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ASSESSMENT OF MEDICATION ADHERENCE OF ASTHMA PATIENTS ON SINGLE MAINTENANCE AND RELIEVER THERAPY: A SYSTEMIC LITERATURE REVIEW

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ABSTRACT

Long-term management techniques are necessary for asthma, a chronic inflammatory airway disease marked by fluctuating airflow restriction and recurrent symptoms. The medication adherence of asthma patients undergoing Single Maintenance and Reliever Therapy (SMART), which combines long-acting β2-agonists and inhaled corticosteroids in a single inhaler for both maintenance and symptom relief, is the main focus of this comprehensive literature review. Research shows that, in comparison to traditional treatment approaches, SMART therapy dramatically reduces exacerbations, enhances asthma control, and lowers total corticosteroid exposure. Nonetheless, poor inhaler technique, complicated treatment plans, a lack of patient education, and constraints in the healthcare system all contribute to medication non- adherence, which continues to be a significant obstacle to the best possible asthma outcomes. Adherence is measured using a variety of techniques, each with its own limitations, such as self-report scales and electronic monitoring devices. Along with methods to increase adherence, such as patient education, motivational interviewing, and pharmacist-led interventions, the review also identifies obstacles unique to SMART therapy,

such as incorrect inhaler use and low patient participation. All things considered, increasing adherence through focused interventions is crucial to optimizing the therapeutic advantages of SMART treatment and improving asthma patients' quality of life. This review also highlights the increasing significance of patient-centered and individualized care in the management of asthma. Adherence and treatment outcomes can be greatly enhanced by customized interventions that take into account each patient's unique habits, beliefs, and socioeconomic circumstances. Promising prospects for real-time monitoring and patient assistance are provided by the integration of digital health technology, such as smart inhalers and mobile health apps. Increasing cooperation between medical professionals can improve adherence and provide the best possible treatment results, particularly when pharmacists are involved in long-term care. Future studies should concentrate on creating standardized adherence assessment instruments and assessing creative approaches to get over enduring obstacles in the application of SMART therapy.

KEYWORDS: Asthma, SMART therapy, medication adherence, asthma management.

INTRODUCTION

Chronic inflammation of the airways caused by an excess of mast cells, activated T helper lymphocytes, and eosinophils is the hallmark of asthma. These inflammatory cells secrete mediators that cause mucus production, remodeling, and bronchoconstriction. Cytokines, chemokines, growth factors, lipid mediators, immunoglobulins, and histamine are among the inflammatory mediators that propel this process.[1] Even with high dosages of inhaled corticosteroids, about 5% of patients have uncontrollable asthma. It is crucial to thoroughly evaluate these patients to determine whether there are any things that may be corrected that might be causing their poor controlIt is crucial to diagnose asthma and rule out other airway conditions, including vocal cord dysfunction (also known as "pseudo-asthma") and chronic obstructive pulmonary disease (COPD). A poor reaction is frequently caused by noncompliance with treatment, especially when it comes to inhaled corticosteroids. There may be unidentified exacerbating factors, including unrecognized allergens, occupational sensitizers, dietary additives, drugs, gastro-oesophageal reflux, upper airway disease, or other systemic diseases, that need to be identified and avoided or treated. Psychological factors may be important in some patients, but it is difficult to know whether these are causal or secondary to troublesome disease. Some patients have instability of their asthma, with resistant nocturnal asthma, premenstrual exacerbations or chaotic and unpredictable

instability (brittle asthma). A few patients are completely resistant to corticosteroids, but more patients are relatively resistant and require relatively high doses of corticosteroids to control their symptoms (steroid-dependent). Some patients develop progressive loss of lung function, as in patients with COPD. Management of patients with difficult asthma should be supervised by a respiratory specialist and should involve careful assessment to confirm a diagnosis of asthma, identification and treatment of exacerbating factors, particularly allergens, and recording of peak expiratory flow patterns. A period of hospital admission may be the best way to assess and manage these patients. Treatment involves optimizing corticosteroids therapy, assessing additional controllers such as long-acting inhaled or subcutaneous beta2-agonists or subcutaneous, theophylline and antileukotrienes. In some patients, the use of immunosuppressive treatments may reduce steroid requirements, although these treatments are rarely effective and have side-effects. In the future, the nonsteroid anti-inflammatory treatments now in development may be useful in these patients.[2]

PATHOPHYSIOLOGY OF ASTHMA

There are two stages to asthma: an early phase and a late phase. Early on, when mast cells are exposed to stimuli, IgE antibodies activate them, releasing histamine and other substances that restrict the airways. When lymphocytes release cytokines (IL-4, IL-5, and IL-13), eosinophils and other immune cells are drawn to the area, causing inflammation. After a few hours, the lungs enter the late phase, where additional inflammatory cells build up and exacerbate bronchoconstriction and edema. Breathing becomes challenging over time due to increasing mucus, smooth muscle thickness, and airway remodeling, which may result in long-term airflow restriction.[3]

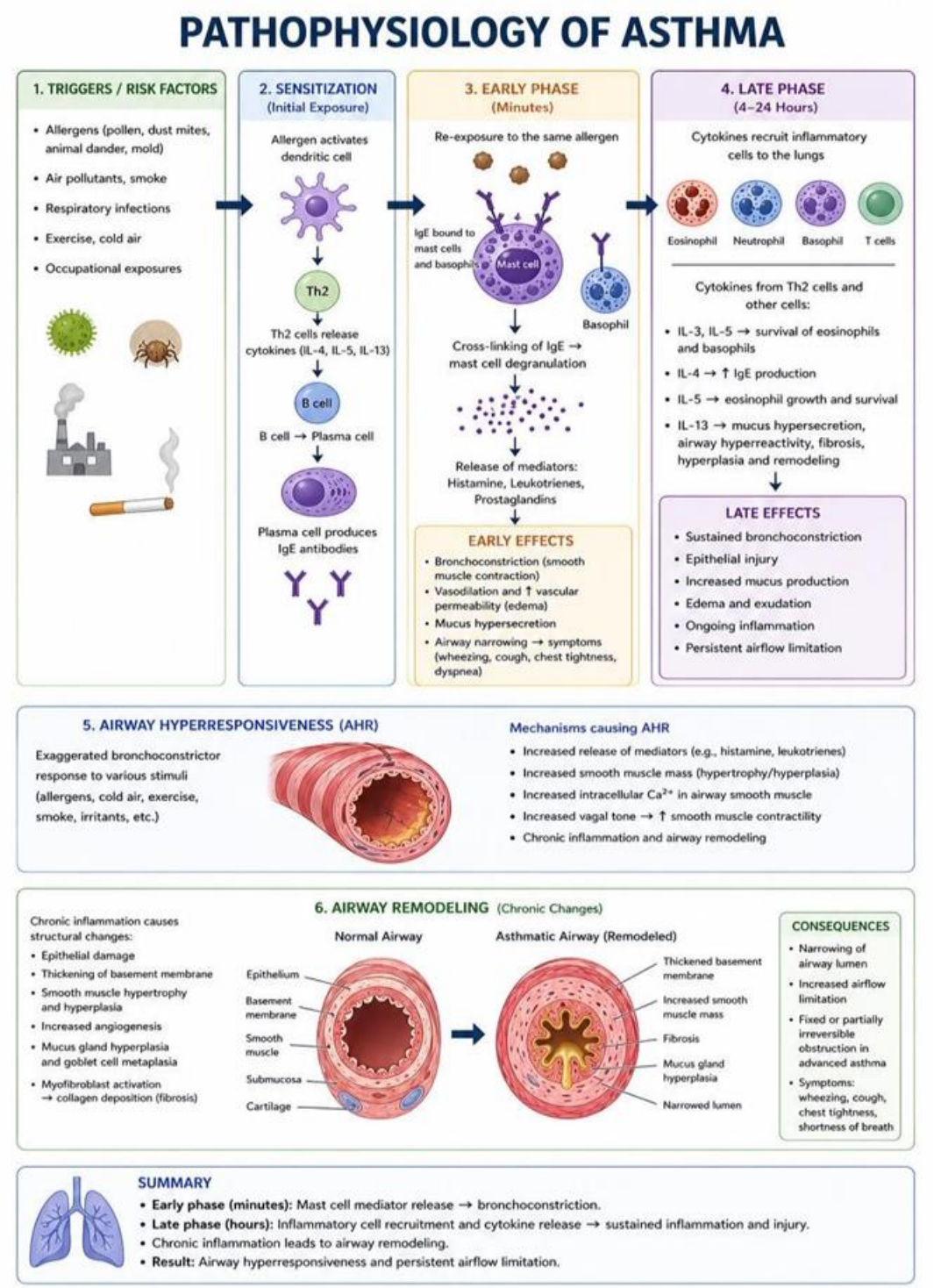


Fig No. 1: Pathophysiology of asthma.

MANAGEMENT OF ASTHMA

β-agonists (both short-acting and long-acting) are bronchodilators with a distinct but complementary mechanism of action (targeting bronchoconstriction of the airway smooth muscle), while ICSs are general anti-inflammatory agents that target airway inflammation, a crucial part of the asthma disease process. While LABAs function as long-term control agents

and are utilized in conjunction with ICS therapy, short-acting β-agonists offer immediate symptom alleviation. Moderate anti-inflammatory and bronchodilating effects are demonstrated by leukotriene modifiers, which block the leukotriene pathway (proinflammatory lipid mediators that, among other inflammatory actions, induce airway smooth muscle tension). Omalizumab is a recombinant humanized monoclonal anti-IgE antibody that binds to effector cells such mast cells and basophils in order to preferentially bind to free IgE, the immunoglobulin molecule that initiates the allergic cascade. Omalizumab, thus, prevents IgE-induced downstream cascade of events, including inflammatory consequences in the airways, in individuals with allergic asthma.e as the severity of their disability increased.

Regardless of age, regular anti-inflammatory treatment with ICSs remains the cornerstone of therapy for individuals with chronic asthma. Patients whose asthma was not sufficiently controlled with low-dose ICSs should be advanced to either medium-dose ICS therapy or low-dose ICS therapy plus a LABA at step 3 (for patients aged 5 years or older). As was previously mentioned, one of the main changes in EPR3 from earlier guidelines is the recognition of potential safety concerns associated with LABA therapy.

Primary care physicians should be aware that, when compared to the greater risk of systemic effects, higher dosages of ICSs for a specific patient may not offer much additional benefit. For instance, a meta-analysis of randomized studies examining fluticasone's efficacy for adults and adolescents with moderate to severe asthma revealed that a dose of 200 µg/d produced the biggest clinical benefit. At dosages of 500 or 1000 µg/d, just a slight improvement was observed, despite a significant degree of individual patient variability. The finding that up to one-third of asthma patients may have some degree of corticosteroid insensitivity and hence may not show a sufficient clinical response even to high-dose therapy further complicates the problem. For patients with poorly controlled asthma, these findings regarding the risks of higher-dose ICS therapy suggest the potential benefits of adjunctive therapies, such as adding a LABA, a leukotriene modifier, or theophylline to medium-dose ICS therapy at step 4 or adding omalizumab therapy to high-dose ICS therapy plus a LABA at step 5. However, many treatments are also linked to safety issues or other drawbacks that need to be balanced against the therapeutic advantages.[4]

SINGLE MAINTENANCE AND RELIEVER THERAPY IN ASTHMA PATIENTS

SMART was linked to a clinically significant lower mean daily dose of ICS (126 mg)

compared with daily budesonide (320 mg), a considerably improved growth rate (mean difference of 1 cm) (P = 0.005), and significant reductions in exacerbations needing medical intervention (P < 0.001).

With an overall risk ratio (95% confidence interval) of 0.68 (0.58–0.80), SMART treatment decreased the risk of the composite exacerbation outcome (exacerbations requiring systemic corticosteroids, hospitalization, or ER visits) in patients aged ≥12 years compared to the same dose of ICS-LABA fixed-dose controller therapy. In contrast, the overall risk ratio of the composite exacerbation outcome with SMART was 0.75 (0.59–0.96) for patients receiving a higher fixed ICS dose with LABA controller treatment.[5]

Controlling and preventing symptoms and exacerbations is the primary objective of asthma therapy in order to attain the best possible lung function and quality of life. This is typically accomplished by using both reliever (short-term symptom alleviation) and maintenance (long-term anti-inflammatory) medications over an extended period of time. According to current guidelines, patients with asthma of at least moderate severity should receive continuous inhaled corticosteroid/long-acting β2-agonist (ICS/LABA) therapy in addition to a rapid-acting bronchodilator as a relief.

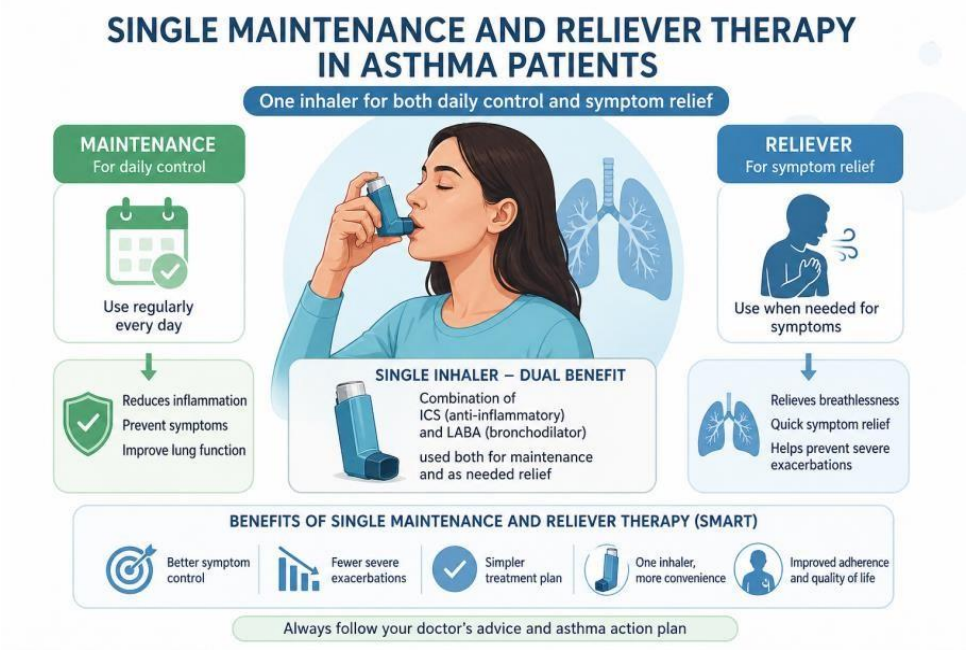
Nonetheless, fixed-dose budesonide/formoterol is offered as a maintenance medication in several nations (and throughout Europe), with necessary modifications administered as relief therapy when symptoms arise. All budesonide/formoterol MRT regimens were linked to a high percentage of reliever-free days and a low frequency of high reliever-use days in routine clinical practice, suggesting that this symptom-adjusted controller regimen produced adequate levels of asthma control.[6]

Regular maintenance inhaled corticosteroids (ICSs) with a short-acting β-agonist inhaler administered as needed for symptom alleviation are the recommended treatment for mild asthma. However, low prescription rates and poor adherence restrict the benefits of regular ICS use in real clinical practice. An alternate approach would be to employ a combination ICS/short-acting β-agonist or ICS/long-acting β-agonist inhaler as a reliever on a symptom-driven basis instead of on a regular maintenance basis.

This strategy aims to improve ICS use in otherwise poorly adherent patients who over-rely on their relief β-agonist inhaler by titrating both the ICS and β-agonist dose according to need.

This approach will only be effective if the β-agonist component relieves symptoms quickly. Evidence suggests that this regimen offers benefits over standard ICS medication and may be a unique, safe, and successful treatment for mild and intermittent asthma.[7]

Every year, the Global Initiative for Asthma (GINA) Strategy Report offers clinicians an evidence-based plan for managing and preventing asthma that can be modified for local conditions (e.g., medication availability). Because of the hazards associated with SABA-only treatment and SABA overuse, as well as the evidence supporting the benefits of inhaled corticosteroids (ICS), GINA advises against treating asthma in adults and adolescents exclusively with SABA. When compared to SABA alone, large trials demonstrate that as-needed combination ICS–formoterol lowers severe exacerbations by >60% in mild asthma, with comparable exacerbation, symptom, lung function, and inflammatory outcomes as daily ICS plus as-needed SABA.[8]



MEDICATION ADHERENCE IN ASTHMA

One of the concerns that must be asked when assessing a patient whose asthma symptoms are not sufficiently controlled despite appropriate therapy is if the patient is truly taking the medicine as directed. Multiple clinic appointments may be required to address the various causes of medication nonadherence. Furthermore, medication compliance may fluctuate over time. The phrase "nonadherence" to asthma therapy refers to a number of related but distinct problems, including improper inhaler technique, nonadherence of the "patient" to prescribed

medication or medications, and nonadherence of the "provider" to asthma treatment and education guidelines—all of which are common issues in asthma care.[9]

Although medication therapy for asthma has been shown to be beneficial, poor treatment adherence may be linked to a higher risk of asthma flare-ups. This study reviewed the literature on the relationship between children's and adults' risk of severe asthma exacerbations and their adherence to asthma controller medication.[10]

Non-adherence is still a major obstacle to asthma treatment, according to the Lancet Asthma Commission. Although pharmacists are becoming more interested in providing more adherence support, medical consultations are still crucial in resolving non-adherence. Studies involving adult asthmatic participants, pharmacist-led or collaborative care treatments, randomized controlled trial designs contrasting interventions with standard pharmacist care, and a medication adherence outcome were all included. The standardized mean difference (d) Recent healthcare initiatives and government policies show that interest in pharmacist-led adherence assistance has increased due to the increasing demand on primary care physicians. was used to analyze the adherence data, and the remaining data was narratively synthesized.[11]

Electronic tracking devices swiftly emerged as the gold standard for gauging inhaler adherence, but high device failure rates may skew results, and awareness of the electronic tracking device may have inadvertently boosted adherence. Second, having access to substantial prescription refill databases allowed for the creation of an even more comprehensive, objective picture of medication-taking behavior. A plethora of research aimed at enhancing adherence was sparked by the realization of the severity of the asthma nonadherence issue. Dosage simplification, patient education, motivational interviewing, adherence feedback, provider communication skill training, and mobile communication technology usage.[12]

The mainstay of maintenance asthma treatment is inhaled corticosteroids (ICS). Nevertheless, ICS adherence is still low. Healthcare professionals find it difficult to identify individuals with treatment-resistant or refractory asthma, which is commonly described as asthma that does not respond to high-dose therapy, due to the high percentage of patients who do not take their ICS as prescribed. Patients with moderate-to-severe asthma who are uncontrolled on high-dose ICS and long-acting β2 agonists may be prescribed newer, frequently more costly

medications as a result, even though it is likely that they would have achieved similar asthma control with optimal adherence to ICS instead.[13]

FACTORS AFFECTING MEDICATION ADHERENCE

"Sticking to a plan" for perceived benefit is what is meant by adherence. This idea is used for people who have accepted and incorporated a doctor-recommended plan.[14]

These include patient-provider relationship factors (dissatisfaction with health care providers, lack of trust, and lack of patient involvement), medication factors (complexity of medication regimen, high medication costs, and poor labeling instructions), patient factors (old age, male gender, low education level, physical and mental status, and health literacy [HL]), and health care system factors (inability or difficulty in accessing pharmacy, lack of follow-up, and poor treatment by untrained staff).[14]

The majority of people with asthma have poor treatment adherence, which may be a major contributor in the disease's poor outcomes, decreased health-related quality of life (HRQL), and expensive expenses.[15]

Adolescents' adherence behavior has also been found to be significantly influenced by the doctor-patient relationship. More specifically, the healthcare provider's job is to help their asthma patients by establishing and preserving a relationship of trust and by offering specific information and guidance.

Two categories of behaviors were found in relation to asthma treatment adherence: purposeful and inadvertent. Adolescents who intentionally choose not to follow their treatment plan because of worries or a lack of faith in medical professionals are said to be intensive. Adolescents' health-related risk-taking behaviors, such as smoking and drinking alcohol, or their overall disregard for the consequences of their actions, are also linked to medication non-adherence. Instead of following treatment, people who don't trust medicine avoid triggers or put up with symptoms.

When therapy is not administered because of ignorance, improper inhaler technique, or forgetfulness, it is considered unintentional. Adolescents stated that maintaining routines is challenging due to their active, busy, and occasionally chaotic lifestyle. Both behavioral types require different types of interven-tion. From both types, those who do not adhere to treat-ment intentionally are the most difficult to treat, hence, bothtypes require tailored

intervention strategies.[16]

METHODS TO MEASURE MEDICATION ADHERENCE

There are several ways to assess adherence in asthmatic patients. For instance, determining whether medication is ordered and subsequently picked up or dispensed at the pharmacy is one way to gauge the start of therapy. This approach has drawbacks since data dispensing does not demonstrate if a patient actually begins taking the drug.[17]

Because undiscovered poor adherence leads to poor asthma outcomes, it is critical to accurately identify drug nonadherence. However, because there is no standardized way to assess adherence, it might be difficult to identify poor adherence in clinical practice. Patient self-report is the most economical approach, although it is widely known that patients often overreport their level of adherence.[9]

EMDs are typically the most objective way to monitor implementation over time. According to some experts, they are the "gold standard" for measuring adherence in COPD or asthma patients in an objective manner. Some of these devices can monitor the quality of the inhaling method and provide feedback and reminders in addition to recording each dosage.[17]

The most common way to gauge adherence to asthma treatment is to look at how often prescription drugs are refilled. However, refill records do not distinguish between the point of discontinuance and the conclusion of a treatment term. Consequently, the rates of persistence may be overestimated by this strategy. All things considered, the majority of currently employed techniques include advantages as well as a number of drawbacks that reduce their usefulness in figuring out the actual adherence rates.[17]

Electronic monitoring devices and dose counts from analog counters were the two objective indicators of adherence. In both studies, research assistants fitted an electronic monitor to dry powder inhalers (DPI) and metered dose inhalers (MDI) and instructed study participants to return the monitors in a postage-paid envelope after four weeks. Additionally, patients were called to remind them to return the deviations. The Smartdisk (Nexus6, Franklin, OH) was utilized for DPI and the Doser Electronic Monitor (Meditrack, MA) for MDI in the COPD trial.

Only patients utilizing an inhaler device without an electronic monitor had their dose counts recorded using analog counters. The study coordinators recorded the date and number of

remaining doses on the analog counter of the device or by counting the number of non-punctured dose capsules (tiotropium inhaler) at the baseline interview. They then recorded the date and doses utilized during a follow-up interview. When the patient started using a new inhaler (for example, when their prescription was updated), the electronic monitors were attached to the inhaler. Between the baseline interview and 30 days later, this might happen at any time. Adherence was calculated using these objective metrics by dividing the total number of doses taken over the course of four weeks by the number of recommended doses. According to convention, adequate adherence was considered as around 80% of the total doses provided.[18]

An 8-item Morisky Medication Adherence Scale questionnaire that was previously available served as the basis for the knowledge and attitude assessment.13 There were fourteen questions in all, eight of which were knowledge-based and six of which were attitude-based.[14]

Patients' knowledge, attitudes, and beliefs regarding bronchial asthma are acknowledged as important factors influencing their health-related behaviors.

This lack of understanding is regrettable given that an increasing number of people are currently afflicted with this illness. Lack of information of asthma among patients and their caregivers can cause delays in starting the right therapy, which raises morbidity and death.[19]

To our knowledge, the validity of the 8-item Morisky Medication Adherence Scale (MMAS-8) has not been demonstrated for patients with asthma, however it is valid and reliable for patients with hypertension. The study's objective was to ascertain the MMAS-8's criteria validity in asthmatic patients.

Asthma control, quality of life, and asthma flare-ups during the previous year were among the health outcomes. Patients' self-completion of the Asthma Control Test (ACT) was used to assess asthma control. In a clinical setting, the ACT is a relevant and dependable instrument that aids doctors in identifying individuals with uncontrolled asthma.[20]

BARRIERS AND CHALLENGES IN SMART THERAPY ADHERENCE

Nearly half of all asthma patients do not have their illness under control, despite the availability of effective inhaler medication. Increased symptoms, health care use, and financial hardship are linked to suboptimal control. Many eHealth-based asthma self-

management apps have not been successfully incorporated into everyday practice, despite mounting evidence of their usefulness and efficacy. Adoption failure can be caused by a number of factors, including data privacy concerns or a lack of drive or expertise.[21]

If an inhaler has inbuilt or attached electronic components that can track medication dosage, time, and, in some situations, the suitability of the inhaling pattern, it might be considered "smart."[22]

Inhaler usage errors are common, especially in older asthmatic patients. Inhaler technique errors and their causes, as well as inhaler technique self-perception versus actual performance, were compared between old and non-elderly asthmatics in this study.[23]

Oral corticosteroids (OCSs) are used by many patients with severe or uncontrolled asthma in addition to long-acting β2-agonists (LABA) and inhaled corticosteroids (ICS), either chronically to maintain acceptable levels of asthma control or occasionally to treat exacerbations. Numerous severe and incapacitating acute and long-term side effects have been linked to the long-term or frequent use of OCS for asthma.[24]

Increased usage of relievers is a sign of poor asthma control and may exacerbate symptoms because the instant symptom relief may cause patients to put off or even avoid seeking medical attention. The Global Initiative for Asthma (GINA) 2019 guidelines4 indicate a paradigm shift regarding the use of relievers for asthma management and advise against following conventional care algorithms that increase patients' dependence on short-acting β2-agonists (SABAs) because frequent and frequent use of these medications raises the risk of exacerbations. Our interest in investigating the relationship between increased usage of relief inhalers and healthcare utilization (HCU) was sparked by this paradigm change.[25]

The recommendation for patient education and routine physician review is a fundamental part of many asthma care guidelines. To assess the efficacy of asthma education initiatives, several controlled experiments have been carried out. Although these programs increase patient understanding, it is less clear how they affect health outcomes. At its most basic level, education is restricted to imparting knowledge about asthma, its causes, and its management.[26]

Inhaler usage errors are common, especially in older asthmatic patients. For younger patients, prior regular inhaler training was linked to improved actual performance, but not for older

patients. Elderly asthmatics may require specially designed inhaler education programs, as regular training was previously linked to a much larger percentage of patients demonstrating proper or acceptable technique, but only in non-elderly asthmatics.[27]

As the number of persons with chronic illnesses and ailments that require long-term care in the community rises, patient education is becoming a crucial component of service delivery. Patient demands were taken into consideration when designing the customized patient education program. It was effective in increasing understanding of the asthma disease process.[28]

STRATEGIES TO IMPROVE MEDICATION ADHERENCE

Each of the aforementioned elements is amenable to asthma education, according to several research conducted globally that have assessed the effects of patient education. As a result, patient education is now crucial to managing asthma in people of all ages.[28]

Clinic for Community Health Ole has made an effort to lower obstacles to medication adherence related to language, cost, and access to treatment by: 1) making drugs available from the clinic at a discounted price; and 2) offering one-on-one consultations.[29]

Without requiring more time or money, patient-centered methods are linked to improved treatment outcomes and patient retention. The goal of motivational interviewing (MI), a patient-centered counseling technique that can be rapidly included into patient interactions, is to increase patients' drive to change if they are not ready to do so.[30]

Even with the availability of efficient treatments, managing asthma is still difficult since it depends on patient and healthcare provider (HCP) behavior. Notably, pharmacists can offer long-term follow-up treatment for the efficient management of chronic diseases like asthma. Pharmacists are an essential component of the health care team in the primary care environment.[31]

CONCLUSION

The reviewed literature makes it abundantly evident that asthma is a complicated chronic inflammatory illness that needs to be managed consistently over an extended period of time in order to obtain the best possible control and enhance the quality of life for patients. Poor drug adherence continues to be a significant obstacle to excellent treatment outcomes, even with the development of powerful pharmacological therapy, particularly inhaled corticosteroids and combination regimens. According to the data, uncontrolled asthma, more exacerbations, and greater healthcare utilization are largely caused by improper inhaler use, patient ignorance, and inconsistent adherence.

The results also highlight the clinical advantages of Single Maintenance and Reliever Therapy (SMART), which has been a successful tactic for lowering corticosteroid exposure, decreasing exacerbations, and enhancing overall disease control. However, patient compliance and appropriate inhaler technique are critical to its success. Patient-related actions (both purposeful and inadvertent), healthcare system constraints, prescription complexity, and socioeconomic difficulties were found to be some of the factors influencing adherence. Accurate assessment and intervention are further complicated by the lack of established techniques for monitoring adherence.

In conclusion, a multimodal strategy that incorporates patient education, streamlined treatment plans, frequent follow-up, and improved patient-provider communication is needed to improve medication adherence in asthma patients. Addressing adherence hurdles can be greatly aided by the integration of digital health tools, pharmacist-led treatments, and individualized counseling techniques. Enhancing these tactics in conjunction with evidence-

based treatments such as SMART can greatly improve long-term clinical results, lower disease burden, and improve asthma management.

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