INTRODUCTION

Asthma and Allergic Rhinitis (AR) are the disorders affecting a large population of our society. Both of these conditions are often observed together in the affected individuals, having mutual pathophysiology. Several mechanisms have been suggested to elaborate on their disease process with the involvement of inflammatory cells like mast cells and eosinophils, inflammatory mediators like leukotrienes, histamine, and tryptase. Asthma is a chronic inflammatory disorder of airways, presenting with variable symptoms related to the inflammation and hyper responsiveness of airways, while AR can present with rhinorrhea, enlargement of nasal turbinates and tenderness, conjunctival injection, and pallor. It is managed through minimizing the exposure to the allergen, pharmacotherapy, and immunotherapy.

ABSTRACT

Objectives: Our objective was to evaluate the effect of Montelukast on the symptoms of asthma and allergic rhinitis (AR), assess its effect on the individual quality of life (QoL), and estimate the proportion of participants having adverse effects.

Methods: This prospective, open-label study conducted at Dow University of Health Sciences, Ankle Saria Hospital and Sindh Government Hospital Liaquatabad, Karachi, from August 2018 to September 2019, included patients aged ≥18 years with a clinical diagnosis of Asthma, AR, or both. Patients were given a 10 mg Montelukast tablet each day and then called for follow-up in the fourth week, where the questions related to the improvement in the symptoms of asthma or AR were asked. Patients were also asked about the improvement in QoL and any adverse effects.

Results: A total of 694 patients were registered of which 138(19.8%) had AR, 294(42.4%) had asthma, while 273(39.3%) had both. Mean age was 41.1±14.63 years and 352 (50.7%) were male and 342(49.3%) were females. On a follow-up visit, there was a sufficient improvement in 351 asthmatics (63.9%), and 288 patients with AR (70.1%) overall, strong or marked improvement in the day (n=342,62.3%) and night time (n=331,60.3%) asthma symptoms. Overall improvements in QoL were very good or good in 419 patients. Montelukast was well-tolerated here with adverse effects (like abdominal discomfort, fever, fatigue, headache, rash, and upper respiratory tract symptoms) seen in 125 patients (18.01%).

Conclusion: Montelukast was very effective in improving the symptoms and QoL of the individuals suffering from asthma and/or AR.

KEYWORDS: Allergic rhinitis, Asthma, Hypersensitivity, Montelukast, Quality of life.

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AR tops the list of the most commonly associated comorbidities with asthma as reported in the literature that 80% asthmatics also carry AR as a coexistent “ghost” diagnosis which in most cases remains underdiagnosed. A study from the United States reported AR symptoms in 72% of individuals with asthma, and interestingly 53% of these subjects were undiagnosed with AR. Epidemiologically, overall the existence of asthma is 30% in patients primarily diagnosed with AR, while that of AR is 70% in asthmatics. A similar kind of data from a study conducted in Japan reported the existence of AR in as many as 67.3% asthmatics.

Montelukast, a Leukotriene (LT) antagonist, has a therapeutic role in the treatment of Asthma and AR by acting on Cysteinyl leukotriene-1 and 2 receptors. It is a widely used drug that was first approved in 1998 for use in the United States, indicated mostly in the prophylaxis and treatment of asthma, including the prevention of exercise-induced bronchoconstriction and AR with a recommended oral dosage of 10mg once-daily in adults.

Montelukast effectively improves the QoL by addressing the symptoms in the patients, proving to be a good replacement of drugs like inhaled corticosteroids (ICS) and long-acting beta2 agonists (LABA). As per a study published in 2019, it plays a great role in the improvement of QoL by addressing the symptoms potently, as compared with a placebo group.

Asthma and AR lie in the category of conditions that need lifelong therapy because of the symptomatic relapses, which is a cause as well as a reason for the lack of compliance. A patient friendly mode of management was the need of the hour since so long. Montelukast came as the answer, a single-dose therapy along with many other advantages. We have focused on analysing the role of montelukast in two of the hypersensitivity disorders, along with sorting out all the pros of using this drug and assessing the traits that make it a first-line therapy in the aforementioned indications.

**METHODS**

This is a prospective, open-label study conducted at Dow University of Health Sciences, Ankle Saria Hospital and Sindh Government Hospital Liaquatabad Karachi, Pakistan, from August 2018 to September 2019. Both males and females, aged ≥18 years with a clinical diagnosis of Asthma or AR giving informed consent were included in the study. Pregnant or breast-feeding patients, those having a history of previous adverse reactions to montelukast, history of hyper-eosinophilic disorder other than an atopic disease, or any significant active pulmonary pathology other than asthma were excluded. The study was approved by the institutional review board (No.: DUHS/IRC/2018-003). The trial was also registered at www.clinicaltrials.gov. (Identifier: NCT03380975).

When patients signed the informed consent, a brief history was taken at registration. They were asked about the diagnosis and its symptoms, either having asthma, AR, or both. The severity of asthma was divided into categories of intermittent and persistent (mild, moderate, and persistent) according to recent guidelines. While AR was categorized as intermittent or persistent based on the duration of symptoms. Individual quality of life (QoL), assessment about sleep, work, everyday life, and physical activity was done at registration.

Patients were given a 10 mg Montelukast tablet (Aireez®), each day and then called for follow-up in the fourth week. On a follow-up visit, general improvement in asthma and AR symptoms, improvement of day and night-time asthma symptoms, and specific improvement in AR symptoms were evaluated. General improvements were categorized as very good, good, satisfactory, sufficient, or not sufficient. Specific improvements in symptoms or QoL domains were categorized as strong, marked, moderate, or none. Patients were also asked about the improvement in QoL and any adverse effects occurring during the therapy. All adverse events occurring during the study period were recorded.

Data were entered and analysed by using SPSS version 23.0, where frequency and percentages were calculated for gender, family history, the severity of asthma and AR, concomitant medications usage, symptoms, QoL categories, adverse effects of montelukast, and improvement in symptoms and QoL.

**RESULTS**

A total of 694 patients were included in the study from August 2018 to September 2019 after taking informed consent. In terms of diagnosis,
138 (19.8%) had AR, 294 (42.4%) had asthma, while 273 (39.3%) had both. The mean ± SD of age was 41.1 ± 4.63 years which included 50.7% males and 49.3% females. The majority of participants (62.4%, n=433) had no family history of asthma. When the severity of asthma and AR were assessed, most of them had a persistent disease with further categorization as shown in Table-I. Montelukast tablet was given to all the patients despite their ongoing medications, details of which are presented in Table-I.

Almost the entire study population showed both the day and night-time symptoms on presentation, with cough being the most prevalent one. On a follow-up visit, there was a sufficient improvement in 351 asthmatics (63.9%), strong or marked improvement in the day (n=342, 62.3%) and nighttime (n=331, 60.3%) asthma symptoms (Table-II).

The symptoms of AR were variable including sneezing, runny nose, nasal congestion, watery eyes, and red/burning eyes. On a follow-up visit, there was a sufficient improvement in 288 patients of AR (70.1%) (Table-III). Overall improvements in QoL were very good or good in 419 patients (Table-IV).

As per our results, Montelukast was well-tolerated here since in this large group of patients, 125 patients (18.01%) had one or more adverse effects reported including abdominal discomfort (2.6%, n=18), fever (2.2%, n=15), fatigue (5.2%, n=36), headache (5.6%, n=39), rash (1%, n=7), and symptoms of upper respiratory tract infection (1.4%, n=10).

**DISCUSSION**

The participants involved in our study showed a marked improvement in their QoL which was significantly affected before the commencement of

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**Table-I: Patient baseline characteristics at week 4 (n=694).**

| Characteristic                  | n (%)     |
|--------------------------------|-----------|
| **Gender**                     |           |
| Male                           | 352 (50.7) |
| Female                         | 342 (49.3) |
| **Duration (Mean ± SD) of disease** | 31.08 ± 61.69 |
| **Family History of Asthma**   | 204 (29.4) |
| **Diagnosis**                  |           |
| Asthma alone                   | 294 (42.4%) |
| Allergic rhinitis alone        | 138 (19.8%) |
| Asthma and Allergic rhinitis   | 273 (39.3%) |
| **Asthma (n=549)**             |           |
| Intermittent                   | 185 (33.7) |
| Mild                           | 203 (36.9) |
| Moderate                       | 161 (29.3) |
| **Allergic Rhinitis (n=411)**  |           |
| Intermittent                   | 243 (59.1) |
| Persistent                     | 169 (41.1) |
| **Concomitant Medications**    |           |
| Antileukotrienes               | 286 (41.2) |
| Inhaled Corticosteroids        | 217 (31.3) |
| Oral Corticosteroids           | 140 (20.2) |
| Long-acting inhaled beta2-agonists | 81 (11.7) |
| Short-acting inhaled beta2-agonists | 42 (6.1) |
| Short-acting oral beta2-agonists | 49 (7.1) |
| Ipratropium                    | 163 (23.5) |
| Theophylline                   | 206 (29.7) |
| Others                         | 32 (4.6)   |
| Average inhaler Puff per day ± SD | 2.60±1.03  |

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**Table-II: Symptoms of patients with asthma before and after administration of montelukast at Week 4 (n=549).**

| Characteristic                  | n (%)     |
|--------------------------------|-----------|
| **On presentation**            |           |
| **Day-time asthma symptoms**   |           |
| Cough                          | 528 (95.1) |
| Wheezing                       | 440 (79.3) |
| Chest tightness                | 382 (68.8) |
| Shortness of breath            | 322 (58.0) |
| Others                         | 1 (0.1)    |
| **Night-time asthma symptoms** |           |
| Cough                          | 507 (91.4) |
| Shortness of breath            | 407 (73.3) |
| Nocturnal awakening            | 266 (47.9) |
| Others                         | 2 (0.2)    |
| **On follow-up**               |           |
| **Improvement in day symptoms of asthmatics** |   |
| Strong                         | 233 (42.4) |
| Marked                         | 109 (19.8) |
| Moderate                       | 78 (14.2)  |
| None                           | 4 (0.7)    |
| **Improvement in night symptoms of asthmatics** |   |
| Strong                         | 196 (35.7) |
| Marked                         | 135 (24.6) |
| Moderate                       | 77 (14.0)  |
| None                           | 7 (1.2)    |
| **Asthma overall improvement** |           |
| Very good                      | 182 (33.1) |
| Good                           | 169 (30.7) |
| Satisfactory                   | 45 (8.1)   |
| Sufficient                     | 23 (4.1)   |
| Not sufficient                  | 5 (0.7)    |

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the treatment with montelukast. Overall, a strong improvement was observed in the day, night and overall symptoms of asthma. Moreover, the majority of participants also showed improvement in AR symptoms on the follow-up i.e. sneezing, cough, nasal, and ocular ones.

Our study is similar to the work of Philip G et al., where marked improvement was observed in nasal and ocular symptoms after the two weeks treatment with montelukast 10 mg, the same study also concluded that this significant reduction in the symptoms of AR imposed a positive impact on asthma-related problems of the patient who were dealing with both the disorders. Montelukast particularly has a positive impact on cough and all the discomforts associated with it, and this is quite evident in our patients as well.

After the computation of results, headache was found to be the most prevalent among all the adverse effects of this LT antagonist. Findings of
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Haarman MG et al. somewhat validates this as they also reported headache as the most common adverse effect along with others like abdominal pain, aggression, abnormal behaviour, rash, and muscle spasm.\textsuperscript{16} As computed in our results, believed to be one of the contributors in AR oxide production, imbalance of which is montelukast maintains the balance in nitric oxide (like zileuton).\textsuperscript{17} These comprise of two main groups of CysLT1R antagonist (like montelukast, pranlukast, and zafirlukast) and 5-lipoxygenase inhibitors (like zileuton).\textsuperscript{18} As far as AR is concerned, montelukast maintains the balance in nitric oxide production, imbalance of which is believed to be one of the contributors in AR pathogenesis.\textsuperscript{16} As computed in our results, other authors have also demonstrated a good role of LT receptor antagonists in the management of asthma and AR symptoms. Once-daily oral dosage of montelukast significantly improves the airway function in asthmatics.\textsuperscript{19} Similarly, it also proves beneficial in reducing daytime ocular symptoms with a delayed impact on night-time symptoms of AR.\textsuperscript{20}

There are several reasons that make montelukast stand out as a part of the treatment regimen of asthma and AR and the topmost of them is the ease in compliance for the patient as it is far easier to use a drug once-daily orally in comparison with other drugs. Secondly, this also shortens the extended side-effect profile (like that after long-term steroid usage).

Limitations of the study: Although this study has tried to cover the role of montelukast in the treatment of asthma and AR but there are some limitations that can be listed in order to get worked on in the future, as the evaluation of short and long-term side effects associated with the use of montelukast, contraindications, toxicities, and continuous monitoring of the patient while on treatment. There was no control group or a placebo drug to compare the effects and be sure that the outcome is only due to the tested drug. Further research is needed in order to emphasize the importance and safety of this drug. Moreover, there is some gap in research regarding the role of montelukast in the treatment of several other allergic disorders to consolidate the theories behind the mechanisms and adverse effects of its use in these conditions.

CONCLUSION

Montelukast is effective in improving the symptoms and QoL of the individuals suffering from asthma and Allergic Rhinitis.

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Authors’ Contributions:

FFZ: Worked on concept and design of study and questionnaire and he is also the responsible and accountable for the accuracy or integrity of the work.
MA, AH, SM: Contributed in data collection and reviewed the paper. They are also responsible and accountable for the accuracy and integrity of the work
All authors have read and approved the final draft of the manuscript.