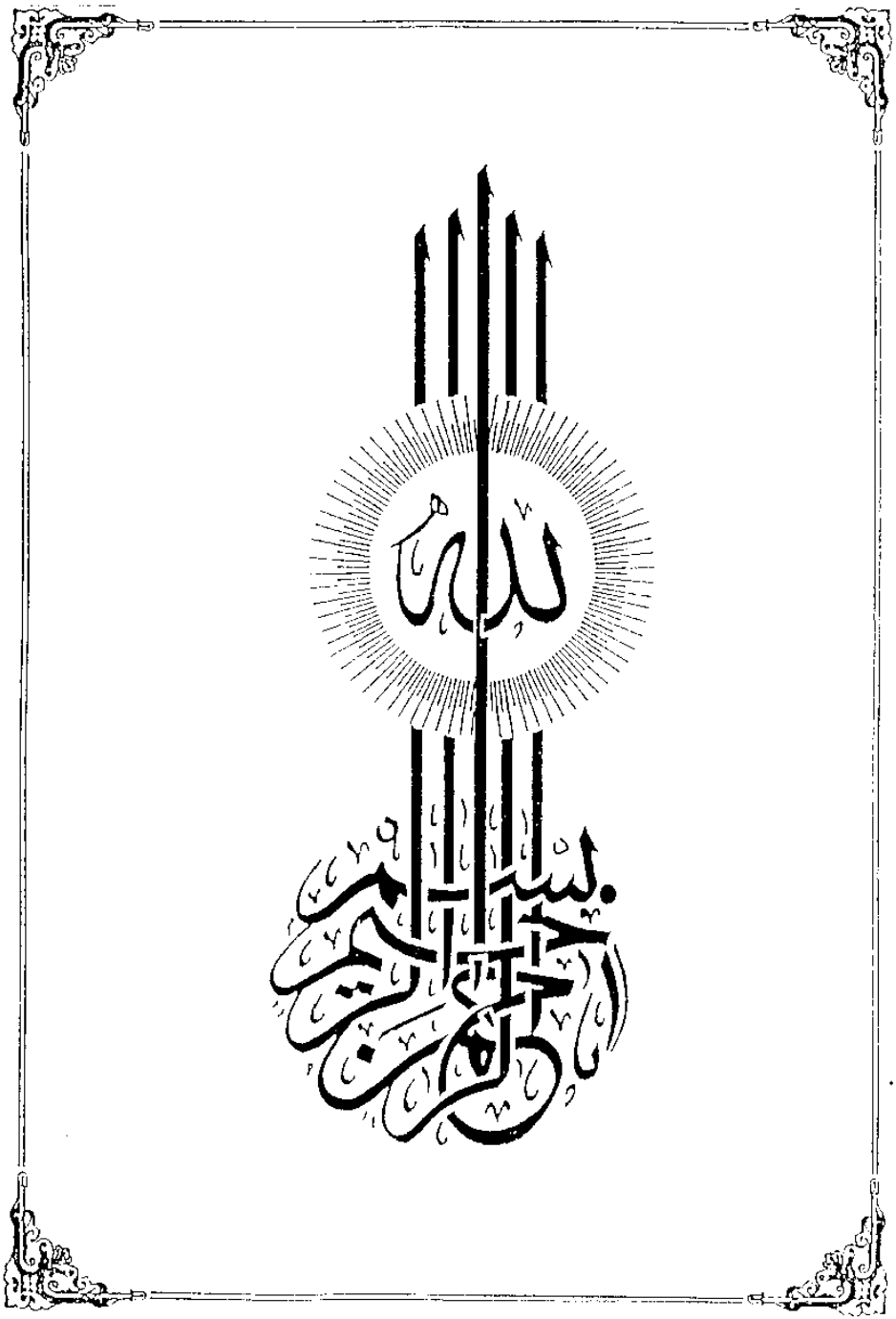

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Introduction

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Bronchial hyperreactivity is defined as an exaggerated bronchoconstrictive response to inhaled methacholine or histamine in much smaller doses than that required to produce in normal individuals ***(Mocklem, 1990).***

Bronchial inhalation challenges are used for identification of airway hyperreactivity in patients with no evidence of airway obstruction on routine pulmonary function testing, for this purpose many agents are used, methacholine being the most widely used and preferable one ***(Chai, etal. 1977).***

Airway hyperreactivity has been previously described in patients with asthma, chronic obstructive lung disease, cystic fibrosis, tuberculosis and sarcoidosis ***(Bechtel, etal. 1981)*** .

Bronchial hyperreactivity was found to be far more common amongst the elderly than previously recognised ***(Horsley, etal. 1993).***

Many studies have shown that viral respiratory infections play an important role in airway hyperresponsiveness and precipitate the symptoms of asthma .

Busse (1994) stated that viruses increase airway responsiveness in non asthmatic patients .

Apart from atypical bacteria and mycobacteria , no studies discussed the role of bacterial chest infection in BHR .

Aim of the work

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The aim of our work is to study bronchial hyperreactivity in old patients having bacterial chest infection .

Review of Litrature

Bronchial Hyperreactivity
BHR

Definition :

BHR Can be defined as an exaggerated airway narrowing in response to a wide variety of stimuli ***(Boushey, et al 1980).***

These stimuli include endogenous mediators such as acetyl choline,histamine , Leukotriens, prostaglandin and bradykinin and also exogenous stimuli such as dry air, acid aerosols, hypotonic and hypertonic aerosols ***(Sheppard , 1989).***

BHR can also defined as an exaggerated bronchoconstriction reaction of smooth muscles of airways narrowing on exposure to a small quantity of non allergic stimulus that doesn't provoke such a reaction in normal subjects ***(Postana , et al. 1989).***

Kaliner and Lemanske, (1993), defined bronchial hyperresponsiveness as an exaggerated airway reactivity to a variety of irritating stimuli which may be natural exposures (cold air, exercise , irritating chemicals , laughing and coughing) or to provocation's such as histamine, metha-choline, PGF2 a, adenosine, and cold air.

Mechanism :

The following are some of the possible mechanisms that determine BHR : -

1 - Alteration in smooth muscle responsiveness :

Asthmatic airway are more responsive to all bronchoconstrictor mediators that act on airway smooth muscle receptors due to the underlying abnormality in asthmatic airways resides in the smooth muscles and an inherent defect may exist in hyperreactive airway smooth muscle which would account for BHR ***(O'Byrne, 1992)*** .

Increased airway narrowing could occur simply as a result of alterations in mechanical factor in the airway which include a decrease in baseline airway caliber , decrease in the load against which airway smooth muscles contracts and increase in airway thickness ***(Sheppard, 1989).***

2 - Mucosal Edema :-

Edema of the airways may increase the responsivenes for geometric reasons , since submucosal thickening will greatly exaggerate the increased airway resistance that will occur with constriction of airway smooth muscle ***(Hogg ,et al. 1987).***

Edema of airway mucosa is due to increased capillary permeability with leakage of serum proteins into interstitial areas. Histamine, PGE2, LTC4, LTD4, PAF, and bradykinin are all capable of causing increased capillary permeability ***(Kaliner and Lemanske, 1993).***

3- Epithelial Damage : -

The mechanism for epithelial damage has not been systematically examined, although several mediators might participate ***(Kaliner and Lemanske, 1993).***

However it was found that ; while loss of airway epithelium in asthmatics may result in BHR , transient BHR can occur with an intact and functioning epithelium ***(O'Byrne, 1992).***

Eosinophil-derived mediators can cause epithelial damage, induce mast cell degranulation, and contribute to many of the pathogenic features, of asthma ***(Redwan ,et al. 1994).***

Mast cell degranulation is accompanied by the production of superoxide anion, which may lead to the production of hydrogen peroxide and other active radicals that may be responsible for BHR ***(Susann, et al.1994).***

4 - Autonomic Nervous System and BHR :-

Increased cholinergic tone and ∝-adrenergic responsinveness and decreased B-adrenergic responsiveness and non adrenergic inhibitory input are possible determinant's of BHR ***(Kaliner and Lemanske, 1993).***

Para - sympathetic Nerves :

Normal bronchial tone is mediated by vagal constrictive influences ***(Kaliner and Lemanske, 1993).***

Paraganglionic fibres, originating in the vagus nuclei travel via the vagus nerve to the ganglia adjacent to the airways and blood vessels, from these , postganglionic fibres travel to the smooth muscles, blood vessels , mucous glands and possibly the goblet cells ***(Morgeneroth, 1987).***

Upon stimulation of the vagus nerve, acetylcholine is released from the nerve endings. Cholinesterase, which is localized close to the site of release, blocks the action of acetylcholine very rapidly so that this substance is only of importance for regulation of airway smooth muscle close to its point of liberation and it's suggested that BHR is due to over activity of parasympathetic nervous system but there is no convincing evidenc that this is correct ***(O'Byrne, 1992).***

Studies on experimental animals have postulated that mediators such as histamine were capable of stimulating vagal afferent nerves found interlaced among the epithelial - cell lining of the airway , and upon provocations, histamine causes a reflex - vagally mediated - glandular secretion ***(Kaliner and Lemanske, 1993).***

Sympathetic Nerves :

The sympathetic nerve supply to lungs originates from upper thoracic preganglionic fibres that end in the extra pulmonary satellite ganglia . Post-ganglionic fibres can be visualized in the walls of the airway and surrounding blood vessels by fluorescent histochemical test for catecholamine ***(Richardson and Beland ,1976).***

Sympathetic nerves do not directly innervate airway smooth muscle in humans, but do supply airway autonomic ganglia, suggesting that sympathetic nerves can modulate neurotransmission through these ganglia. Adrenergic receptors are present presynaptically and on airway smooth muscle and are stimulated by circulating rather than neurally released catecholamines ***(O'Byrne, 1992).***

Two receptors determine sympathetic influence on BHRα and B receptors ***(Kaliner and Lemanske, 1993).*** It appears that B-blocker by itself is insufficient to cause significant bronchial hyperreactivity in health subjects. The airways narrowing and the increase in bronchomotor responsiveness after B-blocker in patients with

asthma could be due to unopposed bronchoconstrictor activity at the parasympathetic nervous systems, or unopposed bronchoconstrictor activity of the sympathetic nervous system mediated through alpha receptors ***(Boushey , et al. 1980).***

In Vivo , the role of ∝ - receptor stimulation in bronchial reactivity has been studied by assessing the ability of ∝-adrenergic antagonists to prevent bronchoconstriction induced by histamine. In patients with asthma ∝- adrenergic activity has an important role in the regulation of mucous secretion in the airway ***(Nadel , et al. 1979).***

Nonadrenergic Noncholinergic Mechanisms (NANC)

Autonomic control of human airways is more complex than it was previously recognized, for in addition to classic cholinergic and adrenergic pathways, neural mechanisms that are neither cholinergic nor adrenergic have been described ***(Richardson, 1981)*** .

The proposed NANC include ; nonadrenergic inhibitory nerves, vasoactive intestinal peptide, noncholinergic excitatory nerves, substance P, calcitonin gene related peptide, axon reflexes and other neuropeptides ***(Barnes, 1986).***

a - Nonadrenergic Inhibitory Nerves :-

In human airway smooth muscle this non adrenergic inhibitory nerve system is the only direct neural bronchodilator pathway from the trachea to the smaller bronchi since there is no functional sympathetic innervation and stimulation of this pathway produces pronounced and long lasting bronchodilatation, a response that can be inhibited by ganglion blockers ***(Barnes, 1986).***

(Said , 1982) claimed that vasoactive intestinal peptide is at least one of the neurotransmitters of nonadrenergic inhibitory nerves in airways, but ***O'Byrne,(1992),*** stated that the neurotransmitter of this inhibitory nervous system is not yet known and its role in controlling airways in asthma has been difficult to study.

b - Non Cholinergic Excitatory Nerves And Substance P:-

A non-cholinergic excitatory nerves were found in only one of eight airways tested so that this neural mechanism may not be easily demonstrable in humans ***(Lundberg, et al, 1983)***.

Substance P, an amino acid peptide, can contract airway smooth muscle, enhance bronchial mucosal edema and stimulate mucous secretion and may be the neurotransmitter for this NANC excitatory nervous system in human lung ***(Barnes, 1984).***

c - AXON Reflexes :-

Damage of airway epithelium that occur even in well controlled asthmatic airways exposes afferent nerve endings that are stimulated by inflammatory mediators.

The C-Fiber endings may be sellectively stimulated by bradykinin and prostaglandins produced in the inflammatory reaction which could result in a reflex cholinergic bronchoconstriction or may result in release of sensory neuropeptides from sensory collaterals in the airways ***(Barnes, 1986).***

The hypothesis of axon reflex in explanation of BHR has not been tested in asthmatic subjects ***(O'Byrnes 1992)***.

5 - Airway Inflammation And BHR :

Biopsy studies of the airways of asthmatics after allergen challenge have shown the following observations :

Within minutes of allergen exposure, mast cells degranulate and release mediators detectable in the bronchoalvealor lavage fluid, such as histamine, PGD2, and tryptase, the superficial vessels swell and become permeable, and edema is formed . Many additional factors have been identified that can activate mast cells, recruiting them to participate in inflammatory reactions unrelated to allergen exposure ***(White , 1993).***

The Mechanism by which inflammatory mediators released by inflammatory cells cause airway hyper- responsiveness is not known ***(O'Byrner 1992).***

Cytokines are extracellular signalling proteins , many of them are glycosylated