Review of Literature
Asthma is one of the most common chronic diseases in the world. It is estimated that around 300 million people in the world currently have asthma (GINA)\(^27\).

**PRESENT WORLD SCENARIO OF BRONCHIAL ASTHMA:**

The National Health Interview Survey (NHIS) data on asthma prevalence in the United States of America demonstrate an almost doubling of asthma prevalence over the last quarter century, from 3.2 percent per 100 population in 1981 to 5.5 percent per 100 in 1996. The current data show a significant modification of prevalence by gender, in that males tend to predominate in the younger age group, whereas gender ratio equalize in the pubertal years, and females predominate throughout the rest of the adult life. One third of those affiliated with asthma are children under the age of 18 years\(^28\). A study conducted in 2006 by Sidney S Burman\(^29\) shows that there has been a sharp increase in the global prevalence, morbidity, mortality, and economic burden associated with asthma over the last 40 years, particularly in children. Approximately 300 million people worldwide currently have asthma, and its prevalence increases by 50% every decade.

There are only a few studies from India on epidemiology of asthma. In a study from Mumbai, conducted as part of the European Community Respiratory Health Survey, asthma prevalence in adults aged 20-44 years was reported to be 3.5% using ‘clinician diagnosis’ and 17% using a very broad definition (which included prior physician diagnosis and/or a positive bronchoprovocation test)\(^181\). According to the National Family Health Survey-2 report the estimated prevalence of asthma in India is 2468 per 100,000 persons\(^182\). As per the survey
conducted and published in 2006 by Agarwal A.N et al, asthma was present in 2.28%, 1.69%, 2.05 and 3.47% of a total of 73605 respondents respectively at Chandigarh, Delhi, Kanpur and Bangalore, with an overall prevalence of 2.38%\textsuperscript{183}. A projected estimate of 6.62 lakh in urban areas and 251.58 lakh in rural areas by 2011 was reported by Murthy KRJ et al\textsuperscript{183}.

The increasing number of hospital admissions for asthma, which are most pronounced in young children, reflect an increase in severe asthma, poor disease management, and poverty. Worldwide, approximately 180,000 deaths annually are attributable to asthma, although overall mortality rates have fallen since the 1980s. Most asthma deaths occur in those ≥ 45 years old and are largely preventable, frequently being related to inadequate long-term medical care or delays in obtaining medical help during the last attack\textsuperscript{29}.

Asthma is a syndrome rather than a condition. It is an episodic disease, with acute exacerbations, interspersed with symptom-free periods. Typically most attacks are short lived, lasting minutes to hours, and clinically the patient seems to recover completely after an attack. However there can be a phase in which the patient experiences some degree of airway obstruction daily which is termed as chronic asthma. This phase can be mild, with or without superimposed severe episodes, or much more serious with severe obstruction persisting for days or weeks, the latter condition is know as acute severe asthma.
Chronic asthma can be defined as a chronic inflammatory disease of the airways that is characterized by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli\textsuperscript{30}.

According to the Global Initiative for Asthma Management and prevention (GINA), a definition of Asthma is given as; “Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness (AHR) that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment”\textsuperscript{31}.
PATHOPHYSIOLOGY OF ASTHMA

CHARACTERISTICS OF CLINICAL ASTHMA

Symptoms (Figure 1)
A. Airway obstruction
B. Inflammation
C. Hyperresponsiveness

The concepts underlying asthma pathogenesis have evolved dramatically in the past 25 years and are still undergoing evaluation as various phenotypes of this disease are defined and greater insight links clinical features of asthma with genetic patterns. Central to the various phenotypic patterns of asthma is the presence of underlying airway inflammation, which is variable and has distinct but overlapping patterns that reflect different aspects of the disease, such as intermittent versus persistent or acute versus chronic manifestations. Acute symptoms of asthma usually arise from bronchospasm and require and respond to bronchodilator therapy. Acute and chronic inflammation can affect not only the airway caliber and airflow but also underlying bronchial hyperresponsiveness, which enhances susceptibility to bronchospasm.

Figure 1: The Interplay and Interaction between Airway Inflammation and the Clinical Symptoms and Pathophysiology of asthma.
PATHOPHYSIOLOGY AND PATHOGENESIS OF ASTHMA:

Airflow limitation in asthma is recurrent and caused by a variety of changes in the airway. These include Bronchoconstriction, airway oedema, AHR and airway remodeling.

Bronchoconstriction:

In asthma, the dominant physiological event leading to clinical symptoms is airway narrowing and a subsequent interference with airflow. In acute exacerbations of asthma, bronchial smooth muscle contraction occurs quickly to narrow the airways in response to exposure to a variety of stimuli including allergens or irritants. Allergen-induced acute bronchoconstriction results from an IgE-dependent release of mediators from mast cells that includes histamine, tryptase, leukotrienes, and prostaglandins that directly contract airway smooth muscle. Aspirin and other nonsteroidal anti-inflammatory drugs can also cause acute airflow obstruction in some patients, and evidence indicates that this non-IgE-dependent response also involves mediator release from airway cells. In addition, other stimuli (including exercise, cold air, and irritants) can cause acute airflow obstruction. The mechanisms regulating the airway response to these factors are less well defined, but the intensity of the response appears related to underlying airway inflammation. Stress may also play a role in precipitating asthma exacerbations. The mechanisms involved have yet to be established and may include enhanced generation of pro-inflammatory cytokines.

Airway Edema:

As the disease becomes more persistent and inflammation more progressive, other factors further limit airflow (Figure 2). These include
edema, inflammation, mucus hypersecretion and the formation of inspissated mucus plugs, as well as structural changes including hypertrophy and hyperplasia of the airway smooth muscle. These latter changes may not respond to usual treatment.32

Figure 2: Factors Limiting Airflow in Acute and Persistent Asthma.

Airway Hyperresponsiveness:

AHR—an exaggerated bronchoconstrictor response to a wide variety of stimuli—is a major, but not necessarily unique, feature of asthma. The degree to which AHR can be defined by contractile responses to challenges with methacholine correlates with the clinical severity of asthma.

The mechanisms influencing AHR are multiple and include inflammation, dysfunctional neuroregulation, and structural changes;
inflammation appears to be a major factor in determining the degree of AHR. Treatment directed toward reducing inflammation can reduce AHR and improve asthma control.

**Airway remodeling:**

Briefly, features of airway remodeling include:

- Inflammation.
- Mucus hypersecretion.
- Subepithelial fibrosis.
- Airway smooth muscle hypertrophy.
- Angiogenesis.

In some persons who have asthma, airflow limitation may be only partially reversible. Permanent structural changes can occur in the airway (Figure 2); these are associated with a progressive loss of lung function that is not prevented by or fully reversible by current therapy. Airway remodeling involves an activation of many of the structural cells, with consequent permanent changes in the airway that increase airflow obstruction and airway responsiveness and render the patient less responsive to therapy\(^3^4\). These structural changes can include thickening of the sub-basement membrane, subepithelial fibrosis, airway smooth muscle hypertrophy and hyperplasia, blood vessel proliferation and dilation, and mucous gland hyperplasia and hypersecretion. Regulation of the repair and remodeling process is not well established, but both the process of repair and its regulation are likely to be key events in explaining the persistent nature of the disease and limitations to a therapeutic response.
PATHOPHYSIOLOGIC MECHANISMS IN THE DEVELOPMENT OF AIRWAY INFLAMMATION:

Inflammation has a central role in the pathophysiology of asthma. As noted in the definition of asthma, airway inflammation involves an interaction of many cell types and multiple mediators with the airways that eventually results in the characteristic pathophysiological features of the disease: bronchial inflammation and airflow limitation that result in recurrent episodes of cough, wheeze, and shortness of breath. The processes by which these interactive events occur and lead to clinical asthma are still under investigation. Moreover, although distinct phenotypes of asthma exist (e.g., intermittent, persistent, exercise-associated, aspirin-sensitive, or severe asthma), airway inflammation remains a consistent pattern. The pattern of airway inflammation in asthma, however, does not necessarily vary depending upon disease severity, persistence, and duration of disease. The cellular profile and the response of the structural cells in asthma are quite consistent.

**Inflammatory Cells**

**Lymphocytes**

An increased understanding of the development and regulation of airway inflammation in asthma followed the discovery and description of subpopulations of lymphocytes, T helper 1 cells and T helper 2 cells (Th1 and Th2), with distinct inflammatory mediator profiles and effects on airway function (Figure 3). After the discovery of these distinct lymphocyte subpopulations in animal models of allergic inflammation, evidence emerged that, in human asthma, a shift, or predilection, toward the Th2-cytokine profile resulted in the eosinophilic inflammation characteristic of asthma. In addition, generation of Th2 cytokines (e.g.,
interleukin-4 (IL-4), IL-5, and IL-13) could also explain the overproduction of IgE, presence of eosinophils, and development of AHR. There also may be a reduction in a subgroup of lymphocytes, regulatory T cells, which normally inhibit Th2 cells, as well as an increase in natural killer (NK) cells that release large amounts of Th1 and Th2 cytokines\textsuperscript{35, 36}. T lymphocytes, along with other airway resident cells, also can determine the development and degree of airway remodeling. Although it is an oversimplification of a complex process to describe asthma as a Th2 disease, recognizing the importance of \( n \) families of cytokines and the chemokines has advanced the understanding of the development of airway inflammation\textsuperscript{37, 38}.

\textbf{Figure 3:} Airway Inflammation
Mast cells:

Activation of mucosal mast cells releases bronchoconstrictor mediators (histamine, cysteinyl-leukotrienes, prostaglandin D2) 39, 40, 41.

Although allergen activation occurs through high-affinity IgE receptors and is likely the most relevant reaction, sensitized mast cells also may be activated by osmotic stimuli to account for exercise-induce bronchospasm (EIB). Increased numbers of mast cells in airway smooth muscle may be linked to AHR 42. Mast cells also can release a large number of cytokines to change the airway environment and promote inflammation even though exposure to allergens is limited.

Eosinophils:

Increased numbers of eosinophils exist in the airways of most, but not all, persons who have asthma 43, 44 and 45. These cells contain inflammatory enzymes, generate leukotrienes, and express a wide variety of pro-inflammatory cytokines. Increases in eosinophils often correlate with greater asthma severity. In addition, numerous studies show that treating asthma with corticosteroids reduces circulating and airway eosinophils in parallel with clinical improvement. However, the role and contribution of eosinophils to asthma is undergoing a reevaluation based on studies with an anti-IL-5 treatment that has significantly reduced eosinophils but did not affect asthma control 46. Therefore, although the eosinophil may not be the only primary effector cell in asthma, it likely has a distinct role in different phases of the disease.
Neutrophils:

Neutrophils are increased in the airways and sputum of persons who have severe asthma, during acute exacerbations, and in the presence of smoking. Their pathophysiological role remains uncertain; they may be a determinant of a lack of response to corticosteroid treatment. The regulation of neutrophil recruitment, activation, and alteration in lung function is still under study, but leukotriene B4 may contribute to these processes.

Dendritic cells:

These cells function as key antigen-presenting cells that interact with allergens from the airway surface and then migrate to regional lymph nodes to interact with regulatory cells and ultimately to stimulate Th2 cell production from naive T cells.

Macrophages:

Macrophages are the most numerous cells in the airways and also can be activated by allergens through low-affinity IgE receptors to release inflammatory mediators and cytokines that amplify the inflammatory response.

Resident cells of the airway:

Airway smooth muscle is not only a target of the asthma response (by undergoing contraction to produce airflow obstruction) but also contributes to it (via the production of its own family of pro-inflammatory mediators). As a consequence of airway inflammation and the generation of growth factors, the airway smooth muscle cell can
undergo proliferation, activation, contraction, and hypertrophy-events that can influence airway dysfunction of asthma.

**Epithelial cells:**

Airway epithelium is another airway lining cell critically involved in asthma\(^{53}\). The generation of inflammatory mediators, recruitment and activation of inflammatory cells, and infection by respiratory viruses can cause epithelial cells to produce more inflammatory mediators or to injure the epithelium itself. The repair process, following injury to the epithelium, may be abnormal in asthma, thus furthering the obstructive lesions that occur in asthma.

**INFLAMMATORY MEDIATORS:**

**Chemokines:**

They are important in recruitment of inflammatory cells into the airways and are mainly expressed in airway epithelial cells\(^{38}\). Eotaxin is relatively selective for eosinophils, whereas thymus and activation-regulated chemokines (TARCs) and macrophage-derived chemokines (MDCs) recruit Th2 cells. There is an increasing appreciation for the role this family of mediators has in orchestrating injury, repair, and many aspects of asthma.

**Cytokines:**

These direct and modify the inflammatory response in asthma and likely determine its severity. Th2-derived cytokines include IL-5, which is needed for eosinophil differentiation and survival and IL-4 which is important for Th2 cell differentiation and with IL-13 is important for IgE formation. Key cytokines include IL-1β and TNF-α, which amplify
the inflammatory response, and GM-CSF, which prolongs eosinophil survival in airways. Recent studies of treatments directed toward single cytokines (e.g., monoclonal antibodies against IL-5 or soluble IL-4 receptor) have not shown benefits in improving asthma outcomes.

**CysteinyI-leukotrienes:**

They are potent bronchoconstrictors derived mainly from mast cells. They are the only mediator whose inhibition has been specifically associated with an improvement in lung function and asthma symptoms\(^54\), \(^55\). Recent studies have also shown leukotriene B4 can contribute to the inflammatory process by recruitment of neutrophils\(^56\).

**Nitric oxide (NO):**

It is produced predominantly from the action of inducible NO synthase in airway epithelial cells; it is a potent vasodilator\(^57\), \(^58\). Measurements of fractional exhaled NO may be useful for monitoring response to asthma treatment because of the purported association between Fractional Exhaled Nitric oxide (FeNO) and the presence of inflammation in asthma\(^59\).

**Immunoglobulin E (IgE):**

IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic diseases and the development and persistence of inflammation. IgE attaches to cell surfaces via a specific high-affinity receptor. The mast cell has large numbers of IgE receptors; these, when activated by interaction with antigen, release a wide variety of mediators to initiate acute bronchospasm and also to release pro-inflammatory cytokines to
perpetuate underlying airway inflammation\textsuperscript{39, 60}. Other cells, Basophils, dendritic cells, and lymphocytes also have high-affinity IgE receptors. The development of monoclonal antibodies against IgE has shown that the reduction of IgE is effective in asthma treatment\textsuperscript{7, 34}. These clinical observations further support the importance of IgE in asthma.

**C-reactive protein:**

C-reactive protein (CRP) is a protein found in the blood in response to inflammation (an acute-phase protein). CRP is produced by the liver and by fat cells (adipocytes). It is a member of the pentraxin family of proteins. It is not related to C-peptide or protein C.

CRP rises up to 50,000-fold in acute inflammation, such as infection. It rises above normal limits within 6 hours, and peaks at 48 hours. Its half-life is constant, and therefore its level is mainly determined by the rate of production (and hence the severity of the precipitating cause). Raised levels of CRP have been reported to be significantly associated with respiratory symptoms and non-allergic asthma but not with allergic asthma\textsuperscript{61}. In recent times, assessment of high sensitive CRP (hs CRP) has been employed to measure the low levels of CRP using laser nephelometry.

This test gives results with sensitivity down to 0.04mg/L. Increase in serum CRP levels measured by high sensitive assays may be associated with airflow obstruction and airway inflammation, and may serve as a surrogate marker of airway inflammation in asthma\textsuperscript{62, 63}.  

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MANAGEMENT OF ASTHMA: LINE OF TREATMENT

AVAILABLE:

Asthma management guidelines define control in terms of meeting each of a series of "treatment goals", including symptoms, rescue β₂-agonist use, exacerbations, lung function and adverse effects of medication. However, these goals are based on expert opinion, rather than being evidence based\textsuperscript{64}.

The goal of asthma treatment is to achieve and maintain clinical control. Medications to treat asthma can be classified as controllers or relievers\textsuperscript{65}.

**Controllers** are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects. They include inhaled and systemic glucocorticosteroids, leukotriene modifiers, long-acting inhaled β₂-agonists in combination with inhaled glucocorticosteroids, sustained-release theophylline, cromones, anti-IgE, and other systemic steroid-sparing therapies. Inhaled glucocorticosteroids are the most effective controller medications currently available.

**Relievers** are medications used on an as-needed basis that act quickly to reverse bronchoconstriction and relieve its symptoms. They include rapid-acting inhaled β₂-agonists, inhaled anti-cholinergics, short-acting theophylline and short-acting oral β₂-agonists (SABA) and long acting β₂-agonists (LABA). The development of long-acting inhaled bronchodilators and the production of oral sustained-release preparations of shorter acting drugs has made it more difficult to simply
categorize drugs as controllers or relievers; nevertheless this naïve classification is of value in the education of patients and in the production of management plans and educational literature.

Asthma medications can be roughly divided into two groups. The first group includes medications that reverse the constriction of bronchial tubes (bronchodilators). The second group includes medications aimed at preventing future attacks. These medications are often called as anti-inflammatory drugs. Simply said they can be divided into two general classes: long term control medications used to achieve and maintain control of persistent asthma and quick-relief medications used to relieve acute symptoms and exacerbations.

**MANAGEMENT OF CHRONIC ASTHMA**

**Drugs used for the Relief or Suppression of Symptoms (Relievers).**

**β₂ Adrenergic Agonists:**

The β₂ agonists are bronchodilators that give symptomatic relief but have no major beneficial effects on the underlying bronchial wall pathology. Indeed regular use of short acting β₂ agonists has been questioned because of the possibility that such treatment might have a detrimental effect on the control of asthma, possibly by increasing bronchial hyperresponsiveness either during treatment or soon after its withdrawal. Since β₂ agonists only give symptomatic relief, there seems little reason to encourage patients to take them regularly. If regular treatment is necessary for relief of symptoms this should stimulate the prescription of an anti-inflammatory preparation or an increase in its dose.
Inhaled short acting $\beta_2$ agonists (SABA):

The $\beta_2$ agonists relax airway smooth muscle and enhance mucociliary clearance. They also decrease vascular permeability and may modulate mediator release from mast cells and basophils, but they do not have any clinically relevant beneficial effects on the underlying chronic inflammatory disorder of the asthmatic airways. SABA should be used as necessary to relieve symptoms. Regular treatment with these compounds should be avoided wherever possible, unless the results of clinical trials of such treatment prove otherwise\textsuperscript{67-72}. The International Consensus report on Diagnosis and Management of Asthma\textsuperscript{73} suggests that if a patient has to use a SABA more often than 3 times a week this indicates asthma of sufficient severity to warrant regular treatment with an anti-inflammatory or prophylactic drug. The British guidelines\textsuperscript{74} suggest that this form of treatment would be appropriate if a bronchodilator inhaler has to be used more than once a day. It follows therefore that inhaled bronchodilator therapy alone should be used by patients with mild asthma. The inhalation of SABA prior to exercise is often necessary to prevent Exercise induced asthma.

The most commonly used $\beta_2$ agonists are Salbutamol, Terbutaline and Fenoterol. Fenoterol is not recommended these days because of reported side effects\textsuperscript{71, 75}.

Long acting $\beta_2$ agonists (LABA):

Slow release oral formulations of Salbutamol and Terbutaline are available and these increase the duration of tablets. Prodrugs are also now available which, when given orally, also greatly increase the duration of bronchodilation (e.g. Bambuterol).

In general, however, inhaled therapy is preferable to oral since the inhaled route allows more rapid onset of bronchodilator activity with a
minute fraction of the dose necessary to achieve the similar clinical response via the oral route; this therefore reduces the risk of adverse effects\textsuperscript{76}.

The production of $\beta_2$ agonists with a long duration of action when administered by inhalation has created a new era of bronchodilator therapy\textsuperscript{77}. Salmeterol and Formeterol are some of the LABA preparations available for inhalation. These LABA have the advantage of being effective when used twice daily. Although their role in the routine management of the asthmatic patient is far from clear. They do not have clinically relevant anti-inflammatory effects and therefore should not be used as the primary treatment of Asthma, since patients who require more than the occasional us of SABA should be treated with anti-inflammatory drug, usually an Inhaled corticosteroid\textsuperscript{73, 74, 77}. LABAs are used in combination with Inhaled Corticosteroids (ICS) for long-term control and prevention of symptoms in moderate or severe persistent asthma. Of the adjunctive therapies available, LABA is the preferred therapy to combine with ICS. Ultra long acting drugs like Indacaterol are under phase III trials and has got great promise for the future.

**Theophylline:**

In the early 1980 and early 1970’s, Theophylline was the most commonly prescribed bronchodilator. Theophylline relaxes the smooth muscle by inhibition of phosphodiesterase and probably via other mechanisms\textsuperscript{78}. A serum Theophylline concentration of 10-20µg/mL was recommended, since below this range bronchodilation is unlikely and above it, symptoms of toxicity are common\textsuperscript{79, 80}. There is an additive bronchodilator effect when Theophylline is given in combination with
Review of Literature

β₂ agonists and in an attempt to decrease adverse effects low doses of Theophylline preparations have been used in combination with Salbutamol or Terbutaline. However this therapeutic approach requires regular β₂ agonist which should be avoided in the treatment of asthma whenever possible. Theophylline has shown to increase the contractility of the diaphragm and render it less susceptible to fatigue, and also to increase the maximal transdiaphragmatic pressure. However, these actions of the drug are not likely to be of much clinical significance in asthma, except perhaps in severe acute episodes. Theophylline has shown to effect changes in the activity and functions of macrophages and Lymphocytes. Theophylline has been shown to reduce eosinophil infiltration of the airway and to produce a reduction in eosinophil activity after prolonged treatment. However the role of Theophylline in the treatment of basic underlying eosinophilic inflammation of asthma has yet to be determined, and may be minimal. In the future, low-dose Theophylline in combination with other drugs may become more established in the management of mild to moderate chronic asthma.

Anticholinergic agents:

The drugs of this category (muscrranic antagonists) most widely used in the treatment of reversible airway disease are ipratropium bromide and oxitropium bromide. Recent studies have also shown that Tiotropium bromide helps in improving airflow in the management of asthmatic patients. It is generally accepted that they are more effective in chronic obstructive pulmonary disease than in chronic Asthma. In chronic stable asthma, ipratropium bromide produces a smaller response of delayed onset compared with salbutamol, although older asthmatics

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may respond better to anticholinergic agents than do younger patients. In chronic asthma these drugs are usually reserved for use in patients who have not responded to conventional doses of ICS, when they are added to the treatment regimen as regular inhaled therapy. Ipratropium bromide is of much greater value in the treatment of severe acute episode than it is in the routine treatment of most patients with chronic asthma.

**Drugs with Anti-Inflammatory Properties: The Controllers or the Preventers:**

**Sodium Cromoglycate and Nedocromil Sodium:**

Sodium cromoglycate was first synthesized and its use in asthma reported in a small trial in 1967. Its clinical efficacy was established in both adults and children in a series of clinical trials performed in different parts of the world although in recent years its use has been almost completely restricted to the treatment of childhood asthma. Sodium cromoglycate is preferred mainly because it is virtually free of side-effects. This drug continues to be prescribed as first choice treatment for asthmatic children, particularly those with exercise–induced asthma, despite reports of early treatment failure and greater efficacy of low dose ICS. Sodium cromoglycate has no role in acute severe asthma.

Nedocromil has an extremely good safety record, although it has a reportedly unpleasant taste. The role of this drug in the management of chronic Asthma is difficult to define. It has little place in primary treatment, since its anti inflammatory properties and clinical efficacy are inferior to those of ICS. However, it may be of value in patients not well
controlled by conventional doses of ICS and should be used as a cortico-
sparing agent in patients on oral and high-dose ICS \cite{112,113}.

Compared with sodium Cromoglycate, the evidence suggests that
it is at least as good, or even superior, in the treatment of adult chronic
asthmatics\cite{114-116}. Like sodium cromoglycate it has no role in the
treatment of acute severe asthma.

**H₁-receptor antagonist:**

Although effective in the treatment of allergic rhinitis
antihistamines have little place in the treatment of asthma. The evidence
for and against the use of these drugs in asthma has been extensively
reviewed and it is apparent that the few patients who may benefit from
these compounds are young atopic individuals with mild seasonal
symptoms\cite{117}.

Ketotifen is a commonly used drug, especially in under developed
countries. It is a non-competitive H₁ – receptor antagonist and in vitro
has an inhibitory effect on mast cells similar to that of sodium
cromoglycate.

**Inhaled corticosteroids:**

ICS have been used in the treatment of asthma for nearly half a
century \cite{118,119}. The early treatment of both acute and chronic asthma was
with Adrenocorticotropin. However, following the development of a
number of glucocorticosteroids, prednisolone became the standard oral
therapy, and hydrocortisone and methylprednisolone have become
established as the most commonly chosen corticosteroids for I.V.
administration. Beclomethasone dipropionate and Budesonide are
commonly prescribed ICS for the treatment of asthma. Recently, approximately a decade later, Fluticasone propionate was marketed as a more potent drug than Budesonide. There can be doubt that the development of ICS has revolutionalized asthma therapy. The introduction of topical ICS therapy thus allowed withdrawal of systemic corticosteroid therapy in the majority of patients previously treated with these drugs and allowed a considerable reduction in dose in those patients with very severe disease acquiring treatment with high doses of prednisolone.

ICS has now become first line of therapy in the treatment of chronic asthma in most countries. They are most effective therapy available and have been shown to have beneficial effects on bronchial wall inflammation and AHR as well as symptoms.

Bronchial biopsies of patients being treated with ICS have shown a reduction in the number and activation of inflammatory cells in the airway \textsuperscript{120, 122} and also restoration of the disrupted epithelium and normalization of the ratio of ciliated cells to goblet cells \textsuperscript{120}. ICS reduces airway responsiveness to both direct and indirect stimuli. It has been reported that a single dose of ICS does not protect against Exercise induced asthma but a more prolonged therapy does\textsuperscript{122,123}. Corticosteroids presumably improve airway responsiveness by reducing the underlying inflammation, although any component of the airway disease caused by structural changes in the bronchial wall, such as thickening of the basement membrane and airway muscle hypertrophy, may be irreversible. Indeed there is now evidence that if ICS therapy for asthma is delayed the response, as judged by objective measurements of pulmonary function, is less good than when this treatment is given.
quickly after the diagnosis has been made. There are findings which have led to the concept of early intervention with ICS in the treatment of asthma. Early treatment is also important since it has been shown that objective response to ICS therapy is significantly better in patients treated soon after the onset of symptoms compared with treatment delayed by 2 years or more.

Numerous controlled clinical trials have now established that corticosteroids are effective in controlling symptoms of asthma and reducing the number and severity of exacerbations.

This proven efficacy of ICS, coupled with the knowledge that inflammation is found even in patients with very mild asthma, has led to the use of these drugs at a much earlier stage in treatment. A low dose of ICS is effective in mild asthma as is a once daily therapy. The various guidelines of asthma therapy recommend this form of treatment for any patient symptomatic enough to require the use of a bronchodilator inhaler more than once daily.

High-dose ICS is now frequently used in many countries for treatment of patients with more severe disease. It significantly reduces the need for maintenance oral corticosteroids, and many patients with ‘difficult to control’ chronic asthma have benefited from this treatment. ICS are effective in the treatment of asthma because they control bronchial wall inflammation, although this may take many weeks to be achieved. Whether ICS reduces the mortality from asthma remains to be demonstrated. Even though studies have shown it to be so (Saskatchewan Study), the numbers studied were too small to come to a firm conclusion. Patients have been reported to be responding fairly
well to ICS, there is a small minority who appear to be resistant or less responsive to these drugs. This type of condition has been named steroid-resistant asthma\textsuperscript{136}.

**Leukotriene Antagonists:**

Several orally administered Leukotriene antagonists have been released on the market, and it is likely that other variants will soon be available. It is possible that these drugs, Montelukast, Zileuton and Zafirlukast, may have a role in the treatment of mild asthma or as corticosteroid-sparing drugs. A more in depth study is required to determine their role in asthma.

**Systemic Corticosteroids:**

Corticosteroids are used in asthma on account of their anti-inflammatory properties. The anti-inflammatory actions include reduction in permeability and dilatation of blood vessels and suppression of accumulation of neutrophils; other effects include reduction in the number of circulating monocytes, eosinophils and basophils and extravascular sequestration of lymphocytes, together with the inhibition of fibroblast proliferation.

Oral corticosteroids, usually prednisolone, are the mainstay for treating and aborting acute exacerbations of asthma. Most patients who have had a severe attack of asthma previously, can recognize the symptoms. Such patients should be given prednisolone in advance and told to take it as soon as an attack is about to commence.
Based on the patient’s demographics the dose of prednisolone has to be adjusted. Usually a practice of $30-60$ mg is advised daily and then tapered by $5$ mg daily.

Oral corticosteroids are also necessary for the long term management of chronic asthma. But long term usage should be avoided as much as possible by maximizing other treatments and also by using short intermittent courses. But in some patients control of asthma is near impossible without regular prednisolone. In such cases, the dose of prednisolone should be kept as low as possible and periodic attempts have to be made to wean the patient off the drug$^{65}$.

Parenteral hydrocortisone is used primarily in the management of the acute severe attack. It usually takes several hours to have its optimum effect on airways; this probably depends on the severity of mucosal inflammation and plugging of lumen.

Other uses of parenteral corticosteroids are in the occasional management of chronic asthma and in patients who are unreliable in taking their medications. Intermittent injections of ACTH have been administered in the management of severe childhood asthma so that a long term suppression of adrenal gland is avoided. Due to the advent of cromoglycate and ICS, the need or this therapy has been reduced drastically.

An overall review of the medications for the management of asthma as dictated by NHLBI which is evidence based, can be given as follows:$^{32}$
Medications for asthma are categorized into two general classes: long-term control medications used to achieve and maintain control of persistent asthma and quick-relief medications used to treat acute symptoms and exacerbations.

LONG-TERM CONTROL MEDICATIONS:

Corticosteroids: Block late-phase reaction to allergen, reduce airway hyperresponsiveness, and inhibit inflammatory cell migration and activation. They are the most potent and effective anti-inflammatory medication currently available (Evidence A).

ICS’s are used in the long-term control of Asthma. Short courses of oral systemic corticosteroids are often used to gain prompt control of the disease when initiating long-term therapy; long-term oral systemic corticosteroid is used for severe persistent asthma.

Cromolyn Sodium and Nedocromil: Stabilize mast cells and interfere with chloride channel function. They are used as alternative, but not preferred, medication for the treatment of mild persistent asthma (Evidence A). They can also be used as preventive treatment prior to exercise or unavoidable exposure to known allergens.

Immunomodulators: Omalizumab (anti-IgE) is a monoclonal antibody that prevents binding of IgE to the high-affinity receptors on basophils and mast cells. Omalizumab is used as adjunctive therapy for patients ≥12 years of age who have allergies and severe persistent asthma (Evidence B). As indicated by several studies involving asthma patients between the age of 11 to 50 years, who were already receiving treatment
with glucocorticosteroids and LABA, anti-IgE appears to be safe as an additional therapy\textsuperscript{137}.

**Leukotriene Inhibitors:** Include LTRAs and a 5-lipoxygenase inhibitor. Two LTRAs are available—montelukast (for patients ≥1 year of age) and zafirlukast (for patients ≥7 years of age). The 5-lipoxygenase pathway inhibitor zileuton is available for patients’ ≥12 years of age; liver function monitoring is essential. LTRAs are alternative, but not preferred, therapy for the treatment of mild persistent asthma (Step 2 care) (Evidence A).

LTRAs can also be used as adjunctive therapy with ICSs, but for youths ≥12 years of age and adults they are not the preferred adjunctive therapy compared to the addition of LABAs (Evidence A). Zileuton can be used as alternative but not preferred adjunctive therapy in adults (Evidence D).

**LABAs:** Salmeterol and formoterol are bronchodilators that have duration of bronchodilation of at least 12 hours after a single dose.

- LABAs are not to be used as monotherapy for long-term control of asthma (Evidence A).
- LABAs are used in combination with ICSs for long-term control and prevention of symptoms in moderate or severe persistent asthma (step 3 care or higher in children ≥5 years of age and adults) (Evidence A for ≥12 years of age, Evidence B for 5–11 years of age).
➢ Of the adjunctive therapies available, LABA is the preferred therapy to combine with ICS in youth’s ≥12 years of age and adults (Evidence A).

➢ In the opinion of the Expert Panel, the beneficial effects of LABA in combination therapy for the great majority of patients who require more therapy than low-dose ICS alone to control asthma (i.e., require step 3 care or higher) should be weighed against the increased risk of severe exacerbations, although uncommon, associated with the daily use of LABAs.

➢ For patients ≥5 years of age who have moderate persistent asthma or asthma inadequately controlled on low-dose ICS, the option to increase the ICS dose should be given equal weight to the option of adding LABA.

➢ For patients ≥5 years of age who have severe persistent Asthma or Asthma inadequately controlled, the combination of LABA and ICS is the preferred therapy.

➢ LABA may be used before exercise to prevent EIB (Evidence A), but duration of action does not exceed 5 hours with chronic regular use. Frequent and chronic use of LABA for EIB is discouraged, because this use may disguise poorly controlled persistent asthma (Evidence D).

➢ In the opinion of the Expert Panel, the use of LABA for the treatment of acute symptoms or exacerbations is not currently recommended (Evidence D).

**Methylxanthines:** Sustained-release theophylline is a mild to moderate bronchodilator used as alternative, not preferred, adjunctive therapy with ICS (Evidence A). Theophylline may have mild anti-inflammatory effects. Monitoring of serum theophylline concentration is essential.
QUICK-RELIEF MEDICATIONS:

**Anticholinergics:** Inhibit muscarinic cholinergic receptors and reduce intrinsic vagal tone of the airway. Ipratropium bromide provides additive benefit to SABA in moderate-to-severe asthma exacerbations. May be used as an alternative bronchodilator for patients who do not tolerate SABA (Evidence D).

**SABAs:** Albuterol, levalbuterol, and pirbuterol are bronchodilators that relax smooth muscle. Therapy of choice for relief of acute symptoms and prevention of EIB (Evidence A).

**Systemic Corticosteroids:** Although not short acting, oral systemic corticosteroids are used for moderate and severe exacerbations as adjunct to SABAs to speed recovery and prevent recurrence of exacerbations (Evidence A).

There is only so much that the physician can do in the treatment of bronchial Asthma. In order to reinforce the effect of the medications provided and also if possible to reduce the dosage of the medications taken, it is imperative that other alternative therapies are taken as add on therapy to bring about improvement in chronic asthma.
COMPLEMENTERY AND ALTERNATIVE THERAPIES:

There are many complementary and alternative treatments that claim to treat asthma. However, because there have been few or no research studies on most of them, the effectiveness and safety of many are unknown. Some of the complementary and alternative therapies are:

HERBS AND VITAMINS:

It is believed that some Chinese herbs, like *ding-chan tang*, can decrease inflammation and relieve bronchospasm. *Ma Huang* (Ephedra), a common herb used in dietary supplements, has been used for years as a bronchodilator. Ephedra was recently banned by the United States Food and Drug Administration (US FDA)\(^1\)\(^3\)\(^8\). This is because it is said to cause constriction of blood vessels, increase the heart rate and blood pressure. Another study conducted by using a combination of three Chinese herbs, named as ASHMI, concluded that the intervention was a safe and effective alternative in the treatment of Asthma\(^1\)\(^0\). Some studies have also shown that vitamin C improves asthma symptoms\(^1\)\(^1\).

ACUPUNCTURE:

Its historic origin is an integral part of traditional Chinese medicine\(^1\)\(^2\). There are some reports that acupuncture can help in the treatment of asthma but further studies are ongoing. It is possible to envisage acupuncture as part of allopathic treatment for asthma when a scientific explanation emerges for its effects in neurophysiological or biochemical terms.
BIOFEEDBACK:

Learning to increase the amount of air inhaled has reduced fear and anxiety during an asthma attack for some asthmatics. Biofeedback is a system that uses electronic monitoring devices that feed information back to an individual to teach him or her to control body functions that normally happen automatically. Studies have shown that biofeedback may influence heart rate variability, which in turn may improve lung function and airway flow resistance seen in patients with asthma\textsuperscript{13}.

LIVE FISH CURE:

In India, the Bathini Goud family of Hyderabad treats Asthma by putting a live Murrel fish with herbal medications in the mouth of the asthma patient. A specially formulated herbal medicine is kept in the mouth of the live Murrel fish and in turn slipped into the mouth of the patient. The fish being live and slippery makes it easy to swallow. It is a treatment taken for a duration of 4 years along with diet restrictions which is said to cure asthma\textsuperscript{14}.

NATUROPATHIC THERAPIES:

For the breathing difficulties of asthma, naturopathy therapy includes\textsuperscript{15,139}:

- Oxidative naturopathic treatments such as ultraviolet blood irradiation and ozone therapy. These treatments’ goal is to rapidly rebalance the immune system for improvements in breathing, and reduced reliance on drug medications.
- Allergy testing/neutralization and oxidative naturopathic treatments to reduce underlying cause of asthma.
Dietary supplementation with natural anti-inflammatory such as omega-3 fatty acids.

Dietary changes to avoid foods that may lead to an allergic reaction, increased risk of asthma attack, or increased immune response.

Homeopathic remedies which can reduce immune response to allergens\(^{15}\).

**HYPNOSIS:**

Also known as hypnotic suggestion or hypnotherapy, involves placing the patient in an altered state of consciousness. Hypnosis can train a patient’s mind to relax when necessary, and the technique may be used anywhere. Children are especially good candidates for this technique because they tend to be hypnotized more easily than adults. Not all people are susceptible to hypnosis.

A controlled study done in 1968 had 127 patients in the hypnosis group and 125 controls who were taught breathing exercises. Results were assessed by daily dairy recordings of wheezing, bronchodilator usage, FEV\(_1\) and vital capacity (VC).

The average score for wheezing, bronchodilator usage was found to be reduced in both the groups but the reduction was seen to be more in the hypnosis group. The changes in FEV\(_1\) and VC between the groups were closely similar\(^{16}\).
BREATHING TECHNIQUES AND ASTHMA

PRANAYAMA:

Pranayama is a Sanskrit word meaning "lengthening of the prana or breath". The word is composed of two Sanskrit words, Prāna, life force, or vital energy, particularly, the breath, and "āyāma", to lengthen or extend. It is often translated as control of the life force. When used as a technical term in yoga, it is often translated more specifically as "breath control" as postulated by Sivananda swami.  

Pranayama is the fourth stage in Patanjali’s eight stage yoga discipline (141). With reference to yoga, prana can be described as something that flows continuously from somewhere inside us, filling us and keeping us alive: it is vitality. Pranayama is the measuring, control, and directing of the breath, and thus of energy within the organism, in order to restore and maintain health and to promote evolution. There are five forms of prana. They have different names according to the bodily functions with which they correspond.

These forms of prana are:

Udana-vayu: corresponding to the throat region and the function of speech.
Prana-vayu: corresponding to the chest region.
Samana-vayu: corresponding to the central region of the body and the function of digestion.
Apana-vayu: corresponding to the region of the lower abdomen and the function of elimination.
Vyana-vayu: corresponding to the distribution of energy into all areas of the body. Vayu is a sanskrit term meaning "air" or "breath". Emphasis is laid on two of these forms: prana-vayu and apana-vayu.

**Prana and Apana:**

That which enters the body is called *prana* and that which leaves is called *apana*. The term *apana* also refers to the region of the lower abdomen and all the activities that take place there. *Apana* is waste matter that accumulates because of many factors, some of which lie within our control.

The practice of yoga aims to reduce these impurities. People who are short of breath, cannot hold their breath, or cannot exhale slowly are seen as having more *apana*, whereas those who have good breath control are considered to have less *apana*. An overabundance of *apana* leads to problems in all areas of the body. We have to reduce the *apana* so that we can bring more *prana* into the body.

When we inhale, *prana* from outside the body is brought within. During inhalation, *prana* meets *apana*. During exhalation, the *apana* within the body moves toward the *prana*. Pranayama is the movement of the *prana* toward the *apana* and the movement of the *apana* toward the *prana*. Similarly, holding the breath after inhalation moves the prana toward the apana and holds it there. Holding the breath after exhalation moves the apana toward the prana.

“*Pranayama is what heart is to the human body*” as stated by B.K. Iyengar.\(^\text{142}\)
The Four Stages of Breathing:

Each cycle of breathing, usually thought of as merely a single inhalation followed by a single exhalation. This may be analyzed into four phases or stages, each with its distinct nature and its traditional Sanskrit name. The transitions from inhaling to exhaling and from exhaling to inhaling involve at least reversals in direction of the movements of muscles and of expansive or contractive movements of lungs, thorax and abdomen. The time necessary for such reversals can be very short, as may be observed if one deliberately pants as shortly and rapidly as he can. Yet they can be long, as one may notice if he intentionally stops breathing when he has finished breathing in or breathing out. The effects of this pause especially when they become lengthened, at first deliberately and then spontaneously seem remarkable. Thus in analysis of the four stages of breathing special attention is paid to these pauses, how to lengthen them and how to profit from them.

1. INHALATION (Puraka):

A single inhalation is termed puraka. It is a process of drawing in air; it is expected to be smooth and continuous. If a person should pause one or more times during the process of a single inhalation, the process might be spoken of as a broken puraka rather than as a series of purakas.

2. PAUSE AFTER INHALING (Abhyantara Kumbhaka) FULL PAUSE:

Kumbhaka consists of deliberate stoppage of flow of air and retention of the air in the lungs, without any movement of lungs or
muscles or any part of the body and without any incipient movements. A beginner may experiment by using some force to keep such pause motionless. Quite elaborate instructions and techniques have been worked out for this purpose.

3. Exhalation (Rechaka):

The third stage, exhalation, is called rechaka. Like inhalation, it too should be smooth and continuous, though often the speed of exhalation is different from that of inhalation.

Normally, muscular energy is used for inhaling whereas exhaling consists merely in relaxing the tensed muscles. Such relaxing forces air from the lungs as they return to a relaxed condition. However, a person can force air out with muscular effort; so when he sits or stands erect and has his abdominal muscles under constant control, muscular effort may be used for both inhaling and exhaling.

Especially if one deliberately smooths the course of his breathing and holds the cycles in regular or definitely irregular patterns, he is likely to use muscular energy at each stage, including the pauses. However, in a condition of complete relaxation, one should expect effort to be needed only for inhaling.

4. PAUSE AFTER EXHALING (Bahya Kumbhaka) EMPTY PAUSE:

The fourth stage, the pause after exhaling, is also called kumbhaka, especially when the stoppage is deliberate or prolonged. The fourth stage, the empty pause, completes the cycle which terminates as the pause ends and a new inhalation begins.
REVIEW OF THE EFFECT OF VARIOUS BREATHING EXERCISES ON CHRONIC BRONCHIAL ASTHMA

To support the use of Pranayama in asthma, numerous studies were conducted which show contradictory results on the beneficial effects of breathing exercises on bronchial asthma.

I. EFFECT OF PRANAYAMA ON BRONCHIAL ASTHMA:

1.1 Effect of Pranayama on Pulmonary function tests:

Using a comparison of Pranayama breathing exercises and respiratory physiotherapy breathing exercises, similar to the present study in terms of intervention was done as early as in 1978. Tandon MK conducted a study on eleven patients with severe chronic airways obstruction who were given training in yogic breathing exercises and postures. A matched group of 11 patients were given physiotherapy breathing exercises. After initial assessment of all patients had been completed, both the physiotherapy and the yoga groups were given training in the various physiotherapy and yogic maneuvers by a trained physio – therapist and a yogic teacher under medical supervision.

Both groups received training for one hour three times a week for the first four weeks, twice a week for the next four weeks, and once a week thereafter for a total of nine months. Both groups of patients were followed up at monthly intervals for nine months with pulmonary function tests and inquiry into their symptoms. Forced Expiratory Volume in 1 second (FEV₁) and Vital Capacity (VC) were the only two parameters measured of lung functions with the help of Godart Expirograph Spirometer. Mean FEV₁ at baseline in the yoga group was 0.965 L and at follow up showed a change of +0.022 L which was not
significant statistically. The Physiotherapy group had a baseline mean \( \text{FEV}_1 \) of 0.83 L which showed a change of -0.0815 L (p<0.1) at follow up. The VC of the yoga group at baseline was 2.565L and at follow up showed a change of +0.072, which was not significant. The physiotherapy group showed a baseline mean for VC as 2.438 and at follow up the value was +0.1127 (p<0.1). So the two groups showed no significant change from the control values after training in yoga or physiotherapy breathing exercises.

Some other studies on effect of yoga on healthy subjects have shown an improvement in the parameters of pulmonary functions\(^{144, 145}\). As published in 2008, a short term study was conducted by Makwana K \( et \ al, \) where fourteen normal volunteers between the ages of 19 to 27 underwent a twelve day course in the practice of yoga\(^{144}\). The observations in the form of Forced Vital Capacity (FVC), Breath Holding time (BHT) and Residual volume (RV) were recorded before and at the end of the practice period of twelve days. The mean group FVC prior to yoga was 4253.57ml ± 1478.88 and the post yoga group was 4767.86ml ±1575.36 (p = 0.03), which was clinically and statistically significant. The mean group BHT at TLC before yoga was 53.78sec ±27.23 and after yoga the BHT at TLC was 76.21sec ±42.2 (p < 0.001), which was also significant. The mean group BHT at RV before yoga was 27.57sec ±8.13 and after completion of yoga BHT at RV measured 31.64sec ±9.38 (p=.143) which was not significantly different. In conclusion, this study suggested that a practice of yoga for even a short duration of time showed an overall improvement in respiratory function similar to those found in more long term studies, suggesting that beginners of yoga can also receive health benefits and improved lung function. In order to come to a firm conclusion about the
benefits of yoga on lung functions, the study could have had a bigger sample size, be of a longer duration and a controlled study.

Effect of pranayama was studied in 20 males and 10 females suffering from perennial asthma (Murthy KRJ et al)\textsuperscript{18}. The mean age of the males was 32 years and of females was 25 years. The mean duration of asthma was 7 years in males and 5 years in females. Initial data regarding the clinical symptoms, dosages of drugs and Spirometry (absolute values, predicted percentages and response to bronchodilator aerosol) were recorded and were repeated every 15 days for 75 days. All were taught pranayama (rechaka, puraka with kumbaka) under supervision in the institute for half an hour every day in the morning. The assessment was made on the basis of the mean clinical symptom score, mean dosage of drugs and mean FEV\textsubscript{1}; mean percent predicted FEV\textsubscript{1}, FVC, ratio of FEV\textsubscript{1} by FVC (FEV\textsubscript{1}/FVC) percent and PEFR of the particular fortnight as compared to the initial values. The results of this study indicated that though there was a statistically significant increase in the absolute values of the different parameters of ventilatory function, a reduction in the dosages of drugs and decrease in symptom-score but airway obstruction as noted by FEV\textsubscript{1}/FVC percent remained unchanged. This study was not a controlled study and since the dosage of bronchodilator was decreased, this can be attributed to the FEV\textsubscript{1}/FVC percent remaining unchanged. The mean duration of asthma in this study was low so.

Nagarathna R and Nagendra HR, in 1985\textsuperscript{20}, conducted a study with fifty three patients with asthma, who underwent training for two weeks in an integrated set of yoga exercises, including breathing exercises, suryanamaskar, yogasana (physical postures), pranayama.
(breath slowing techniques), dhyana (meditation), and a devotional session, and were told to practice these exercises for 65 minutes daily. They were then compared with a control group of 53 patients with asthma, matched for age, sex, and type and severity of asthma, who continued to take their usual drugs. Patients were between the age group of 9-47 years with a mean of 26.4 years. By the end of the study 25 patients had dropped out. Parameters assessed were the number of attacks, severity, dosage of drugs used and PEFR. Using students’ t’ test inter group comparison showed a highly significant improvement in the number of attacks per week and drug treatment scores in the patients who practiced yoga. The control group had a mean initial value for number of Asthma attacks per week as 2.9 ± 3.01 and after follow up the value was reduced to 2.1 ± 2.7 (p <0.005), whereas in the yoga group the mean initial value was 3.55 ± 2.98 and after intervention there was reduction to 0.83 ± 2.49 (p < 0.005) which was statistically significant. The severity score of the control group was 1.6 ± 0.75 at the start of the study and reduced to 1.05 ± 0.85 after follow up. In the yoga group the score was 1.47 ± 0.66 as the initial value and after follow up it was 0.75 ± 0.8. The p value was non significant. The drug treatment score of the control group was 6.22 ± 7.18, initially and at follow up it was 7.9 ± 9.9, in the yoga group the initial score was 10.26 ± 13.16 and after intervention it showed a reduction to 2.08 ± 4.09. Here a statistically significant improvement in the drug score was seen in the yoga group (p< 0.005). The PEFR of the control group was 264.2 L/min ± 117.2 and at follow up increased to 290.8 L/min ± 12.2, where as the yoga group the initial PEFR was 290.1 L/min ± 93.1 and at follow up increased to 362.8 L/min ± 107.6 (p=0.03). It can be noted that the subjects of the yoga group had a baseline PEFR of 290.1 L/min, which may indicate a better asthma control than the subjects of the control
group. Since there was high rate of dropouts, 25 out of 54 patients, this resulted in a relatively small sample from whom the results had to be derived.

An integrated approach of yoga training programme of 2-4 weeks for 570 asthmatic subjects was followed up for 3 to 54 months was conducted by Nagendra et al. The yoga training programme consisted of yoga practices like yogasanas, pranayama, meditation, kriyas including the theory and lectures on yoga. The patients were allowed to decrease their dosage of bronchodilators over a period of time and those on corticosterone were encouraged to slowly shift to non steroidal bronchodilators and then taper off. The parameters assessed were the number, duration of and severity of attacks per week, PEFR.

Nagendra et al divided the results into 3 groups, based on the regular, irregular and discontinued practitioners of yoga. In the regular group (n=232), the number of attacks per week initially was 4.92 ± 5.48 and after follow up was reduced to 1.43 ± 2.52 (p<0.005). Duration of attacks at baseline was 11.91 ± 16.95 and at follow up the duration of attacks was recorded as 5.53 ± 10.64 (p<0.005). There is a significant improvement in the duration of attacks but the unit for the duration has not been mentioned. Severity of attacks based on their classification was recorded as 1.53 ± 0.92 at baseline and at follow up there was a reduction to 1.05 ± 0.90 (p<0.005) which was significant. Medications per week was recorded as 12.44 ± 11.55 at baseline wherein a decrease in the number of medications per week was seen at follow up as 6.40 ± 10.86 (p<0.005). The medications considered here, were the bronchodilator tablets or even the ayurvedic preparation taken by patients. Thus it is difficult to assess the reduction of medication when
two different types of therapy are taken into account together. Intake of cortisone tablets were assessed separately, where a reduction in the number was seen from 193.52 ± 203.44 at baseline to 55.16 ± 123.38 at follow up. A p value <0.005 was considered to statistically significant. The PEFR measured at baseline was measured to be 266.03 ± 122.15 which then increased to 328.92 ± 133.29 at follow up, with p < 0.005 which is clinically and statistically significant. BHT was another parameter assessed in this study where an improvement was seen from 23.70 seconds at baseline to 28.96 at follow up. A p value of <0.005 was considered to be significant both clinically and statistically.

It can be said that at a BHT of about 28 seconds at baseline shows a study group who was probably having mild asthma. The number of dropouts has been heavy, where out of 570 patients only 280 were assessed at the follow up. Nagendra et al have also recorded a fairly significant improvement even in those patients who were irregular proponents of yoga. But in those who had discontinued yoga there was no improvement of any parameters. No other pulmonary function tests were done to assess the extent of improvement in the improvement of asthma, which are better indicators of assessment. In this way they have tried to establish the long term efficacy of the integrated approach of yoga therapy in the management of bronchial asthma.

Nagrathna R and Nagendra HR along with Seethalaxmi conducted a study in 1991, using a yoga chair breathing for acute episodes of bronchial asthma. Study was on 86 patients of bronchial asthma, who had an average of 4.9 attacks per week. Here an attack was defined as an episode of wheeze and dyspnoea, which normally in the study required the patient to use an inhaler or other medication. None of
the patients could get any relief from these attacks without resorting to drugs. Of these 30% of the patients were already on steroids, to overcome their episodes of airway obstruction. These patients underwent an integrated approach of yoga training of 2 week duration spread over 3 years. The training program also consisted of yoga chair breathing procedure.

The whole procedure was of the duration of 25-60 minutes. Those patients who developed wheeze were subjected to yoga chair breathing. Peak flow rate was recorded using a Wright’s Peak Flow Meter. Patients who did not get any relief after the second round of relaxation were then allowed to take their rescue medications. Based on the results the patients were divided into 3 groups. The improved group, who had symptomatic relief with no wheezing and increased or no change in PEFR, the partially improved group, who felt partially improved but had reduced PEFR, and the No change group. Results did show a statistically significant improvement in the PEFR in one group, as seen in the previous study conducted by Nagrathna R et al. The PEFR in the Improved group increased from 112.6 L/min± 54.4 to 138.2L/min± 82.7 (p< 0.001). The other groups did not show any such variation. This study is an uncontrolled study. It is difficult to assess how many of the 86 patients improved their PEFR.

A study of the effect of yoga therapy in forty six patients with bronchial asthma conducted by Jain SC and Talukdar B in 1993 showed a significant increase in exercise tolerance and pulmonary functions. This study included assessment of both qualitative and quantitative parameters. All patients were taught yoga on an indoor basis for a period of forty days. Follow up was conducted at the end of
one year. At follow up PFT included FEV\textsubscript{1} and PEFR. At baseline the PEFR was 28.5L/min ± 46.7 which should a significant increase to 36.8L/min± 57.2. FEV\textsubscript{1} values at baseline was 40.8±8.27 of the percentage predicted which showed an increase to 52.6±7.18 of the percentage predicted (p<0.01). They have concluded that yoga helps as an economical mode of rehabilitation in bronchial asthma. This was an uncontrolled study where the follow up after 40 days of training was done at the end of 1 year. We can conclude that the effect on PFT is inconclusive.

A German study on the long term effects of breathing exercises and yoga in patients with bronchial asthma was conducted in 1994\textsuperscript{148}. To compare the effects of breathing exercises (BE) or Yoga (Y) on the course of bronchial asthma, thirty six subjects with a mild bronchial asthma were studied. The patients were randomly divided into three groups. Two of the groups participated in a 3 week training program of BE or Y while the third group rested without any additional treatment (control group). At the end of the training period the patients were asked to practice BE or Y on their own. Drug therapy and lung function parameters before and after a beta 2-agonist metered dose inhaler (Albuterol, ALB) were recorded prior to the training programme and at 4 weeks intervals for 4 months thereafter. The response to the beta 2-agonist was documented continuously in twenty eight patients. The mental state of the patients was elucidated by questionnaires.

Prior to the study a significant effect of inhaled ALB on the FEV\textsubscript{1} was shown without any significant between group differences. Both, BE and Y, caused a significant amelioration of the mental state but only the BE induced a significant improvement of lung function parameters.
compared to the individual baseline values. The FEV₁ increased significantly by 356.3 +/- 146.2 ml (p < 0.05) and the VC by 225.0 +/- 65.5 ml (p < 0.01). These long-term changes were not significantly different from the actual response to ALB. BE decreased the RV significantly by 306.3 +/- 111.6 ml (p < 0.05), an effect significantly higher compared to the beta 2-agonist (p < 0.01). They concluded that BE in combination with ALB has an additive effect.

Khanam AA et al, in 1996 investigated the effect of yoga on pulmonary functions including BHT on only 9 subjects. Yoga training was given for 7 days. The pulmonary functions of FEV₁, FVC, FEV₁/FVC and PEFR showed no change from the baseline. In case of another parameter that was measured BHT showed significant improvement (p<0.01) after intervention with yoga. Study was a short term and not a controlled study with only a small sample size.

Vedanthan et al, 1998 17, conducted a study on seventeen adult asthmatics who were university students in the age group of 19 to 52 years. They were randomly assigned to a yoga group (n=9) and a control group (n=8). Breathing and relaxation techniques including Pranayama, yogasanas and meditation were taught to the yoga group 3 times a week for 16 weeks for duration of 45 minutes. All participants in each group kept daily symptom and medication diaries, performed AM and PM peak flow readings, completed weekly questionnaires and underwent weekly Spirometry. The Pulmonary function tests included FEV₁, FVC, FMEF₂₅₋₇₅% (Forced Mid expiratory flow) and PEFR. At baseline the FVC in the yoga group was recorded as 4.31L± 1.06, which increased to 4.39L±1.12 at 4 weeks and to 4.51L±1.18 by the end of 6 weeks. But statistically it did not show any significance. In the control group, there
was an initial decline in FVC from 4.99L± 1.55 to 4.97L±1.67 but there was an increase to 5.63L±1.40 by the end of 6 weeks, but this variation was not significant. FEV$_1$ in the yoga group fluctuated between 3.22L± 0.68 at baseline to 3.10L± 0.86 in between to rise to 3.29L± 0.82 by the end of the study. In the control group a similar type of variation was recorded where the FEV$_1$ at baseline was 4.02L± 1.64 to decrease to 3.60L± 1.57 midway and then increase to 4.19L± 1.05 by the end of the study. The FMEF$_{25-75%}$ in the yoga group followed a similar trend, where the baseline value of 2.95L±1.26 decreased to 2.36L± 1.15 and then increased to 2.57L± 0.98 at 6 weeks. But the increase was still less then at what it was at baseline. In the control group there was an increase in the FMEF$_{25-75%}$ from a baseline value of 3.11L± 1.30 to 3.64L± 1.86 at 6 weeks. But all the values obtained of PFT were not statistically significant.

Thus no significance was derived from both the groups in this study. As confessed by the authors themselves, the possible reason for lack of statistical differences in the various parameters may be due to the fact that the sample size was too small, their pulmonary physiology was basically normal to start with and because the subjects needed to practice yoga over a longer period.

In 2002, it was published that Manocha et al conducted a double blind parallel group study where subjects were allotted either in the Sahaja yoga group and the other in the control group$^{150}$. One of the parameters assessed in this study was the lung function tests (described in detail under 1.7). At the end of intervention 21 subjects were tested in the yoga group and 26 subjects in the control group. The Spirometric parameters showed no significant changes where lung functions were
concerned or in the case of Peak expiratory flow rate, which was measured at home by the subjects. FEV₁ did increase marginally in the yoga group (-4.2) as compared to controls but the p value of 0.3 was not significant. The FEV₁/FVC ratio too increased marginally in the yoga group (- 0.008) when compared to that of the controls but again the p value was 0.5. Despite the statistical data, it was seen that in 9 subjects of the yoga group there was an increase of FEV₁/FVC from 48% at baseline to 66% at the end of intervention. Where as this change in the FEV₁/FVC was not recorded in the control subjects.

Six adult asthmatics (4 female, 2 male) in the age range of 23 to 48 years (mean age 34 years) volunteered to participate in a study using yoga breathing techniques (YBT). This study by Vedanthan et al. was to study the effect of yoga breathing techniques in relieving mild attacks of Asthma. So here, all the volunteers were taught YBT by a senior Yoga instructor over 2 sessions and were instructed to practice these sessions daily with the help of a prerecorded guiding tape over a period of 2 weeks. Subjects acted as their own controls. During the “control day,” their baseline vital signs were measured, including pulse rate (PR), blood pressure (BP), PEFR and Spirometry. They all then underwent exercise testing by climbing up and down 14 steps indoors with controlled temperature and humidity. Serial Pulmonary Function Test (PFT), BP, and PR were measured and recorded at 1 minute, 7 minutes, and 15 minutes post exercise. On the “control day,” subjects sat on a chair resting after exercise. They were treated by bronchodilator aerosol if their PFT dropped by 30% or more from their baseline values or if they complained of increasing difficulty in breathing during that period. On the “Yoga day,” subjects underwent similar baseline studies as well as exercise testing as outlined above, and all the subjects were requested...
to perform the YBT immediately after they had completed their exercise test. A drop of 20% in FEV₁ (one of the PFT parameters measured) was considered as being consistent with exercise induced bronchospasm (EIB).

Three out of six subjects on the “control day” needed bronchodilator nebulizer treatments to relieve their EIB, whereas only one out of 6 subjects on the “Yoga day” needed a nebulizer treatment. The average time for the PFT to return to baseline from the post-exercise drop was shorter (18 minutes v/s 24 minutes) on the “Yoga day” compared to the “control day.” Five out of 6 subjects subjectively felt better after the YBT compared to none on the “control day.” The study concluded that Yoga Breathing techniques (YBT) can be useful in relieving mild attacks of asthma (145). Here the sample size is too small to bring about a conclusive and significant result in projecting that these yoga breathing exercises were indeed helpful in relieving mild attacks of asthma.

Sodhi C et al 152 also conducted a study in 2009 where the role of yoga breathing exercises, as an adjunct treatment for bronchial asthma was assessed. One hundred twenty patients of asthma were randomized into two groups, yoga training group and control group. Each group included sixty patients. PFT were performed on all the patients at baseline, after 4 weeks and then after 8 weeks. The PFT parameters recorded were; PEFR, FEV₁, FVC, Forced Mid Expiratory flow in 0.25-0.75 seconds (FEF₂₅₋₇₅) and FEV₁/FVC %. Spirometric tests were done 4 hours after the last dose of short acting bronchodilator. The readings were recorded thrice and best of the three was noted.
In analysis Sodhi C et al have taken the percentages of the predicted value rather than the actual values. Yoga group showed a statistically significant increasing trend in % PEFR from 79.81± 10.78 at baseline to 80.75 ± 10.17 at 4 weeks to 82.45 ± 10.17 at the end of 8 weeks (p<0.01). It was reported that the inter group differences were not statistically significant. Percentage of predicted FEV\textsubscript{1} at baseline was 79.63 L ±10.35 and at 4 weeks was measured to be 81.03 ± 9.75, which increased to 83.16± 10.49 by the end of 8 weeks in the yoga group (p < 0.001). The control group did show a decrease in the Percentage of predicted FEV\textsubscript{1} but not statistically significant (p > 0.001). So FEV\textsubscript{1} was higher in the yoga group than in the control group. A similar increase in the percentage of predicted FVC from 84.33 ± 11.05 at baseline to 85.33 ±10.94 at 4 weeks, and to 86.67 ± 10.72 at the end of 8 weeks was reported (p <0.001) in the yoga group. Where as the Control group showed a variable change in %FVC with an overall decrease, which was not significant statistically. The inter group difference was not statistically significant too. Percentage of Forced mid expiratory flow in 0.25–0.75 seconds was higher in the yoga group than in the control group at both points of follow up but the difference between the groups was not found to be statistically significant. Yoga group showed a statistically significant increase in % FEF\textsubscript{25-75} from 75.41 ±10.42 at baseline to 76.88 ± 10.75 at 4 weeks to 79.50 ± 11.75 at 8 weeks (p<0.001) where as the control group showed a statistically significant decrease in the % FEF\textsubscript{25-75}.

Thus, it was concluded by Sodhi C et al that pranayama breathing exercises used adjunctively with standard pharmacological treatment significantly improves pulmonary functions in patients with bronchial asthma. Most of the subjects taken for this study had mild asthma, thus
the effect on patients with severe and chronic asthma needs to be assessed.

A similar study\textsuperscript{153} was conducted by Vemppati R \textit{et al}, randomized controlled trial was conducted on 57 adult subjects with mild or moderate bronchial asthma who were allocated randomly to either the yoga (intervention) group (n = 29) or the wait-listed control group (n = 28). The control group received only conventional care and the yoga group received an intervention based on yoga, in addition to the conventional care. The intervention consisted of 2-wk supervised training in lifestyle modification and stress management based on yoga followed by closely monitored continuation of the practices at home for 6-wk. The outcome measures were assessed in both the groups at 0 wk (baseline), 2, 4 and 8 wk by using Generalized Linear Model (GLM) repeated measures followed by post-hoc analysis. It was found that in the yoga group, there was a steady and progressive improvement in FEV\textsubscript{1} at 8 week and PEFR at 2, 4 and 8 week as compared to the corresponding baseline values. FEV\textsubscript{1} (% of predicted) recorded in the yoga group was 70.2 ± 17.4 at baseline and increased to 73.9 ± 19.6 at week 2. At week 4 it was recorded as 76.1± 20.1 and by week 8 it was 77.9 ± 17.2. There was significant inter group difference in FEV\textsubscript{1}.

Similarly FEV\textsubscript{1}/FVC (% of predicted) values in the yoga group increased from 80.4 ± 11.5 at baseline to 82.6 ± 13.3 at 2 week, at 4 week it was 83.7 ±13.4 but at 8 week it had decreased to 83.1 ± 12.2. The control group FEV\textsubscript{1}/FVC decreased over the follow up period. The average forced expiratory flow rate during the expulsion of 25-75\% of FVC (FEF\textsubscript{25-75}) showed an increase from the baseline to the 4 week assessment. At baseline it was 38.4 (±14.6), at 2\textsuperscript{nd} week it was 42.0 (±
19.4), at the 4\textsuperscript{th} and 8\textsuperscript{th} week it was 45.0. The control group showed a decrease in the FEF\textsubscript{25-75} throughout the different points of measurement. The intergroup difference was statistically significant. There was a significant reduction in EIB in the yoga group. But there was also no significant change in serum Eosinophilic cationic protein (ECP) levels during the 8 week study period in either group. The sample size in each of the group is small. This study by Vempati \textit{et al} has shown that yoga can improve the pulmonary functions in mild to moderate asthma.

The effect of Pranayama on bronchial asthma was assessed in a study conducted by Tarun Saxena \textit{et al},\textsuperscript{154} where fifty patients with bronchial asthma were enrolled into the study. Twenty five were enrolled into the Pranayama group and twenty five patients were taken as controls. The Pranayama group practiced breathing exercises for 20 minutes twice daily for twelve weeks, whereas the control group practiced meditation for 20 minutes twice daily for twelve weeks.

After twelve weeks of intervention it was seen that the Pranayama group showed a significant reduction in symptoms, improvement in FEV\textsubscript{1} and PEFR (p < 0.001) when compared to the control group\textsuperscript{148}. Symptoms recorded were cough, wheezing and dyspnoea. There was a significant reduction in the symptoms in the yoga group (p<0.01) but no reduction was recorded in the control group (p>0.05). FEV\textsubscript{1}% in the yoga group was 72 ± 1.7 at baseline but after 3 months of intervention, it increased to 84±2.29 (p<0.001). Whereas in the control group the FEV\textsubscript{1}% values increased from 73± 2.07 to 75± 2.56 but it was statistically not significant. The PEFR (L/min) values in the yoga group increased from 250 ±13.4 at baseline to 390±15.5 at the end of 12 weeks (p<0.001). The control group did not show a significant increase in the
PEFR at the end of the follow up. At baseline the PEFR was 252±15.3 and increased to 260±15.0 by the end of 12 weeks. They concluded that breathing exercises were helpful in bronchial asthma. This study has taken only FEV₁% as a measurement of lung functions and all subjects who were on medications were asked to discontinue their drug therapy.
1.2. EFFECT OF PRANAYAMA ON ADOLESCENTS WITH BRONCHIAL ASTHMA:

There were two studies conducted on adolescents with asthma. What was different from our study is that the age group was from the adolescent section of patients. A study conducted by Madanmohan et al.,\textsuperscript{145} on forty student volunteers between the ages of 12 to 15 years was enrolled into the study. The subjects were randomly divided into two groups of twenty each. One group was taught Pranayama and the other group acted as the control. Pulmonary functions comprising of FEV\textsubscript{1}, FEV and PEFR were measured in both the groups before and after 6 months. FEV\textsubscript{1} values at baseline was 1.84 (± 0.07) and after 6 months was 2.12 (±0.09); FEV\textsubscript{1} at baseline was 1.85 (±0.07) and after pranayama improved to 2.21 (± 0.09), whereas PEFR at baseline showed a mean of 271 (± 14.82) and after 6 months was 336.16 (± 19.04) with a p value of < 0.001. In the control group, the changes in these parameters were statistically insignificant. Thus, in this study it was concluded that Pranayama was beneficial in the improvement of pulmonary functions of children. The sample size needs to be bigger to come to a firm conclusion.

Another yoga related asthma study was also conducted on adolescents. The purpose of this study was to investigate the effect of yoga exercise on health-related physical fitness of school children with asthma. The study, conducted by Chen et al in 2009\textsuperscript{155}, employed a quasi-experimental research design in which 31 voluntary children aged 7 to 12 years were purposively sampled from one public elementary school in Taipei County. Of the 31 children enrolled 16 were assigned to the yoga group and 15 were taken as control. The fitness scores were
assessed at the time of pre-exercise (baseline) as well as at the seventh and ninth week following the completion of intervention. A total of 30 subjects (exercise group: 16, control group: 14) completed the follow-up. Compared to the normal children population, the study subjects (n = 30) were all below the 50\textsuperscript{th} percentile on all five physical fitness items of interest. There was no significant difference in scores between the two groups at baseline (pre-exercise) for all five fitness items. The control group had a higher mean value of BMI than the exercise group, but both groups were in the range of 35-55 percentile of the normal child population. There was a positive association between exercise habit after school and muscular strength and endurance among asthmatic children. Compared to the control group, the exercise group showed favorable outcomes on flexibility and muscular endurance. Such favorable outcomes sustained even after adjustment for age, duration of disease and steroid use, which were unequally distributed between two groups at baseline. There was a tendency that all item-specific fitness scores increased over time in the exercise group. The GEE (generalized estimating equations) analysis showed that, the yoga exercise indeed improved flexibility and muscular endurance after 7 weeks of intervention. After 2 weeks of self-practice at home, the yoga exercise continued to improve BMI, flexibility, muscular strength, and cardiopulmonary fitness. It was conducted with a small group of subjects but this study shows that further studies can be conducted in adolescents to bring about a control of asthma.
1.3 EFFECT OF PRANAYAMA ON DYSPNOEA SCORE AND SYMPTOMS:

As mentioned earlier, Tandon M K\textsuperscript{143} conducted a study on eleven patients with severe chronic airways obstruction who were given training in yogic breathing exercises and postures which was matched with another group of 11 patients who were given physiotherapy breathing exercises. Along with PFT, any changes in the chest symptoms were assessed. Tests were conducted on a monthly basis which culminated at nine months. Analysis in changes in symptoms after treatment was done by taking into consideration the assessment of improved exertion tolerance, quicker recovery after exercise, easier control over dyspnoea, overall improved chest condition and easier sputum evacuation. The exercise tolerance was greatly improved in the yoga group (p<0.03) in comparison to the Physiotherapy group. The ability to recover more quickly after exercise was also better in the yoga group (p<0.026). The yoga group had a much better control severe dyspnoea (p<0.006) as compared to the physiotherapy group. The sputum evacuation was equally improved in both the groups (p=NS) but the chest condition was more improved in the yoga group. Again, the sample size is small to differentiate the effects between the two groups.

It was stated that a significantly greater number of patients reported that with the help of yogic breathing exercises, they could control an attack of severe shortness of breath without having to seek medical help. This was not the case in the physiotherapy group. So the authors have concluded that the training in yoga is beneficial to patients with chronic severe airways obstruction.
Jain SC and Talukdar B in 1993\textsuperscript{147} showed a significant improvement in exercise tolerance and dyspnoea score in his study on 46 indoor patients. Exercise capacity was measured by 3 tests: (i) 12 minute walk test (12-md); (ii) physical fitness index (PFI) by modified Harvard step test; and (iii) Exercise-Liability index (ELI). Yoga therapy programme resulted in a significant increase in the pulmonary functions (as stated earlier) and exercise tolerance. The 12 minute walk test showed an increase in the distance by the subjects after training in yoga. At baseline the distance was 482.4± 101.5 meters where as at follow up, the distance increased to 520.2± 91.6 with a p value of <0.01. The physical fitness index also increased from 29.9±12.2 to 45.1±11.3 at follow up (p <0.01). The exercise induced bronchial liability index decreased significantly from 63.8±18.9 to 52.5±14.3 at follow up (p<0.01). A one-year follow-up study of 31 subjects showed a good to fair response with reduced symptoms score and drug requirements in these subjects.

Dyspnoea scale was assessed by using the MRC dyspnoea scale. After one year follow up it was seen that out of 31 moderate to severe asthma patients, 19 were in the category of mild asthmatics, 7 in the moderate category and 5 patients in the severe category from the earlier 8 patients. This is not a controlled study where there is a need to see the effect on controls.
1.4. EFFECT OF PRANAYAMA ON EXACERBATIONS OF ASTHMA.

As mentioned earlier\(^{19}\), in 1986 Nagarathna et al, a long term study with 570 patients with a follow up for 3 to 54 months was conducted. These patients had duration of asthma of \(23 \pm 19.44\) years. For follow up they had divided patients into regular practitioners, irregular practitioners and those who had discontinued yoga. Of the 570 patients, 232 were regular practitioners who had \(4.92 \pm 5.48\) attacks per week. At follow up the number of attacks was reduced to \(1.4 \pm 2.52\) \((p<0.005)\). This was a statistically significant decrease in the exacerbation per week. But even the irregular practitioners of yoga and those who had discontinued the practice of yoga showed a decrease in the number of attacks per week. The irregular practitioners of yoga have shown a reduction in the number of attacks from \(4.24 \pm 3.21\) attacks to \(2.24 \pm 3.15\) attacks per week. Interestingly, the discontinued group too showed a decrease in the number of attacks from \(4.08 \pm 2.77\) attacks to \(2.42 \pm 3.94\). Both the groups have a statistically significant result. So therefore, it is inconclusive whether yoga helps in improving the exacerbations of Asthma, according to this study.

In 1991, Nagrathna et al, conducted a study with 86 patients of bronchial asthma (146). These patients had an average attack of 4.9 per week. The patients in this uncontrolled study were taught yoga techniques to relieve attacks of wheeze or breathlessness without resorting to medications. The type of technique taught was yoga chair breathing which lasts for around 25 to 60 minutes. Based on the results the patients were divided into 3 groups. The Improved group, who had symptomatic relief with no wheezing, the Partially Improved group,
who felt better, and the No Change group. In the Improved group the number of episodes was 78 with a duration of only 29.8 seconds, that were relieved by the yoga chair technique and a p value of <0.003. Similarly, The Partially Improved group had 21 episodes that were relieved but the duration was increased to 35.6 seconds (p<0.05). In the No change group the number of episodes was 10 but the duration was 41 seconds (p <0.05). 70% of the episodes were shown to have been successfully relieved within a mean time of 30 minutes. Thus they recorded a significant reduction in the number of attacks in the 15 days of practice and in the long term follow up. The study has concluded that the patients showed great confidence and tried this technique before resorting to medication.
1.5 EFFECT OF PRANAYAMA ON THE USE OF BETA ADRENERGIC INHALERS:

Vedanthan et al, 1998\textsuperscript{17}, for a period of 16 weeks conducted a study on two groups of adult asthmatic patients which was of a complete random design. It was a blinded trial as the principal investigators did not know who were undergoing yoga therapy. There were 9 subjects in the yoga group and 8 in the control group. A weekly symptom questionnaire and pulmonary functions was assessed. The usage of medication was also recorded. In the control group none of the subjects reduced their use of inhalers instead 2 of the subjects increases the use of $\beta$ adrenergic inhalers. In the yoga group, of the 4 subjects on $\beta$ adrenergic inhalers, 2 showed no change in the dosage whereas the remaining 2 decreased the dosage. This study is insufficient in data where sample size is concerned and needs to be more detailed regarding the actual dosage of the inhalers. Vedanthan et al have concluded that Yoga techniques are a beneficial adjunct to the medical management of asthma.

Vempati R et al, in 2009\textsuperscript{153}, screened 132 potential subjects out of which 72 subjects were eligible. At the end of the 1 week run-in 60 were included. These subjects were divided into a yoga (intervention) group with 30 subjects and a control group with another 30 subjects.

But at the end of the study only 57 subjects were analyzed as there was 1 drop out in the yoga group and 2 from the control group. The outcome measures were assessed at 2, 4 and 8 weeks. The outcome measures included the intake of rescue medication and Spirometry which was earlier discussed in 1.1. In the case of rescue medication, the subjects were asked at the beginning to record the number of times they
had to use a bronchodilator inhaler. For subsequent usage of the drugs, the subjects were told to enter in their diary every time they had to use their drug. At any point of time, the frequency of rescue medication was calculated as the average number of times that the medication had to be used in a day. The frequency of rescue medication used showed a significant decrease over the 8 week period in both the groups. The p value being <0.001 for the yoga group and <0.05 for the control group. But the decrease in rescue medication use was achieved relatively earlier and was more marked in the yoga group than in the control group. There was significant difference in the usage of rescue medicine at the 2 and 4 week between the 2 groups as there was significant decrease in the frequency in the yoga group. Thus Vempati et al have postulated that yoga in bronchial asthma does reduce rescue medication usage earlier than in the case of conventional treatment. A longer duration of follow up is probably required to ascertain the efficacy of yoga in reducing the intake of rescue medication.
1.6. EFFECT OF PRANAYAMA USING THE PINK CITY LUNG EXERCISER (PCLE):

Numerous studies were conducted on subjects having bronchial asthma using a device called the Pink city lung exerciser. This device mimics Pranayama breathing technique. It consists of a mouth piece attached to a disc that contains a selection of apertures of 2-5 mm, anyone of which can be selected, through which inspired and expired air pass. The apertures carry a one way valve which halves the cross sectional area of the aperture during expiration and thus imposes a 1:2 ration on the duration of inspiration and expiration, although the inspiratory/expiratory ratio is unchanged.

Singh V et al conducted studies on mild asthmatics using a PCLE\textsuperscript{156}. Eighteen patients with mild asthma were assessed in a randomized, double blind, placebo controlled cross-over trial. After baseline assessments, they were trained in pranayama using the PCLE for 15 minutes twice a day for 2 weeks. So during the active period they were trained to breathe through the PCLE and during the control period they used a matched placebo device. At the end of the study period, 4 subjects had withdrawn from the study. FEV\textsubscript{1} was measured at two points during baseline.

FEV\textsubscript{1} increased from 3.23 L± 0.70 at baseline to 3.46L± 0.87 at the end of 2 weeks in the PCLE group, PEFR increased from 466 L/min ± 100 at baseline to 475 L± 99 in the PCLE group, symptom score was found to be reduced from 2.11 ±0.83 at baseline to 1.48± 0.75 at end of the study in the PCLE group and inhaler use decreased from 1.69 puffs/day ± 11.37 to 1.33 puffs ± 1.08 in the PCLE group at the end of
the follow up. Though there was improvement in the pulmonary function parameters, symptom scores and in the inhaler use between the PCLE group and the placebo group, the difference was small and not significant. However, $PD_{20}$ increased by .55 (SEM 0.36) doubling doses after PCLE, compared with 0.56 (0.36) doubling doses after placebo; this difference of 0.96 doubling doses (95% CI 0.23, 1.69) was statistically significant ($p=0.013$). In the questionnaire assessment at the end of the study, 15 of the 18 subjects reported benefit from the exercise devices, 9 of whom preferred the PCLE. The only side effect reported in this study was of mild dyspnoea by one subject during the use of the PCLE. But the study also mentions respiratory tract infections in two of the patients who used the PCLE device and the sample size should have been bigger with duration of follow up of at least 6weeks.

A similar study was conducted by Singh V in 1987\textsuperscript{157}, using the PCLE on twelve mild asthmatics to show the effect on Peak expiratory flow rate. This was then compared with the effect of a lung exerciser using a hot, humid air. The effect on PEFR was also seen with a placebo device. It was seen that five of the twelve asthmatics increased their PEFR using the PCLE, in comparison to the eight patients who improved with the lung exerciser using hot, humid air. With this study they concluded that slow breathing alone and also in combination with hot humid air has a non-specific bronchoprotective or bronchorelaxing effect. It is difficult to make such a conclusive statement as the sample size was too small and there was no control group included.

S Cooper \textit{et al} in 2003\textsuperscript{21} said that patients with asthma are interested in the use of breathing exercises but their role is uncertain. The effects of Buteyko breathing technique, a device which mimics
pranayama (a yoga breathing technique), and a dummy pranayama device on bronchial responsiveness and symptoms were compared over 6 months in a parallel group study. Methodology was that ninety patients with asthma taking ICS were randomized after a two week run-in period to Eucapnic Buteyko breathing, use of a Pink City Lung Exerciser to mimic pranayama, or a PCLE placebo device. Subjects practiced the techniques at home twice daily for six months followed by an optional steroid reduction phase. Primary outcome measures were symptom scores and change in the dose of methacholine provoking a 20% fall in FEV$_1$ during the first six months. Results showed that sixty nine patients completed the study.

Primary outcome measure of symptom score showed that in the PCLE and placebo group the symptoms remained relatively stable but was seen to be reduced in the Buteyko group. The median change in daily symptom scores at 6 months was 0 (-1 to 1) in the placebo group, -1(-2 to 0.75) in the PCLE group and -3 (-4 to 0) in the Buteyko group; the difference between the 3 groups was found to be significant (p=0.003). There was little change recorded the in PD 20 from baseline during the study. The estimated intergroup difference at 3 months and at 6 months was not found to be significant. In Buteyko versus control the estimated difference was recorded to be -0.3 at 3 months and 0.1 at 6 months, whereas in the PCLE versus control group it was estimated to be -0.03 at 3 months and 0.6 at the end of 6 months. The secondary outcome measures included assessment of FEV$_1$. FEV$_1$ measured showed no change in the different groups. Mean change in FEV$_1$ was seen to be 0.001 in the Placebo group, 0.06 in the Buteyko group and increased value of -0.002 in the PCLE group but not significantly so. Conclusion drawn was that the Buteyko breathing technique can
improve symptoms but does not appear to change bronchial responsiveness or lung function in patients with asthma. No benefit was shown for the Pink City Lung Exerciser. Even though this study uses a PCLE that mimics asthma, it is always prudent to practice pranayama as it is without the help of any devices. That is why some review of studies done by authors exclude any clinical trials conducted using devices that mimic breathing exercises\(^{22}\).
1.7. EFFECT OF PRANAYAMA ON QUALITY OF LIFE IN ASTHMA:

In 2002, a parallel group, double blind, randomized controlled trial was undertaken by R Manocha, to assess the effectiveness of this therapy as an adjunctive tool in the management of Asthma in adult patients who remained symptomatic on moderate to high doses of inhaled steroids. Subjects were randomly allocated to Sahaja yoga and control intervention groups. Both the yoga and the control interventions required the subjects to attend a 2 hour session once a week for 4 months. Allocation of groups was by randomized permuted blocks with a block size of four. The study group undergoing training Sahaja yoga was taught meditation which is a state called “thoughtless awareness” or “mental silence”. Meditation was conducted for a period of 10 to 20 minutes a day. The control group, on the other hand included relaxation methods, group discussion and cognitive behavior therapy-like exercises. The treatment with inhaled corticosteroids, long acting β-agonists, and/or Theophylline was continued unchanged throughout the study. The outcome assessments at baseline were PEFR, symptoms, bronchodilator usage, Asthma Quality of Life Questionnaire (AQLQ), Profile of Moods Assessment (POMS) and Spirometry with Methacholine challenge test. These assessments were repeated at the end of intervention and 2 months after the end of intervention.

59 subjects were randomized out of which 21 subjects completed the Sahaja yoga intervention and 26 subjects completed the control arm. At the end of the treatment period the level of airway hyperresponsiveness had improved by 1.6 doubling doses in the yoga intervention group and by 0.2 doubling doses in the control group with a
p value of 0.047. 2 months after the end of treatment there was no longer significant inter group difference. The improvement in AQLQ score at the end of the treatment period was 0.41 units greater in the yoga group than in the control group with a p value of 0.07, which just failed to reach statistical significance. After 2 months after end of treatment the intergroup difference between groups was even less significant with a p value of 0.3. The POMS scale showed greater beneficial changes (where tension and fatigue was concerned) in the yoga group than in the control group.

A randomized, controlled, double-masked clinical trial was conducted by Sabina AB et al in 2005. Random assignment was made to either a four week yoga intervention that included postures and breath work or a stretching control condition. Outcome measures were evaluated at 4, 8, 12, and 16 weeks and included the Mini Asthma Quality of Life Questionnaire, rescue inhaler use, spirometry, symptom diaries, and health care utilization. A total of sixty-two participants were randomized to the intervention and control groups, and 45 completed the final follow-up measures. Intention-to-treat analysis was performed. Significant within-group differences in post bronchodilator forced expiratory volume in 1 second and morning symptom scores were apparent in both groups at 4 and 16 weeks; however, no significant differences between groups were observed on any outcome measures. It was concluded that yoga conferred no appreciable benefit in mild-to-moderate asthma. They stated that the circumstances, under which yoga is of benefit in asthma management, if any, remain to be determined.
1.8 EFFECT OF PRANAYAMA ON ABSOLUTE EOSINOPHIL COUNT AND ESR:

Studies on estimation of Absolute Eosinophil count in asthmatics, which have been on breathing exercises as intervention, are very rare. The study that was reviewed below was a singular study that was found and the study design was not well defined.

Sathyaprabha TN et al in 2001 conducted a study on the efficacy of Naturopathy and Yoga on bronchial asthma\textsuperscript{139}. A total number of thirty seven patients (19 men, 18 women) with mean age 35.06 yrs (men), 40.74 yrs (women) enrolled into the study, for a period of 21 days. The treatment included diet therapy, Nature cure treatment and Yoga therapy. The various parameters including lung function test were measured at baseline and once a week. Results showed that there was significant improvement in lung functions, ESR and Absolute eosinophil count. The patients reported a feeling of well being, freshness and comfortable breathing. Naturopathy and yoga helps in inducing positive health, alleviating the symptoms of disease by acting at both the physical and mental levels.

**PHYSIOTHERAPY BREATHING EXERCISES FOR ASTHMATICS:**

Breathing exercises recommended by physiotherapists have a close similarity to the pranayama breathing techniques. The main aim in therapeutic exercise is\textsuperscript{159}

1. To mobilize secretions.
2. To teach effective coughing and remove secretions.
3. To teach relaxation.
4. To teach breathing control.
5. To teach postural awareness.
6. To mobilize thorax and shoulder girdle.

Breathing exercises are commonly incorporated into the overall pulmonary rehabilitation program of patients with acute or chronic pulmonary disorders. Breathing exercises are designed to retrain the muscles of respiration and improve or redistribute ventilation, lessen the work of breathing, and improve the gas exchange and oxygenation. Active range of motion exercises, to the shoulders and trunk also help expand the chest, facilitate deep breathing, and often stimulate the cough reflex.

The main aim of breathing exercises in physiotherapy:

- Improve or redistribute ventilation
- Increase the effectiveness of the cough mechanism and promote airway clearance.
- Prevent postoperative pulmonary complications.
- Improve the strength, endurance, and coordination of the muscles of ventilation.
- Maintain or improve chest and thoracic spine mobility.
- Correct inefficient or abnormal breathing patterns and decrease the work of breathing.
- Promote relaxation and relieve stress.
- Teach the patient how to deal with episodes of dyspnoea.
- Improve a patient’s overall functional capacity for daily living, occupational, and recreational activities.
For management of pulmonary conditions there are various exercises advocated in physiotherapy:

1. Diaphragmatic breathing.
2. Segmental breathing.

Physiotherapy breathing exercises in asthmatics help to build up the chest muscles involved in respiration. The aim of breathing exercise is to relax the chest muscles that are overworked, to teach the patient to use the abdominal muscles and diaphragm for respiration. These exercises help the patient to concentrate on breathing out rather than breathing in.

Pursed-lip breathing acts as a "splint." It creates a back pressure that helps to keep the airways open slightly longer to allow more stale air to escape so that more fresh air can replace it. The technique has the following benefits for those with breathing difficulties:

- It increases the amount of air taken in and let out of the lungs (vital capacity).
- Releases the trapped air from the lungs.
- It extends the time the airways are kept open and makes breathing less work.
- Lengthens exhalation time, which slows breathing.
- Moves old air out of and new air into the lungs.
- Improves gas exchange as more oxygen enters the body and carbon dioxide exits.
- Relieves shortness of breath.
- Improves the posture.
- Relaxes the body.
Many experts advocate pursed-lip breathing for asthmatics. During an asthma attack, less air reaches the lungs as the airways swell and produce excess mucus. This causes the person to work harder to breathe. Pursed-lip breathing can make breathing more efficient, minimizing the effort necessary to breathe by emphasizing the use of the diaphragm and the muscles between the ribs instead of chest and neck muscles. Patients who master the pursed-lip breathing technique may feel a greater sense of control over their respiratory disorder, according to advocates. This sense of confidence may help relax them during flare-ups, which in itself can lessen symptoms. However, as with other breathing techniques, there is little hard data to support claims that pursed-lip breathing can improve a patient's asthma. A number of studies with respiratory physiotherapy breathing exercises have been conducted on bronchial asthmatics.\textsuperscript{25, 143, 148, 154}
2. THE EFFECT VARIOUS TECHNIQUES OF PHYSIOTHERAPY BREATHING EXERCISES ON BRONCHIAL ASTHMA.

Different types of breathing exercises have been advocated by Physiotherapists. There are comparatively few studies dealing with the effect of these exercises on different parameters of bronchial asthma. The studies reviewed below are the effect of different techniques of breathing exercises on certain parameters in bronchial asthmatics.

2.1 EFFECT OF DEEP DIAPHRAGMATIC BREATHING ON BRONCHIAL ASTHMA:

Girodo et al in 1992 introduced a new diaphragmatic breathing technique. Sixty-seven asthmatic adults randomly assigned to deep diaphragmatic breathing training, physical exercise training, or a waiting list control group participated in a 16-week program\textsuperscript{160}. Deep diaphragmatic training resulted in significant reductions in medication use and in the intensity of asthmatic symptoms. Importantly, a nearly 300\% increase in time spent in physical activities also resulted from deep diaphragmatic training.

A follow-up at two months found many patients had returned to earlier medication levels and sedentary habits. They concluded that a strengthened musculature can replace the need for a physical aid in this respiratory habilitation; though adherence to its use may require individually-tailored encouragement.

In 2003, Thomas M conducted a study on 33 adult patients between the ages of 17 to 65 years\textsuperscript{23}. Patients were randomized into one group who were taught diaphragmatic breathing exercises and the
control group was given a 60 minute group session on asthma education by a nurse. Outcome measures were AQLQ, Nijmegen questionnaire and changes in medication dosage. The Breathing retraining group showed statistically significant improvement in the overall AQLQ scores (p=0.018), symptoms (p=0.04), activities (p=0.007) and environment domains (p=0.018) after one month of intervention when compared to the control group. There was significant difference in the emotions score (p=0.205). After 6 months of intervention, there was significant improvement only in the activities domain of the AQLQ when compared to the control group but a strong trend towards improvements in the other outcomes was recorded.

Where the Nijmegen score was concerned, there was reduction in the score in the intervention group at 1 and 6 months but a statistically significant difference was seen only after 6 months. In case of the inhaled corticosteroids and bronchodilator medication there were no significant changes in either of the 2 groups. The p values being 0.49 in the control group and 0.17 in the intervention group.

As recently as in 2009, M Thomas et al conducted a prospective, parallel group, single-blind, randomized controlled trial comparing breathing training with asthma education (to control for non-specific effects of clinician attention). Subjects with asthma with impaired health status managed in primary care were randomized to receive three sessions of either physiotherapist-supervised breathing training (n = 94) or asthma nurse-delivered Asthma education (n = 89). The main outcome was AQLQ, with secondary outcomes including Spirometry, bronchial hyper-responsiveness, exhaled nitric oxide, induced sputum eosinophil count and Asthma Control Questionnaire (ACQ), Hospital
Anxiety and Depression (HAD) and hyperventilation (Nijmegen Q) questionnaire scores. Enrolled subjects were randomized to either breathing training or control groups. The subjects were given 3 sessions each of physiotherapy supervised breathing training or 3 sessions of nurse- provided asthma education.

At the end of 1-month, assessments showed improvement in AQLQ scores in both the groups with no significant intergroup difference (0.78). But at the end of 6 months, assessment showed an improvement from baseline (0.92 to 1.32) compared with a smaller change (0.51 to 0.9) in the control group with a significant between group difference of 0.38 (0.08 to 0.68, \( p=0.01 \)). The secondary outcomes were also assessed at the end of 1 month and 6 months. There was no significant change in methacholine \( PC_{20} \) from baseline in either group (mean change 0.29) doubling doses in BT group (\( p=0.19 \)) and 0.09 doubling doses in control group (\( p=0.72 \)). The between group difference was 0.02 doubling doses (\( p=0.54 \)). Small increase in \( FEV_1 \) was recorded in both the groups with a non significant trend favoring the control group. Minute volume was reduced in both the groups with no significant intergroup difference. The differential eosinophil count did not change significantly in either group with no significant intergroup difference. The questionnaires showed changes from baseline to the time of assessment. Significant improvement in ACQ were observed in both the groups at the one month assessment with no significant intergroup difference (\( p=0.70 \)), there was some improvement in the BT group at 6 months. The between group difference was significant with a \( p \) value of 0.04. The HAD Anxiety and Depression scores in both groups, showed no change 1 month following the intervention. At the 6 month assessment significant between group differences were observed.
focusing the Breathing Training group in the Anxiety score (mean difference is -1.05, p=0.02) and the Depression score (mean difference is -0.75, p=0.03).

The same scenario was seen in the NQ score, at 6 month the difference favored the BT group having a mean difference of -3.16 and a p value of 0.005. Bronchodilator usage was decreased in both the groups with no significant difference between groups (p=0.72). Finally, they summarized that this randomized controlled trial found that the adults with asthma when trained in breathing exercises showed improvement in health status, symptoms and psychological well being after 6 months compared to those who received an asthma education programme. The breathing exercises, as recorded in this study did not alter objective measures of airway hyper responsiveness or inflammation, so cannot replace the need for anti-inflammatory medication. They concluded that the breathing exercises may potentially have a role in patients with suboptimally controlled mild to moderate asthma, but the use of these techniques has to be in tandem with anti-inflammatory pharmacotherapy\textsuperscript{161}. 
2.2 EFFECT OF SHALLOW NASAL BREATHING IN ASTHMATICS:

A double blind, randomized, controlled trial was conducted on fifty seven subjects by Slader CA et al in 2006\textsuperscript{25}, who were randomized to one of the two breathing techniques learned from an instructional video. The primary aim of this double blind study was to compare the effects of breathing exercises focusing on shallow nasal breathing (Group A) with those of non-specific upper body exercises on asthma symptoms (group B). The other parameters assessed were Quality of life (QOL), other measures of disease control, and inhaled corticosteroids dose. This study also assessed the effect of peak flow monitoring on outcomes in patients using breathing techniques. After a 2 week run in period, fifty seven subjects were randomized to one of two breathing techniques. During the following 30 weeks subjects practiced their exercises twice daily and as needed for relief of symptoms. After week 16, two successive ICS down titration steps were attempted. The primary outcome variables were Asthma Quality of Life (QOL) score and daily symptom score at week 12. There was no significant difference between groups where the primary outcome measures were concerned. AOLQ had a baseline between groups p value of 0.04, at week 12 the p value increased to 0.29 and to 0.27 at week 28.

There were small differences favouring group B in daytime symptom scores (p=0.0192) and night-time symptom scores (p=0.0636). The secondary outcome measures of Reliever use showed a dramatic reduction from week 1 after randomization but no significant between group differences was seen at week 12 (p=0.17). The proportion of reliever free days increased in both groups between baseline and week 12 (group A had baseline of 6.7%, week 12 it was 53.5% and p = 0.001, group B: baseline was 8.3%, at week 12 it was 55.3% with a p value of
There was no significant differences between groups (p =0.49 at baseline; p=0.19 at week 12). The other variables of ACQ scores did not show any significant difference at week 12 (p=0.234) however there was a statistically significant improvement in ACQ at week 12 in group B (p=0.0324) but not in group A (p=0.49). No significant intergroup difference was seen in Patient or Physical Global Assessments at week 12, though there was improvement was seen in group B but not group A when compared to the baseline values (p=0.046 and 0.073 respectively). FEV_1 values recorded did not show any significant intergroup differences at week 12 but group B did show a reduction in FEV_1 (0.084L) by week 12 (p=0.0359). The baseline daily dosage of ICS was 800µg for both the groups, at the end of study the dosage was reduced to 200 µg and 187.5 µg in group A and group B respectively. In summary, this study shows that two completely different types of breathing techniques, taught by video, could lead to a similar level of improvement in asthma outcomes particularly those relating to the use of short acting β₂ agonists.

This study did not find any improvement on physiological parameters of airway inflammation. They concluded that that the breathing techniques may be useful in the management of patients with mild asthma symptoms who use reliever frequently, but in the present there was no evidence to show that shallow breathing techniques favour over non-specific upper body maneuvers.
2.3 IMPLEMENTATION OF PAPWORTH METHOD BY PHYSIOTHERAPISTS IN BRONCHIAL ASTHMA:

An integrated breathing and relaxation technique known as the Papworth method has been implemented by Physiotherapists since the 1960s for patients with asthma and dysfunctional breathing, but no controlled trials had been reported. A study by Elizabeth Holloway has tried to evaluate the effectiveness of the Papworth method in a randomised controlled trial. Eighty five patients (36 men) were individually randomised to the control group (n = 46) or to the intervention group receiving five sessions of treatment by the Papworth method (n = 39). Both groups received usual medical care. Assessments were undertaken at baseline, post-treatment (6 months after baseline) and at 12 months. The primary outcome measure was the St George's Respiratory Symptoms Questionnaire (SGRQ). Secondary outcome measures included the Hospital Anxiety and Depression Scale (HADS), the Nijmegen dysfunctional breathing questionnaire and objective measures of respiratory function. Post-treatment and 12 month data were available for 78 and 72 patients, respectively. At the post-treatment assessment the mean score on the SGRQ Symptom subscale was 21.8 in the intervention group and 32.8 in the control group (p = 0.001 for the difference). At the 12 month follow-up the corresponding figures were 24.9 and 33.5 (p = 0.007 for the difference).

SGRQ Total scores and HADS and Nijmegen scores were similarly significantly lower in the intervention group than in the control group. The groups did not differ significantly following the treatment on objective measures of respiratory function except for relaxed breathing rate. Thus, they found that the Papworth method appears to ameliorate
respiratory symptoms, dysfunctional breathing and adverse mood compared with usual care.

Studies have been reported where the Breathing exercises have shown a better result in pulmonary functions when compared to the Pranayama group\textsuperscript{148} where as there also have been studies that show symptomatic improvement in the Pranayama group when compared to the patients having physiotherapy breathing exercise as an intervention\textsuperscript{143}.
BUTEYKO BREATHING TECHNIQUE (BBT):

Buteyko breathing technique was developed by the Russian doctor Konstantin Pavlovich Buteyko. The method is taught as a complementary therapy and several small clinical trials have shown that it can safely reduce asthma symptoms and the need for reliever medication in some people, as well as increasing quality of life scores\textsuperscript{162}. However, improvement takes time and commitment, requiring daily exercises over a period of weeks or months. At the core of the Buteyko method is a series of breathing exercises that focus on nasal-breathing, breath-holding and relaxation.

The \textit{British Guideline on the Management of Asthma 2008}\textsuperscript{74} grants permission for British health professionals to recommend Buteyko, stating that the method "may be considered to help patients control the symptoms of asthma". The guideline also grades clinical research on Buteyko with a 'B' classification - indicating that high quality supporting clinical trials are available. No other complementary therapy has been endorsed by this body for the treatment of asthma\textsuperscript{21, 74, 163}.

The three core principles of Buteyko are reduced breathing, nasal breathing and relaxation.

REDUCED BREATHING:

Almost all of the Buteyko exercises involve slowing breathing rate or reducing breathing volume. The exercises are initially practiced on a regular basis, but are gradually phased out as the condition improves. Instead of relying solely on peak-flow measurements,
Buteyko uses an exercise called the 'Control Pause' (CP) to monitor the status of asthma. The Control Pause can be defined as 'The amount of time that an individual can comfortably pause without resuming breathing after a normal exhalation.' As with many physical exercises, performing the CP properly requires practice, and the measurement varies widely from person to person.

With regular Buteyko reduced-breathing practice, asthmatics tend to find that their CP gradually increases, and in parallel their asthma symptoms decrease.

**NASAL BREATHING:**

The Buteyko method stresses the importance of breathing through the nose, rather than the mouth. Apart from protecting the airways by humidifying, warming, and cleaning the air entering the lungs, breathing through the nose also reduces the tendency to hyperventilate.

The majority of asthmatics and those who suffer with other breathing disorders have problems sleeping at night. This is thought to be linked with poor posture or unconscious mouth-breathing at night, and there are many devices available designed to encourage nocturnal nasal breathing. By keeping the nose clear and encouraging nasal breathing during the day, night-time symptoms can also improve.

**RELAXATION:**

Dealing with asthma attacks is an important factor of Buteyko practice. The first feeling of an asthma attack is scary and often results in a short period of rapid breathing. By controlling this initial ‘over-
breathing’ phase, asthmatics can prevent a ‘vicious circle of over-breathing’ developing and spiraling into an asthma attack. It has been reiterated that this method is not a substitute for medical treatment and reliever medication should be kept handy at all times and used as required. This aspect of Buteyko is merely a change in lifestyle that can minimize the chance of an attack occurring and reduce the severity by remaining calm and in control of breathing.

3. REVIEW OF EVIDENCE OF THE EFFECT OF BUTEYKO BREATHING ON BRONCHIAL ASTHMA

Cooper S et al\textsuperscript{21} have done studies using BBT on asthma patients showing that these breathing techniques are beneficial in asthma. S Bowler \textit{et al}\textsuperscript{164}, in 1998, conducted a prospective, blinded, randomized study comparing BBT with a control group. 39 patients were randomized, out of which 19 were in the BBT group and 20 in the control group. No significant baseline differences were seen between the 2 groups. Participants were between 12 to 70 years with asthma. In addition 20 normal subjects were also included in the study. The main outcome measures were morning PEFR, FEV\textsubscript{1}, end-tidal CO\textsubscript{2}, resting minute volume (MV), and QOL score measured at 3 months. Results showed no change in daily PEFR or FEV\textsubscript{1} in either group. Morning pre-bronchodilator PEFR was similar at both run-in (BBT, 385±90L/min, control, 375±117L/min; \(p=0.3\)) and at three months (BBT, 374 ± 115 L/min; control, 383 ± 103 L/min; \(P = 0.6\)). Pre-bronchodilator percentage predicted FEV\textsubscript{1} was also no different at run-in (BBT, 75% ± 17%; control, 73% ± 19%; \(p=0.4\)) and at three months (BBT, 72% ± 22%; control, 72% ± 15%; \(p = 0.4\)). No significant difference in mean ET CO\textsubscript{2} existed between BBT and control groups either at run-in or at three months. The normal subjects had significantly higher mean ET
CO\textsubscript{2} levels than both the BBT and the control groups. It was seen that at three months the mean MV for the BBT group was significantly less than for the control group (p = 0.004). Three months after intervention, there was a significant difference in beta\textsubscript{2}-agonist use between the BBT group and the control group (p = 0.005). The BBT group had a median reduction in daily adjusted beta\textsubscript{2}-agonist dose of 904 µg and the control group had a median reduction of 57 µg (p = 0.002). No significant difference existed between the mean quality of life score of the two groups at any stage. At three months, there was a trend towards greater improvement in the BBT group: median improvement of 1.2 units in the BBT group compared with 0.4 units in the control group (p = 0.09). These changes were spread fairly evenly across all four domains. Despite a trend in inhaled steroid use there was no significant difference between the groups in absolute daily doses or change in dose at any time. The median reduction in daily dose at the third month, compared with run-in, was 49% for BBT subjects and 0 for control subjects (p = 0.06). A trend toward reduced inhaled steroid use and better quality of life was observed in these patients without objective changes in measures of airway caliber.

Thirty-six adult subjects with mild to moderate asthma were randomized to receive either a BBT or placebo video to watch at home twice per day for 4 weeks. Opat J et al\textsuperscript{165} assessed the asthma-related quality of life, PEFR, symptoms, and asthma medication intake were assessed both before and after intervention. Study results demonstrated a significant improvement in quality of life among those assigned to the BBT compared with placebo (p = 0.043), as well as a significant reduction in inhaled bronchodilator intake (p = 0.008). They concluded that the BBT may be effective in improving the quality of life and
reducing the intake of inhaled reliever medication in patients with asthma.

Hence it is seen from above mentioned review that most of these studies were short term, performed without controls, or qualitative but based on subjective judgments. Most studies had low sample sizes and suffered from one or more methodological deficiencies, such as suboptimal data analysis, high dropout rates, problematic measurement procedures, or insufficient descriptions of methodology and results. Overall effects on parameters of lung function, symptoms, medication consumption, and health care use were generally negligible.
COCHRANE REVIEW OF BREATHING EXERCISES ON ASTHMA:

Holloway EA$^{22}$ reviewed the randomized or quasi randomized controlled trials of breathing retraining in patients with all ages with a diagnosis of asthma. Forty two studies were obtained for assessments, out of which thirty five studies were excluded. A total of seven studies were finally reviewed. All the studies mentioned in the Cochrane review have been already discussed earlier.$^{17, 20, 23, 148, 160, 164, 165}$

Taking each outcome measure in the studies reviewed, Holloway EA gave an in depth analysis of the results obtained. Accordingly, Holloway stated that the improvement in FEV$_1$ reported by two studies was not significantly different between the control group and breathing retraining groups. PEFR was reported by three studies but an improvement was only observed in one.$^{23}$ So it was stated that it was difficult to derive any firm conclusions for the effect of breathing retraining on PEFR in asthma. However as asthma attacks occur intermittently and the airways and not lung tissues are affected, some physiological measurements are not always indicative of the severity of asthma. Quality of life measurements are increasingly being recognised as important outcome measures for a number of chronic conditions.

Minute volume (MV) was reported by one study.$^{164}$ to decrease by 3.7 L. As the intention of the Buteyko and Papworth method of breathing retraining is to reduce the accompanying elements of hyperventilation in asthma patients this is of interest. A significant decrease in the use of ‘rescue beta-2 agonist’ by almost 6 actuations per week was reported by one study.$^{23}$
The study by Bowler, 1998 also reported a decrease in use of beta-2 agonist, however the results were not included in this outcome because the author reported actual total dosage used and the study actively recruited patients who were higher users of beta-2 agonists (> 1400 mcg). Inhaled corticosteroids use was also reported to fall by 49% in this study. At baseline, steroid use was higher in the actively treated arm than in the control group (1500 mcg/day & 1000 mcg/day, respectively). This may have led to a regression to the mean effect causing an apparently better effect in the treated patients. Bowler’s intervention was concentrated into one week’s treatment where BBT was taught and additional encouragement was given by telephone and subsequently outcomes were assessed three months later.

Asthma symptoms scores reported by Vedanthan 1998 did not improve significantly, but there was a trend towards improvement. Asthma exacerbations fell in one study of Nagarathna 1985, but not in another study as reported by Fluge, 1994.

Nagarathna, 1985 measured exacerbations in mean episodes per week; severity of attack was rated from 1 to 3 where 3 was the most severe requiring an injection or admission to hospital. Fluge, 1994 and Opat 2000 measured exacerbations as total counts per group. Fluge stated that three patients in the control group suffered from acute exacerbations requiring oral steroids; however definitions and severity of exacerbations were not described.

Measures of Quality of Life were reported to improve in two studies by Bowler 1998; Thomas 2003 both of which compared breathing retraining with asthma different instruments, the Marks
questionnaire and the Juniper AQLQ; therefore it was not possible to combine them. Also breathing retraining methods used in the two studies were different, namely the BBT and the breathing training element of the Papworth Method. Thomas’ was the only study reporting a ‘numbers needed to treat’ calculation, using the AQLQ, of 2 at one month and 4 at 12 months\textsuperscript{23}.

In addition to the varying techniques of teaching breathing retraining the length and frequency of the treatment interventions also varied considerably with the BBT taught daily for 60-90 minutes in the Bowler 1998\textsuperscript{164} study to 45 minute sessions of yoga breathing training three times a week for 16 weeks in the Vedanthan 1998 study\textsuperscript{17}. In another yoga trial by Nagarathna, 1985, the training programme ran daily for 2.5 hours for two weeks\textsuperscript{20}.

There is little uniformity between the interventions even when the techniques are similar, again making comparisons difficult. Both Bowler\textsuperscript{164} and Thomas\textsuperscript{23} stratified their participants, the former by higher levels of medication and Thomas’ inclusion criteria were those scoring over 23 in Nijmegen questionnaire scores. Outcome measures in these studies will relate only to similar populations with similar characteristics. We can only generalise results to a patient population bearing similar characteristics. Bowler’s results relate to those patients with initial high beta agonist usage and Thomas’ to patients exhibiting more severe symptoms associated with dysfunctional breathing. The applicability of the results of this review are limited with a number of factors contributing to this problem; the small number of studies, small number of participants and a diversity of methods of breathing retraining and outcome measures.
Overall, these studies were too small to provide a reliable estimate of the efficacy of breathing exercises for asthma. Despite the impossibility of running double blind studies with breathing retraining as the intervention, further randomized controlled trials should be undertaken to evaluate the different methods of breathing retraining.

The methods should be fully described for evaluation by patients, the public and professionals. Further studies and larger studies are required including outcome measurements such as health status questionnaires, measurements of symptom free days and the frequency and definitions of exacerbations together with routine physiological measurements and also measures evaluating airway inflammation.

It was concluded that the comparisons and conclusions were difficult to evaluate as treatment interventions and outcome measurements from the seven trials varied considerably. No reliable conclusion was drawn concerning the use of breathing exercises for asthma in clinical practice. But it was found that the improvement in quality of life to be encouraging and recommendation for further studies with detailed description of treatment methods and outcome measurements were suggested. Hence it is seen from above mentioned review that only few randomized controlled trials have tested the effectiveness of breathing techniques for asthma. As breathing techniques on bronchial asthma seem to have great potential this study was conducted to find its effect in patients with bronchial asthma.
**CHARACTERISTICS OF THE STUDIES ACCORDING TO COCHRANE DATABASE OF SYSTEMATIC REVIEW, 2004\(^2^2\)**

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<td>Bowler 1998</td>
<td>DESIGN: Randomised Controlled Trial. Randomly allocated to 2 groups using sealed envelopes.</td>
<td>BBT - active group: n = 19. 9 (47%) female. Age range: 12-68. (mean not stated) Control group: n = 20. 8 (40%) female. Age range: 12-69.</td>
<td>Subjects recruited from an Asthma Foundation publicity campaign and accepted if 'variable difficulty', wheeze or chest tightness with response to beta2-agonist and taking substantial doses of asthma medication.</td>
<td>Active treatment: 19 in the BBT group were given breathing exercises to reduce depth and frequency of breathing and also breath holding exercises. Control: Asthma education, relaxation, abdominal breathing exercises not involving hypoventilation.</td>
<td>Pulmonary function included ETCO(_2) and QOL.</td>
<td>Normal group had significantly higher mean end tidal carbon dioxide (ETCO(_2)) levels than either the BBT or control group in their run-in period and also at the 3 month follow-up. QOL: Indicated trends of improvement. Medication: The BBT group reduction in beta2-agonist. There was a trend to lower inhaled steroid doses in the BBT group.</td>
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### Review of Literature

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<td>Fluge 1994</td>
<td>Randomised controlled trial. Randomly assigned into three equal groups.</td>
<td>3 groups n = 36</td>
<td>Mild to moderate asthma controlled by medication. Breathing groups; physical and respiratory (yoga) exercises. Control/placebo: no therapy.</td>
<td>Pulmonary function and number of acute attacks.</td>
<td>Yoga and physiotherapy led to significant reduction in symptoms; only physiotherapy had a positive influence on lung function; effects persisted at 3-months follow-up.</td>
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<td>Girodo 1992</td>
<td>Randomized controlled trial with a run-in period.</td>
<td>n = 92. 3 parallel groups.</td>
<td>Media solicited volunteers with mild asthma. 16 weeks training, 3 times a week. Breathing group – diaphragmatic breathing. Physical training group Control/placebo group.</td>
<td>Daily medication use, attacks, asthma symptoms, time spent on physical activities.</td>
<td>Diaphragmatic breathing technique found to be superior in all end points.</td>
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<tr>
<td>Nagarathna 1985</td>
<td>Random selection not described.</td>
<td>n = 53</td>
<td>Patients with bronchial asthma. 2 weeks of yoga training and continue till follow up at 30 months.</td>
<td>PFT, number of severity of attacks, drug treatment score.</td>
<td>Yoga group was found to have better lung function.</td>
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<td>Opat 2000</td>
<td>Design: Randomised controlled trial.</td>
<td>n= 108. BBT group and Placebo group.</td>
<td>Patients with mild to moderate asthma recruited through media.</td>
<td>BBT taught through instructional video twice a day for 4 weeks. Control group had to watch a landscape video for 20 mins twice a day.</td>
<td>AQOL, ICS intake, bronchodilator usage, PEF and asthma symptoms.</td>
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<td>Thomas 2003</td>
<td>Design: Randomised controlled trial.</td>
<td>N= 33. Breathing retraining and control group.</td>
<td>Patients with asthma fulfilling the Nijmegen questionnaire.</td>
<td>Breathing retraining, assessed at 1 and at 6 months. Control group had 6 months asthma education from a nurse.</td>
<td>Nijmegen questionnaire, AQLQ.</td>
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<td>Vedanthan 1998</td>
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<td>N= 17. yoga group and control group.</td>
<td>Students with mild to moderate asthma.</td>
<td>Yoga including breathing techniques for 45 mins, 3 times a week for 16 weeks. Control group; no information was given.</td>
<td>PFT, asthma score, medication use.</td>
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