CHAPTER 2

LITERATURE REVIEW

Bateman et al. (2014) evaluated the effect of the addition of a novel LABA, vilanterol to a once daily ICS, fluticasone on the risk of severe asthma exacerbations in patients with uncontrolled asthma. The authors reported that, once daily vilanterol plus fluticasone reduced the risk of severe asthma exacerbations and improved lung function compared with fluticasone alone, with good tolerability and safety profile in adolescents and adults with asthma currently receiving ICS [52].

Sadatsafavi et al. (2014) assessed the risk of asthma related hospitalization in individuals who regularly filled prescriptions for ICS + LABA compared to those who regularly filled prescriptions for either ICS or LABA and compared to those who did not regularly fill such medications. Their study concluded that, regular dispensation of ICS plus LABA was not associated with an increased risk of asthma-related hospitalization [53].

Bollmeier et al. (2013) reviewed the clinical data on the use of long acting muscarinic antagonist (LAMA), tiotropium in patients with asthma. The authors concluded that tiotropium should be considered in patients with asthma who remain symptomatic while receiving high dose ICS and LABA. The authors also noted that tiotropium appear to respond well specifically in patients with high sputum neutrophil levels or with 16Arg/Arg or 16 Arg/Gly polymorphism of the ADRB2 gene [54].

Hiral et al. (2013) studied the impact of patient education provided by the clinical pharmacist regarding asthma, self-management and inhaler techniques in improving the quality of life (QoL) of asthmatic patients in a south Indian tertiary care hospital. The results of their study showed that, clinical pharmacist’s education intervention had a positive impact on the understanding and self-management of
asthmatic patients which helped in improving their health related quality of life (HRQoL) [55].

Papi et al. (2013) compared the efficacy and safety of ICS plus LABA (beclomethasone plus formoterol) with salbutamol as reliever strategies in patients taking beclomethasone-formoterol combination as maintenance treatment. Their results supported in the use of the combination of a single ICS plus LABA for maintenance and relief in patients with moderate to severe asthma and provided encouraging data for the formulation of beclomethasone-formoterol for this use [56].

Sodhi et al. (2013) carried out a study to know the knowledge, attitude and practices of patients with bronchial asthma. The authors concluded that, sustained efforts are required to disseminate knowledge about all aspects of asthma and its management among patient and to dispel their myths and misconception associated with diseases and its therapy [57].

Yoshida et al. (2013) investigated the effects of tiotropium, on pulmonary function in severe asthma patients despite maximal recommended treatments with high dose of ICS and LABA. The study findings suggested that, tiotropium provides a new strategy for the treatment of bronchial asthma and of overlapping asthma and COPD [58].

Zhao et al. (2013) developed the knowledge, attitudes and practices of parents of children with asthma in China in a multi centric study. The study concluded that, the parent’s KAP were poor. A gap was observed between recommended and actual practice, which may be related to inadequate knowledge and poor attitudes toward childhood asthma. They concluded that, improving knowledge and attitudes may encourage better practices among parents of children with asthma [59].

Apfelbacher et al. (2012) explored the psychometric properties (internal consistency, construct validity, discriminative ability) of the Juniper Mini asthma QoL questionnaire and the Sydney asthma QoL questionnaire. They concluded that, correlations between pulmonary function parameters and generic QoL were either weak or absent [60].
Kerstjens et al. (2012) portrayed that, in patients with poorly controlled asthma despite the use of ICS and LABAs, the addition of tiotropium significantly increased the time to the first severe exacerbation and provided modest sustained bronchodilation [61].

Riemersma et al. (2012) compared the effects of a combination of budesonide/formoterol and guideline driven, usual care on BHR and clinical asthma severity in primary care practice. They concluded that, despite a 59% low dose of ICS, BHR and other clinical outcomes remained stable during budesonide/formoterol as both maintenance and reliever therapy [62].

Sabin et al. (2012) compared HRQoL using SGRQ in asthmatics receiving fluticasone, beclomethasone and budesonide. The authors concluded that, there was an evidence for an early QoL improvement to fluticasone, when compared to beclomethasone or budesonide in moderate and severe persistent asthma. Subsequently, the three ICS showed similar improvements in lung functions and dyspnea indices throughout the study [63].

Salvador et al. (2012) developed a standard parental asthma questionnaire based on the asthma pediatric education program. The study reported that, developed a questionnaire by them was a reliable and useful tool to measure the knowledge, attitudes and practices of parents of asthmatic children [64].

Diette et al. (2011) investigated the differences in control of asthma between the patients, who were treated with asthma controller monotherapy versus combination therapy. The authors reported that, there was no significant difference found during a treatment free period between controller monotherapy and combination therapy [65].

Price et al. (2011) conducted a trial to evaluate the effect of LTA as compared with either an ICS for first-line asthma controller therapy or a LABA as add-on therapy in patients already receiving ICS therapy. They suggested that, LTA was equivalent to an ICS as first-line controller therapy and to LABA as add-on therapy for asthma patients [66].
Ramsay et al. (2011) studied the role of LTA in an acute asthma exacerbation. They stated that, in acute asthma exacerbations, the additional administration of oral montelukast resulted in a significantly higher peak expiratory flow (PEF) than that achievable with current standard treatment [67].

Wang et al. (2011) compared the efficacy and safety of tiotropium bromide inhalation and doxofylline oral tablet in the treatment of COPD and concluded that both tiotropium and doxofylline are effective and safe for the treatment of COPD [68].

Mancuso et al. (2010) performed a cross-sectional analysis to determine what patient and clinical factors were associated with these cognitive variables such as knowledge, attitude and self efficacy and assessed the contributions of these cognitive variables to clinical status. They concluded that, these variables, in turn, were independently associated with asthma status [69].

Patel et al. (2010) studied the effect of controller medication as an add-on to ICS and the LABA on the clinical symptom, pulmonary function and compliance in patients with asthma and concluded that, all add-on controller medications helped, with a significant improvement of lung functions and asthma symptoms [70].

Peters et al. (2010) aimed to find an alternative treatment for adults with uncontrolled asthma. The study reported that, when tiotropium was added to an ICS, it improved symptoms and lung function in patients with inadequately controlled asthma. Its effects appeared to be equivalent to those with the addition of salmeterol [71].

Virchow et al. (2010) stated that, treatment with montelukast was generally well tolerated. In patients insufficiently controlled with ICS or ICS + LABAs, daily add-on montelukast improved both asthma control and HRQoL [72].

Anjan et al. (2009) studied the influence of community pharmacist provided patient education in asthmatic patients on treatment outcomes. The authors concluded that, pharmacist provided patient education showed a positive impact on patient’s
knowledge, attitude, practice (KAP), inhaler usage techniques, medication adherence behavior and treatment outcomes [73].

Keith et al. (2009) evaluated the effectiveness of montelukast as add-on therapy for patients diagnosed with asthma who remain uncontrolled while receiving ICS monotherapy or ICS/LABA therapy in a community practice setting. The study concluded that, montelukast add-on therapy is effective for managing asthma [74].

Korn et al. (2009) evaluated the efficacy of add-on montelukast on asthma control and allergic rhinitis symptoms in asthmatic patients still symptomatic with ICS and LABA. Their open label observational study showed, an improvement, after 2 months of add-on therapy with montelukast [75].

Holgate et al. (2008) said that, treatment choices are limited to asthma and many patients have poorly controlled or uncontrolled asthma. Their paper reviewed the evidence for the need of change in asthma management [76].

Iwamoto et al. (2008) stated that, anticholinergics have long been used to treat asthma, although their current role in therapy is supplementary and they concluded that tiotropium bromide is effective for severe asthma with non-eosinophilic phenotype [77].

O'Byrne et al. (2008) evaluated the effect of increasing the dose of ICS versus adding LABA on the time spent with well controlled asthma or poorly controlled asthma. The study reported that, the addition of formoterol to therapy with low dose ICS increased the probability of well controlled asthma compared to a substantial increase in the dose of an ICS [78].

Aaron et al. (2007) portrayed that, the addition of fluticasone plus salmeterol combination to tiotropium therapy does not statistically influence the rates of COPD exacerbation but improved lung function, QoL and hospitalization rates in patients with moderate to severe COPD [79].

American Lung Association Asthma Clinical Research Centers (2007) compared the effectiveness of once daily oral controller therapy with either LTA
(montelukast) or theophylline added to existing medications in patients with poorly controlled asthma. The study reported that, either montelukast nor theophylline control the rate of asthma despite the improved pulmonary function [80].

American Lung Association Asthma Clinical Research Centers et al. (2007) determined whether patients with asthma that was well controlled with the use of ICS twice daily can receive a step-down treatment with once daily montelukast or once daily fluticasone propionate plus salmeterol. They concluded that, asthma, which was well controlled with the use of twice daily inhaled fluticasone can be switched to once daily fluticasone plus salmeterol without increasing the rates of treatment failure [81].

Deykin et al. (2007) sought to determine whether the combination of the LTA, montelukast and the LABA, salmeterol could provide an effective therapeutic strategy for asthma. They concluded that, for the patients with moderate asthma, the combination of LTA and LABA should not be substituted for the combination of ICS and LABA [82].

Sorkness et al. (2007) compared three controller regimens namely fluticasone monotherapy, fluticasone plus salmeterol combination and montelukast on mild to moderate persistent childhood asthma. They reported that, both fluticasone monotherapy and combination therapy achieved greater improvements in asthma control days than montelukast [83].

Um et al. (2007) studied the combination of tiotropium and budesonide in the treatment of COPD. The authors reported that, compared with tiotropium alone, the tiotropium plus budesonide combination was relatively improved HRQoL [84].

Shah et al. (2006) conducted a study to determine if better control of asthma can be achieved by adding a second controller medication and assessed its use to reduce the dose of ICS. Their study revealed that, the addition of montelukast to budesonide is safe and resulted in greater improvement in lung function than high dose of budesonide treatment or the addition of theophylline [85].

Boushey et al. (2005) evaluated the efficacy of intermittent short course corticosteroid treatment guided by a symptom based action plan alone or in addition
to daily treatment with either ICS, budesonide or oral zafirlukast. They concluded that, it may be possible to treat mild persistent asthma with short, intermittent courses of inhaled or oral corticosteroids taken when symptoms worsen [86].

Dupont et al. (2005) studied the effect of montelukast with ICS and LABA in improving asthma control in asthmatic patients. Their pilot study suggested that, addition of montelukast to the combination of ICS and LABA may result in significant improvements in asthma control [87].

Jenkins et al. (2005) compared the relationships between traditional and patient centered endpoints during treatment with three classes of asthma medication namely formoterol, montelukast and fluticasone. The authors found a significant relationship between patient based variables and pulmonary function only for montelukast treatment [88].

Magar et al. (2005) evaluated the impact of patient education on adult asthmatics. The authors performed an individual assessment of patient's needs and two educational group sessions. They concluded that, there was a significant improvement with regard to symptoms free days, number of awakenings, consumption of corticosteroids, consumption of rescue medications and QoL score in the educated group [89].

Urek et al. (2005) investigated the effect of different educational programs in obtaining better asthma control and HRQoL in adult patients with moderate persistent asthma. The authors concluded that, the best overall improvement in the asthma control and QoL was observed in individual verbal instructions method [90].

Zeiger et al. (2005) determined whether montelukast is as effective as fluticasone in controlling mild persistent asthma as determined by rescue free days. In patients with mild persistent asthma, rescue free days and most asthma control measures improved similarly with fluticasone or montelukast over a short term, but with prolonged open-label treatment, asthma control improved more with fluticasone than montelukast [91].
Basagana et al. (2004) assessed the association between asthma prevalence and socioeconomic status at both the individual and center levels simultaneously by using data from 32 centers in 15 countries. The authors concluded that, community influences of living in a low educational area are associated with asthma, independently of the subject’s own educational level and social class [92].

Cowie et al. (2004) determined whether ICS therapy is effective in controlling asthma and examined the rates of asthma control in relation to ICS use outside the realm of randomized controlled trials. The authors concluded that, though ICS therapy can result in asthma control in most individuals with asthma, this may not be attained outside the realm of randomized clinical trials. The use of ICS for asthma in a 'real world' setting appears to reflect disease severity [93].

Hancox et al. (2004) reported a prospective cohort study of approximately 1000 individuals born in New Zealand. They observed that, socioeconomic status in childhood had no significant impact on the prevalence of asthma in New Zealand born child [94].

Juniper et al. (2004) performed a factor analysis to explore the relationships between QoL measured asthma questionnaire and conventional measures of asthma clinical status. Their analysis revealed that, although some weakness of correlation between clinical indices and QoL may be due to noise of measurement, it is mainly attributable to asthma health status being composed of distinct components [95].

Nathan et al. (2004) described the development of the asthma control test, a patient based tool for identifying patients with poorly controlled asthma. In a busy clinic practice with limited time and resources, there is a need for a simple method for assessing asthma control with or without lung function test. Results reinforced the usefulness of a brief, easy to administer, patient-based index of asthma control [96].

Robinson (2004) reviewed the role of the mast cell in asthma and reported that, mast cell produces a variety of lipid mediators, chemokines, cytokines and enzymes that, may interact with airway smooth muscle cells to cause hyper reactivity to constrictive stimuli [97].
Scicchitano et al. (2004) evaluated the efficacy and safety of budesonide plus formoterol for both maintenance and symptom relief compared with a higher maintenance dose of budesonide in patients with moderate to severe asthma. The authors concluded that, budesonide/formoterol single inhaler therapy had good potential to provide a complete asthma management approach with one inhaler, demonstrating a high level of efficacy in asthma patients [98].

Brusasco et al. (2003) recorded the exacerbations and health resource use in patients with COPD during 6 months treatment period with tiotropium, salmeterol or matching placebo. The study concluded that, exacerbations of COPD and health resource usage were positively affected by daily treatment with tiotropium [99].

Casale et al. (2003) evaluated the effect of once-daily budesonide turbuhaler on HRQoL in adults with mild to moderate asthma. The study concluded that, once daily budesonide turbuhaler 200 and 400 µg demonstrated clinically important and statistically significant improvements in HRQoL that, can be maintained with a low dose of 200 µg [100].

Lalloo et al. (2003) evaluated the efficacy and safety of low dose budesonide plus formoterol, compared with an increased dose of budesonide in adult patients with mild to moderate asthma. The study showed that single inhaler therapy with budesonide and formoterol provides greater improvements in asthma control than increasing the maintenance dose of ICS [101].

Meszaros et al. (2003) developed an educational instrument, to assess its impact as an intervention instrument and to examine QoL. The results indicated that, asthma patients experienced lower QoL. The results suggested that, it is necessary to regularly refresh asthma knowledge to assess patient self management plans to achieve long term effectiveness of asthma management [102].

Prasad et al. (2003) interviewed using a questionnaire to determine how well asthma patients in Lucknow informed about their disease. They observed that, the majority of the patients had wrong concepts about etiology and disease management
and the prognosis of asthma. They concluded that, sincere efforts are required to impart health education to the patients [103].

Riccioni et al. (2003) compared montelukast and budesonide on bronchial reactivity in subjects with mild to moderate persistent asthma. The study data demonstrated that, the administration of montelukast provided an important and additional effect on BHR. Oral administration of montelukast represented a significant advantage over the majority of other anti-asthmatic drugs [104].

Ringdal et al. (2003) compared the efficacy and safety of salmeterol/fluticasone propionate with fluticasone propionate plus oral montelukast in asthma patients. Both treatments were well tolerated equally. Combination therapy with fluticasone propionate plus salmeterol produced significantly greater improvements in lung function and asthma control than the addition of montelukast to fluticasone propionate [105].

Vaquerizo et al. (2003) conducted a randomized, double blind trial to study the efficacy of adding oral LTA, montelukast to a constant dose of ICS, budesonide. The authors concluded that, in patients with mild persistent asthma despite ICS treatment, concomitant treatment with LTA significantly improved the asthma control [106].

Yang et al. (2003) investigated the effect of asthma education on QoL in Taiwanese adults with asthma. Authors proved that, asthma education had significant improvement in asthma knowledge and QoL in adult asthma patients [107].

Dempsey et al. (2002) evaluated the effect of adding zafirlukast or low dose theophylline to a beclomethasone dipropionate on BHR as the primary outcome variable. The authors reported that a LTA but not low dose theophylline conferred significant additive anti-inflammatory effects to therapy with a low dose ICS but not to that with a medium dose of an ICS [108].

Goldstein et al. (2002) compared the efficacy and safety of doxofylline, theophylline and placebo in patients with chronic reversible bronchial asthma. The study evidenced that, doxofylline 400 mg is an effective treatment for relieving
airway obstruction and displays a better safety profile with respect to theophylline 250 mg with a favorable risk to benefit ratio [109].

Lipworth et al. (2002) reviewed the second-line controller therapy for persistent asthma uncontrolled on ICS. The authors concluded that, for patients with poor pulmonary function where bronchodilatation is required, the addition of a LABA to ICS would seem to be a logical choice. For the patient whose pulmonary function is less impaired, with evidence of ongoing BHR where bronchoprotection is needed or when there is concomitant allergic rhinitis, then an LTA would be more suitable [110].

Sanjuas et al. (2002) compared the performance of the juniper asthma QoL questionnaire and the Saint George Respiratory Questionnaire (SGRQ) in a sample of asthmatic patients, representative of a broad spectrum of asthma severity. The authors concluded that, the juniper asthma QoL questionnaire and SGRQ have shown high reliability and validity and with the exception of the SGRQ symptoms, a high level of responsiveness [111].

Yamaoka et al. (2002) implemented a program of educating asthma patients and conducted a QoL survey to objectively evaluate the patient’s conditions and observed significant improvements in social, concerns, marks and scales after the education. The usefulness of patient education can be assessed by means of changing the patient’s QoL scores [112].

Yurdakul et al. (2002) compared the efficacy and safety of the second controller medications (formoterol, zafirlukast, SR-theophylline) used in addition to ICS (budesonide) in moderate persistent asthma. At the end of the treatment period, in all the three groups studied, improvements were attained in overall asthma control and there was no statistical difference among the groups [113].

Nelson et al. (2001) compared the addition of a LABA to the addition of an oral LTA for asthma therapy in patients who remain symptomatic on ICS. They observed that, in asthmatic patients who are not controlled sufficiently with ICS
alone, the combination of LABA and ICS is superior to the combination of oral zafirlukast and ICS as stepwise therapy [114].

Lim et al. (2000) undertaken a study to determine whether theophylline added to low dose ICS would be as efficacious as high dose ICS in asthma. They concluded that there was no overall significant differences between the low dose steroid, low dose steroid with theophylline and the high dose steroid groups [115].

Virchow et al. (2000) stated that not all the asthmatic patients can be controlled with the use of high dose ICS since LTA play a pivotal role in the pathogenesis of asthma. In their double blind study, patients taking high dose ICS, LTA improved lung function and asthma symptoms and reduced the risk of asthma exacerbation, therefore, the authors suggested that, the contribution of leukotrienes to asthma symptoms and exacerbations is not adequately controlled by high dose of ICS [116].

Abdulwadud et al. (1999) reported that, a limited asthma education programme in a hospital outpatient setting had a positive impact on patient’s knowledge of asthma, but not on their QoL, self-management skills or attitudes and beliefs about asthma [117].

Gallefoss et al. (1999) assessed the QoL of patients after patient education in a randomized controlled study. They concluded, asthma patients improved their HRQoL and lung function after patient education when compared to the uneducated patients [118].

Evans et al. (1997) compared the benefits of adding theophylline to ICS with those of doubling the dose of ICS in patients with persistent symptoms despite the use of ICS. The authors reported that, for patients with moderate asthma, low dose ICS with theophylline and high dose ICS produced similar benefits. The addition of low dose theophylline to ICS may be preferable and cheaper than increasing the dose of ICS [119].

Pauwels et al. (1997) evaluated the effect by adding inhaled formoterol to both lower and higher doses of ICS, budesonide. The study concluded that, patients who
have persistent symptoms of asthma despite treatment with ICS, the addition of formoterol to budesonide therapy or the use of a higher dose of budesonide may be beneficial [120].

Greening et al. (1994) compared higher dose ICS and the addition of LABA in asthma patients with symptoms on existing ICS. The authors observed a significant difference in favor of the ICS and the addition of LABA [121].