

Asthma characteristics and treatment essay examples

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Background

Asthma is a chronic disease associated with inflammation of the lining of airway and obstruction of lung airflow. It usually involves an increase in the number of inflammatory cells, most commonly eosinophils and to some extent basophils, mast cells, macrophages. (Eds. Brunton, et al., 2009)

Asthma, together with Chronic Obstructive Pulmonary Disease (COPD), is considered as one of the most common obstructive lung diseases

characterized by expiratory airflow obstruction. (eds. Longo, et al., 2012)

An asthmatic patient usually presents with recurrent events of shortness of breath (SOB), chest tightness, and wheezing, “ a high-pitched whistling sound when breathing caused by movement of air through narrow airways”

(MedlinePlus, 2012), a few of its hallmark symptoms. Physiological examination should reveal reversible narrowing of the bronchial airways and a marked increase in bronchial responsiveness to inhaled stimuli.

Pathologically, it is characterized by lymphocytic and eosinophilic inflammation of the bronchial mucosa. “ Remodeling” of the bronchial mucosa is also sometimes evident, seen as the thickening of the lamina reticularis beneath the airway epithelium and hyperplasia of the cells of all structural elements of the lungs. (Katzung, et al., 2009)

There are a number of factors contributing to an attack and exacerbation of asthma or the occurrence of airway hyperreactivity. (Morris, 2012)

Of all the factors, sinusitis is probably the most important exacerbating factor of the symptoms of asthma. Presence of a sinus disease or inflammation could largely trigger worsening of airway symptoms and thus, asthma. Treatment to eliminate such disease must be undertaken to relieve

symptoms of asthma, which usually requires a 10-day antibiotic management. (Morris, 2012)

Asthma may also be induced by outside elements that come in contact with the body, specifically the airways causing obstruction, such as intake of drugs, exposure to allergens and infection with virus. Aspirin-induced asthma is largely owed to the triad of asthma, aspirin and nasal polyps occurring in 5-10% of asthmatic patients. The non-steroidal anti-inflammatory drug (NSAID) is said to induce acute attacks with symptoms of nasal congestion, eye irritation, and flushing of the head and neck. These symptoms may occur later on the third or fourth decade of life. (Morris, 2012)

Another is presence of a viral infection, which mainly affects children. The presence of human rhinovirus C (HRVC) has been found to cause majority of acute asthma attacks in the young. There were also documented evidences connecting a history of rhinoviral infection during infancy to the onset of an asthma attack later on in childhood life, usually as wheezing. (Morris, 2012)

Daily activities and way of life may also be attributed to asthmatic attacks. Occupational factors are associated with 10-15% of adult asthma case, mainly classified as immune-related occupational asthma and non-immune related. The former, being chronic in nature, may occur within months or years after onset of exposure to respiratory irritants while the latter is characterized by an acute attack, which can occur somewhere between the first 24 hours of exposure to the irritants. (Morris, 2012)

Though the nature of the disease is chronic in itself, asthma attacks can either be acute or chronic and can range from mild to severe asthma attacks.

In mild asthma attacks, symptoms occur occasionally and are triggered by a factor such as exposure to allergens, exercise, or viral infection, while severe attacks are associated with episodes of excessive wheezing, dyspnea, orthopnea?, and at night. Though the symptoms are generally regarded as preventable owing to the existence of various effective treatments for the relief of acute bronchoconstriction and its subsequent prevention, the high cost of medication and hospital visits primarily hinder patient adherence to asthma management. (Katzung, et al., 2009)

Asthma and COPD are considered the most common obstructive lung diseases characterized by expiratory airflow obstruction. (eds. Longo, et al., 2012) It affects approximately 24million people in the US and is the most common chronic disease in children (about 7 million in morbidity). It is also the most common cause of hospitalization for the young in the US. (Morris, 2012) Asthma also accounts for 1-3% of hospital visits, 500, 000 hospital admissions per year, more admissions in the young than any other disease or illness, and greater than 5000 deaths annually. (Morris, 2012)

Pathogenesis of Asthma

The respiratory system primarily regulates flow and exchange of respiratory gases (i. e. oxygen and carbon dioxide) in the body. The major organ for respiration is the lungs, which consists of several components such as bronchioles, alveolar ducts, alveolar sacs, and alveoli, responsible for normal inhalation and exhalation. Gas exchange, or respiration, happens as a result of pulmonary ventilation, external respiration (exchange of gases between

lungs and blood), and internal respiration (exchange of gases between blood and the systemic capillaries). (Tortora and Derrickson, 2006)

Pulmonary ventilation, or breathing, happens when there is pressure difference between the atmosphere and the pressure in the lungs. This and the rate of airflow are also influenced by surface tension of the alveolar fluid, compliance of the lungs and airway resistance. (Tortora and Derrickson, 2006)

The alveoli in the lungs are covered with a thin layer of alveolar fluid consisting of a surfactant, which is usually a mixture of phospholipids and lipoproteins. This allows reduction of surface tension between the highly polar molecules of water and that of the gas making it easier to breathe. Compliance, on the other hand, refers to the extent of force required to stretch the lungs and lining of the chest. In general, compliance is related to elasticity of the lungs and surface tension. Lastly, airway resistance refers to the force exerted by the airway smooth muscles, especially the bronchioles, to the normal flow of air in the lungs, much like blood in the vessels. Normal airway resistance allows for a normal rate of airflow and subsequently normal breathing. Any condition that may narrow or obstruct this mechanism in the lungs increases resistance and therefore exerts more pressure to produce same rate of airflow. Such is the hallmark of asthma, an increased airway resistance due to obstruction or collapse of the airways. (Tortora and Derrickson, 2006)

Pathophysiology of asthma is assumed to involve three (3) processes such as: (1) airway inflammation, (2) intermittent airflow obstruction, and (3) bronchial hyperreactivity. (Morris, 2012)

Airway inflammation is mainly immunologic in nature and is attributed to a reagenic immunoglobulin (IgE), which is a class of antibody primarily responsible for type I hypersensitivity. Respiratory irritants such as proteins from dust mite, cockroach, molds, and pollens trigger production of IgE leading to an inflammation of the airway lining.

IgE antibodies in turn bind to mast cells in the airway mucosa, which then trigger production of inflammatory eicosanoids such as histamine, leukotrienes and prostaglandins and other inflammatory mediators producing a full blown allergic response. (Katzung, et al., 2009) Such a response is characterized by: (1) bronchoconstriction and bronchial hyperreactivity of the airway wall, (2) vasodilation and angiogenesis walls of the lungs, (3) plasma leakage and edema of the airway lining, and. (4) mucous hypersecretion and mucous plugs in the lumen

The resulting airflow obstruction is believed to be caused by a variety of changes such as the bronchoconstriction, airway inflammation, and airway remodeling. The first two (2) characterizes an early asthmatic response. Late asthmatic attack, on the other hand, usually follows after hours of the initial acute attack and maybe attributed to the sudden influx of the inflammatory cells to the bronchial mucosa. A long period of inflammation may allow for structural changes and eventual airway remodeling which might lessen chances of reversing airway obstruction. (Morris, 2012)

The obstruction also results to an increased airflow resistance and a decreased expiratory flow rates, which then results to a decreased exhalation and hyperinflation of the lungs. An inflamed or hyperinflated airway helps keep the airways open to maintain expiratory flow. A main disadvantage of this, however, is an increased effort in breathing. (Morris, 2012)

Bronchial hyperreactivity seems to be connected to airway inflammation as the factors that contribute to hyperresponsiveness such as allergen inhalation, ozone exposure, and viral infection would also cause airway inflammation. The increased responsiveness due to allergen exposure triggers the release of more mediators particularly eosinophils and polymorphonuclear leukocytes in the bronchial fluid. The phenomenon being largely associated to the late asthmatic response due to allergen inhalation is thought to be caused by airway inflammation mainly because treatment requires use of the corticosteroids. (Morris, 2012)

Bronchoconstriction associated with an asthma attack is believed to not only stem from the release of mediators but also from their activation of neural or humoral pathways in the brain. Vagal nerves trigger smooth muscle cells in the lungs which causes it to constrict. (Katzung, et al., 2009)

The many mechanisms that trigger an asthma attack allow the utilization various pharmacological treatments with differing modes of action that shall address each mechanism. Examples of this are the use of drugs that prevents binding of IgE to mast cells (mast cell stabilizers), blocks the action of mediators released (antihistamines and leukotriene-receptor antagonists), and relaxes the airway smooth muscle (sympathomimetic

agents). (Katzung, et al., 2009) Drugs having a dilatory effect on bronchial smooth muscles are also used in sudden asthma attacks for a faster relief of the symptoms. (eds. Brunton, et al., 2008)

Treatment of Asthma

The primary goal of treatment for asthma is to prevent an asthma attack using anti-inflammatory drugs centered to the airway. (eds. Brunton, et al., 2008) According to the Standard Treatment Guideline (STG) established in 2008 by the US National Heart, Lung, and Blood Institute in their publication “ Global Strategy for Asthma Management and Prevention”, treatment and management should be aimed at the ff.:

- a. Control asthmatic symptoms
- b. Maintain normal activity levels, as well as exercises
- c. Maintain pulmonary function, if possible normal
- d. Prevent exacerbations of asthma attacks
- e. Prevent side effects of medications
- f. Prevent mortality

(Morris, 2012)

For this reason, pharmacological treatment is centered in the control of asthma attacks (Controllers) and the relief of its symptoms (Relievers) for the maintenance of pulmonary function and subsequently quality of life of the patient. In all stages or classifications, a reliever medication such as rapid-acting inhaled beta-2-agonists is generally recommended. Patient education is also, thus, essential.

Intermittent asthma (Stage 1), characterized by symptoms of attack

occurring less than once a week, brief exacerbations and nocturnal symptoms not more than twice a month, is treated only with the reliever medication. Mild persistent asthma (Stage 2), on the other hand, has symptoms of attack more than once a week but less than once day, with exacerbations affecting activity and sleep and nocturnal symptoms happening more than twice a month and is mainly controlled by using low-dose inhaled glucocorticoids. Stage 3, which is Moderate Persistent Asthma, is characterized by a daily occurrence of symptoms with nocturnal symptoms appearing more than once a week. It is treated with low-to-medium-dose inhaled glucocorticoids AND long-acting inhaled beta-2-agonists. The last stage, Stage 4 or Severe Persistent Asthma, has symptoms experienced daily with both frequent exacerbations and nocturnal symptoms. There is also an evident limitation in one's physical activity.

Severe Asthma is commonly controlled with a three-drug regimen such as: (1) high dose inhaled glucocorticoid, (2) long-acting beta-2-agonists, and one of the following, (3a) sustained-release theophylline, (3b) leukotriene modifier, (3c) long acting oral beta-2-agonists, and (3d) oral glucocorticoids. (Morris,, 2012) Each drug classification is described below.

SYMPATHOMIMETIC AGENTS, specifically β 2-selective agonists or sympathomimetics appear to be of importance in both the control and relief of symptoms of asthma. This is primarily due to the mechanism of action of β 2-adrenergic receptors present in the lungs which is the prevention of bronchoconstriction and relaxation of smooth muscles in the lungs. (eds. Brunton, et al., 2008) They also partly inhibit the release of mediators from alveoli mast cells. The G-protein coupled receptors activate adenylyl cyclase

(AC) to cyclic adenosine monophosphate (cAMP), a secondary messenger responsible for the control of bronchial tone. A release in cAMP in the smooth muscles triggers efflux of intracellular calcium and hyperpolarization of the smooth muscle cells. The resulting cascade of activities ultimately leads to smooth muscle relaxation and bronchodilation. (Katzung, et al., 2009)

It is important that drugs given to asthmatic patients are β 2-selective because the other isotype β 1-adrenergic receptor has an undesired adverse effect on the cardiac smooth muscles (pronounced vasoconstriction). Only β -agonists used with β 1-activity are epinephrine and isoproterenol, even then they are only used for emergency situations. β 2-selective drugs are divided according to their duration of action to rapid/short-acting and long-acting. (Katzung, et al., 2009)

Short acting β 2 agonists such as albuterol, terbutaline and metoproterenol are mainly used to treat acute asthma attacks and therefore considered as asthma relievers. Albuterol or Salbutamol is the most commonly used reliever. On the other hand, long acting β 2 adrenergic agonists are used for longer lasting bronchodilating effects to β 2 receptors for up to 12 hours. Examples of such class of drugs are salmeterol and formoterol, and duration of action is believed to be caused by the drugs lipophilicity. There are also lesser chances of desensitization of β 2 receptors due to chronic use of the drugs than receptors on mast cells and lymphocytes. (eds. Brunton, et al., 2008)

β 2 adrenergic agonists are administered via inhalation to exert a greater local action to the airway smooth muscles. Though not generally recommended, oral therapy using β 2 agonists are sometimes employed in

severe cases. They are particularly useful in children who cannot tolerate metered-dose inhalers (MDI) yet, if used briefly. However, care should still be undertaken to monitor symptoms of tremulousness, muscle cramps, cardiac tachyarrhythmias and metabolic disturbances. (eds. Brunton, et al., 2008)

GLUCOCORTICOSTEROIDS, or systemic glucocorticoids, are used in both acute asthma exacerbations and chronic asthma attacks. Their effect is mainly attributed to their anti-inflammatory activity due in part to inflammatory cytokines. (Katzung, et al., 2009) They are, however, not directly related to smooth muscle relaxation but instead affect bronchial hyperreactivity and thus reduce exacerbations. Their anti-inflammatory effect in asthma is greatly due to inhibition of various allergic mediators such as the eicosanoids and leukocytes, together with the moderating action it has with cytokine and chemokine production. These mechanisms greatly favor the effective use of glucocorticoids in asthma management. (eds. Brunton, et al., 2008)

Inhaled glucocorticoids are more commonly used than oral glucocorticoids and are combined with β 2-agonists. Such drugs are beclamethasone, triamcinolone, flunisolide, budesonide, and fluticasone. Of the mentioned, the last three (3) are the most potent and have the least frequency in use with 1-2 puffs twice or even once daily. (eds. Brunton, et al., 2008) Doses of inhaled glucocorticoids are determined empirically considering severity and potency of glucocorticoid used. As mentioned, glucocorticoids are used in low dose in mild persistent asthma while can be increased during a moderate persistent asthma attack.

As with β 2 adrenergic agonists, use of glucocorticoids should also be

monitored for any untoward effects, the risk of which increases as the dose of the drug increase. Because of its steroidal nature, immune suppression is the most significant concern in glucocorticoid therapy. One of which is oropharyngeal candidiasis. Other side effects include bone resorption, dysphonia and carbohydrate & lipid metabolism. (eds. Brunton, et al., 2008)

While the above two classification of drugs are the most common, other groups of drugs are also considered in the control of asthma attack especially in severe cases.

THEOPHYLLINE is a methylxanthine drug with no established mechanism of action yet. However, it has been proposed that the bronchodilating action of theophylline is attributed to its inhibition of the phosphodiesterase (PDE) enzyme resulting to a higher concentration of cyclic AMP (cAMP) in tissues. This secondary messenger, as previously mentioned is responsible for eventual relaxation of airway smooth muscles. (Katzung, et al., 2009)

LEUKOTRIENE RECEPTOR ANTAGONISTS, Zafirlukast and Montelukast are another set of drugs considered for the management of asthma; the latter being the more commonly used. These drugs act as competitive inhibitor of leukotriene receptors LTD₄ and LTE₄. Zafirlukast is also believed to be an inhibitor of the 5-lipoxygenase enzyme which catalyzes leukotrienes from arachidonic acid. (Morris,, 2012)

Leukotriene, from previous discussions, is believed to play a role in asthma mainly through airway inflammation. They are not generally recommended for rapid broncodilatory effect and should not be used in emergency situations. However, they are believed to be effective in patients with mild asthma and showed significant improvement in pulmonary function and

decrease in frequency of asthma symptoms and exacerbations. (eds. Brunton, et al., 2008)

Other less frequently used drugs are the monoclonal antibody anti-IgE, antimuscarinic drugs, and cromolyn and nedocromil.

MONOCLONAL ANTIBODY treatment is targeted at the first antibody believed to be responsible for the cascade of asthma symptoms, IgE. There is one biological agent already approved for this regimen, Omalizumab, a recombinant humanized monoclonal antibody. The mechanism of action of Omalizumab is to bind to IgE so that resulting bigger molecule may not produce a lock-and-key effect with its IgE receptors on mast cells and basophils, subsequently preventing the allergic reaction. Treatment with Omalizumab is given only to adolescents and adults for moderate-to-severe persistent asthma. (Brunton, et al., 2008)

ANTIMUSCARINIC DRUGS, on the other hand, blocks acetylcholine released in airway smooth muscles ultimately inhibiting their contraction. However, a disadvantage of the use of antimuscarinic drugs is their relatively limited response because they only exert their inhibitory effects on parts that is mediated by the secondary messenger, acetylcholine. The most commonly used antimuscarinic drug in the market is Ipratropium bromide. It is delivered in high doses via inhalation because there is poor absorption systemically owing to its lipid nature. Another such drug which is longer acting is Tiotropium, as with Ipratropium is mainly used in the management of Chronic Obstructive Pulmonary Disease (COPD). (Katzung, 2009)

CROMOLYN & NEDOCROMIL, lastly, are extremely insoluble salts used as

inhalations, which are useful in patients with seasonal symptoms. They effectively inhibit both antigen- and exercise-induced asthma. One disadvantage to these drugs, however, is they have no effect on the smooth muscles of the lung and cannot reverse bronchoconstriction and obstruction. This is the main reason why these drugs are only taken as prophylaxis to asthma attacks. (Katzung, 2009)

Prognosis

Because of a large number of available drugs in the market for asthma, prognosis of asthma is usually positive despite its chronic nature. Mortality usually accounts for poor asthma management by the patient and poor lifestyle. It is related to loss in lung function increased up to 8-folds. Though asthma usually affects most of the young, diagnosed before the age of 18, almost half of them experience a marked decrease and even disappearance in symptoms by their early adulthood, (Morris,, 2012)

Asthma is one of the leading chronic illnesses throughout the world, affecting more than 300 million people across the globe. When uncontrolled, asthma can greatly reduce the quality of everyday life of a person. However, there exists a variety of treatment regimens both old and new for the control of asthma symptoms. Short-acting β 2-agonists are the mainstay relievers for all stages of asthma, while long-acting β 2-agonists and low-dose glucocorticoids are primarily used as controller medications for asthma. Though highly controllable, there are still cases of fatality and reduced activity due to lung function limitation or failure. It is, thus, important to note that patient

adherence to medication, their knowledge of the disease, and vigilance to prevention of asthma attacks greatly affect the patient's quality of life.

REFERENCES

Brunton, L. L., Parker, K. L., Blumenthal, D. K., Buxton, I. L. O., ed., 2008.

Goodman and Gilman's Manual of Pharmacology and Therapeutics. 11th ed. USA: The McGraw-Hill Companies, Inc.

Katzung, et al., B. G., Masters, S. B., Trevor, A. J., ed., 2009. Basic and Clinical Pharmacology. 11th ed. China: The McGraw-Hill Companies, Inc.

Longo, D. L., Kasper, D. L., Jameson, J. L., Fauci, A. S., Hauser, S. L., Loscalzo, J., ed., 2012. Harrison's Principles of Internal Medicine. 18th ed. USA: The McGraw-Hill Companies, Inc.

MedlinePlus, 2012. U. S. National Library of Medicine – National Institutes of Health Online Encyclopedia [online]. California, MD: A. D. A. M., Inc. Available through: <http://www.nlm.nih.gov/medlineplus/ency/article/003070.htm>. [Accessed 26 October 2012].

Morris, M. J., 2012. Asthma. [Web] USA: Medscape, WebMD LLC. Available at <http://emedicine.medscape.com/article/296301-overview>. [Accessed 24 October 2012].

Tortora, G. J., Derrickson, B., 2006. Principles of Anatomy and Physiology. USA: John Wiley & Sons.