REVIEW ARTICLE

Malpractice in Diagnosis and Treatment of Asthma and Steps Need to Be Taken From Physicians to Adhere to Asthma Guidelines

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ABSTRACT

Asthma is a common chronic disease characterized by episodic or persistent respiratory symptoms and airflow limitation. A minority of patients with asthma have uncontrolled or partially controlled asthma despite intensive treatment. These patients present a special challenge because of the extensive diagnostic evaluation that they need, insufficient evidence regarding personalized treatments, and their high consumption of health-care resources. Asthma treatment is based on a stepwise and control-based approach that involves an iterative cycle of the assessment, adjustment of the treatment and review of the response aimed to minimize the symptom burden and risk of exacerbations. Anti-inflammatory treatment is the mainstay of asthma management. In this review we will discuss the rationale and barriers to the treatment of asthma that may result in poor outcomes. The benefits of currently available treatments and the possible strategies to overcome the barriers that limit the achievement of control of asthma in the real-life conditions.

Keywords: Malpractice; asthma; Guidelines.

INTRODUCTION

Over diagnosis is increasingly recognized as a problem in a range of diseases, including asthma [1]. Asthma has traditionally been diagnosed on the basis of history and response to a trial of treatment; however, asthma presents with respiratory symptoms that are common to a wide range of disease processes and are not specific to asthma (table 2). In addition, the physical examination is usually normal, unless a patient is exacerbating at the time of the examination. As asthma is so common, the majority of diagnoses are made in primary care, where access to objective testing in asthma is limited [2]. Even if objective tests are available, there is no gold standard test for asthma and many of the tests that are available (*e.g.* spirometry, fractionated exhaled nitric oxide (*F*eNO) and bronchial provocation tests) do not necessarily exclude asthma even if they are normal, particularly if the patient has started treatment prior to testing [3].

This complexity makes both under- and over-diagnosis an obstacle that clinicians need to work to avoid in asthma. Both possibilities carry costs to both the patient's health and to healthcare systems [4].

Diagnosing Asthma *Current guidelines :* In recent years there has been a move to include objective testing in asthma diagnosis algorithms. The most widely used asthma guidelines worldwide are those issued by the Global Initiative for Asthma (GINA). The current iteration suggests only treating asthma prior to testing of spirometry/peak flow with reversibility if there is clinical urgency, and always documenting the basis on which an asthma diagnosis has been made. If the objective testing does not support a diagnosis of asthma it suggests repeating the tests at a later date or considering alternative tests. The British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN) also regularly publish an asthma guideline,

which is widely used in the UK and other countries. The most recent version still suggests treating first for those with a typical history, although lists a range of other tests for those in whom the diagnosis is unclear. However, also in the UK, the National Institute of Clinical Excellence (NICE) have published a guideline outlining a diagnostic protocol for asthma that includes not only spirometry with reversibility [5].

All three of these guidelines suggest using bronchial provocation testing where asthma is suspected, but where prior investigations have been nondiagnostic. These tests can utilise direct bronchial provocation testing with histamine or methacholine, or indirect provocation with exercise, inhaled mannitol, nebulised hypertonic saline or eucapnic hyperventilation. Although often considered to be "gold-standard" investigations in suspected asthma, challenge tests can be positive in non-asthmatic patients, have a low but meaningful false negative rate, and can be influenced by baseline lung function and inhaled corticosteroid (ICS) therapy. Therefore, they need to be appropriately interpreted on a case-by-case basis. GINA and BTS/SIGN endorse both direct and indirect challenge tests, whereas only direct provocation protocols are currently recommended by NICE [4].

Another important difference between current diagnostic guidelines regards the utility of FeNO testing. This is quite strongly endorsed by NICE, but remains much less emphatically recommended in the other guidelines. This reflects a lack of consensus within the respiratory community regarding the utility of FeNO testing: although a potentially valuable surrogate marker of lower airway inflammation, it is influenced by extrinsic factors such as diet and smoking, as well as comorbid pathology such as nasal polyposis. Moreover, the absence of clear normative values can make identifying a pathological FeNO level challenging. These different approaches reflect the lack of consensus within the respiratory community about how to diagnose asthma, and differing opinions regarding the usefulness of FeNO and other

measures of type 2 inflammation in making the diagnosis [6].

Overdiagnosis of Asthma

Over-diagnosis defined as a patient does not have asthma and treated mistakenly as asthmatic patient when in fact another disease is attributed for the symptoms. Over-diagnosis can be defined as not recognized asthmatic patient with a sustained clinical remission[7].

Estimates of the overdiagnosis of asthma vary, probably in part due to the different populations studied and the varying definitions and approaches to diagnosing asthma within the studies. The most comprehensive analysis, to date, is that published by [7], which re-examined 613 Canadian adults with a diagnosis of asthma. Those included underwent an assessment with pre-and post-bronchodilator spirometry, and had a bronchial provocation test if this did not confirm asthma. If this was negative, asthma medication was reduced and the provocation test repeated.

If still negative, asthma medication was stopped and the provocation test repeated again. If all of these tests were negative, participants were reviewed by a chest physician to make a final diagnosis of asthma or an alternative cause for their symptoms. The patients were followed up for a year, including repeat provocation tests at 6 months and 1 year, and if they had symptoms at any point during follow-up were encouraged to be seen by the study physician and spirometry was repeated at that stage. Asthma was ruled out in 33% of participants at the end of this diagnostic algorithm and after 12 months 30% remained off asthma medication. Although subjects were approached at random by an automated phone message, there is a possibility that patients who had doubts about their asthma diagnosis were more likely to agree to participate in the study, thus overestimating the extent of overdiagnosis. However, some of the inclusion criteria could also have resulted in an underestimate (*e.g.* excluding those with an asthma diagnosis made more than 5 years ago). The figure of 30% is not dissimilar to other published data: a study of patients in primary care in the UK by [8] found that one third of

patients labelled as having asthma had normal spirometry and provocation tests.

Obese patients are known to have more respiratory symptoms than the non-obese, and so one might expect them to have an even greater rate of overdiagnosis of asthma [9] examined both over- and under-diagnoses in the morbidly obese by recruiting 86 patients who were undergoing pre-operative screening for bariatric surgery. 32 of the participants had a physician diagnosis of asthma, with the remainder free of an asthma diagnosis. They underwent pre- and post-bronchodilator spirometry, FeNO measurement, impulse oscillometry and a methacholine provocation test. Asthma was diagnosed when symptoms were present in the presence of either significant reversibility in their FEV1 with a shortacting β2-agonist (SABA) or a positive provocation test. 40% of patients with a prior diagnosis of asthma did not meet these criteria, although it is possible that some of those patients did still have asthma, in particular as not all patients agreed to stop their inhaled therapy prior to testing. Interestingly, underdiagnosis was also present: 31% of patients with no diagnosis of asthma had asthma symptoms plus a positive test. The authors concluded that symptoms were "unreliable for an adequate diagnosis of asthma" in this population.

The consequences of overdiagnosis : One of the problems of misdiagnosis is that there may be an alternative diagnosis that is not made in a timely fashion. Some of the final diagnoses in the study by [10], such as ischemic heart disease, subglottic stenosis and pulmonary hypertension, were serious and could lead to patient harm if unrecognized . In addition to this risk, patients are often on long term inhaled therapy unnecessarily, leading both to potential side-effects and significant ongoing healthcare costs as these drugs are likely to be issued for many years after a diagnosis of asthma. In the past, many "mild" asthma patients were simply on an as required SABA inhaler, but increasingly this is discouraged with daily ICS therapy recommended for all but a few. This represents a burden to the patient (taking an inhaler twice daily long term) and could

conceivably cause side effects such as an increased risk of adrenal suppression, diabetes, cataract formation and pneumonia [4].

If the wrong diagnosis is made patients are also likely to remain symptomatic, and potentially have their asthma treatment "stepped up", adding to both the cost and the potential for side-effects. The most significant direct harm from overdiagnosis is likely to be in patients whose symptoms have led to them being inappropriately commenced on OCS. Although extremely useful in the short-term management of significant asthma exacerbations, and previously in the care of the relatively small group of asthma patients with genuine severe asthma that is refractory to inhaled medication, medium- to long-term OCS use is associated with significant treatment-related morbidity. A recent systematic review of the published literature found significantly increased likelihood of bone and muscle, psychiatric, cardiovascular, ocular and metabolic disease in asthma patients receiving long-term OCS therapy [3]. At a societal level, overdiagnosis of asthma may lead to significant opportunity cost, as resources required elsewhere are inappropriately spent on overdiagnosed asthma. This is of particular relevance as high-cost therapies such as targeted biologic drugs and bronchial thermoplasty come into more widespread use. The direct costs related to asthma in Europe have been estimated at EUR 17.7 billion per annum, mostly related to outpatient care and drug costs. One Canadian study has completed a cost analysis of direct costs (doctor visits and asthma-related drugs) to estimate the cost– benefit of screening patients with a physician diagnosis of asthma with objective testing [2]. They calculated a saving of CAD >35 000 (approximately EUR 23 700 or GBP 21 150) per 100 patients screened. In the UK, NICE published a guideline on the diagnosis of asthma, attempting to make a protocolised objective testing standard care for all patients with suspected asthma, and has assessed the cost of its diagnostic protocol as GBP 92 per patient (EUR 103). It anticipates an associated saving of GBP 12 million per year in England alone (EUR 13.5 million), assuming

that 33% of patients diagnosed with asthma do not have the condition (this assumption was based on the study of **[10].**

Underdiagnosis of Asthma

The estimates of underdiagnosis of asthma vary widely from as little as 19% to as much as 73%. The largest study, to date, was carried out in Copenhagen in 2000, and involved questionnaires being sent to over 10 000 randomly selected subjects aged 14–44 years of age. Those who reported symptoms suggestive of asthma were further assessed according to the GINA recommendations at the time, which included tests of reversible airflow obstruction. 493 were diagnosed with "definite asthma", and of these 50% had not been diagnosed previously **[11]**. Underdiagnosis may be due to medical professionals failing to recognise the disease, and perhaps attributing symptoms to obesity, deconditioning, cardiac disease or other causes. The patient may appear well with no abnormality on examination and if objective tests for asthma are carried out, particularly as a one off or when the patient is already on treatment, they may be falsely reassuring or misunderstood by the treating physician as excluding asthma. One might speculate that because asthma is so prevalent, patients are less likely to be referred to specialists for confirmation of the diagnosis when it is unclear, whereas patients with suspected diseases that are less familiar may be more likely to be referred. While this may account for some underdiagnosis, it appears that a substantial proportion of patients simply don't ever report their symptoms to a doctor **[4]**.

The consequences of Underdiagnosis asthma:
Asthma that is undiagnosed is also untreated, and this is likely to result in patients with ongoing symptoms. Patients may avoid exercise, may miss work and be less productive, and their quality of sleep and overall quality of life are likely to be adversely affected. These patients are likely to have unsuppressed airway inflammation and eosinophilic airway inflammation is associated with more asthma exacerbations, which may lead to the requirement for OCS and potentially hospitalisation. It is possible that patients may also die of asthma prior to diagnosis, or on their

first presentation of asthma. The UK national review of asthma deaths examined 195 deaths attributed to asthma between 2012 and 2013 [12]. Importantly, 38% of these patients had four or fewer inhalers with a steroid component issued in the previous year, indicating that undertreatment was a probable important factor in their deaths. Almost half of the patients that died of asthma were being managed as "mild" or "moderate" asthma. While this does not directly deal with underdiagnosis, it is an important reminder that even in the developed world undertreatment of asthma remains a problem. As well as the impact on quality of life and risk of exacerbations, patients whose asthma is untreated may also be at risk of airways remodeling. Before ICS were routinely prescribed in asthma, the natural course of the disease was for a decline in FEV1 over time and the patient's degree of obstruction was related to the duration and severity of their asthma. [4].

Asthma misdiagnosis appears to be widespread. This is in part due to the wide differential diagnosis for common respiratory symptoms and the lack of a standardized approach to diagnosis or gold standard test for asthma. It remains a clinical diagnosis, requiring the synthesis of history, examination, physiological tests and possibly trials of treatment. The risks of overtreatment, missing an alternative diagnosis and the financial cost of long-term unnecessary medicines make overdiagnosis a considerable problem. Overdiagnosis is likely to be reduced by the routine use of objective tests of airflow obstruction or bronchial hyperreactivity before any treatment is commenced. This is likely to be further improved by including a measure of airway type 2 inflammation, such as FeNO. Priority should be given to prospectively testing diagnostic algorithms that include combinations of these measures, and increasing access to these tests from primary care. Underdiagnosis is more difficult to address, and is equally concerning given the potential risks to the patient of delayed treatment. Public health campaigns to encourage patients to present to primary care if they have symptoms of asthma may be required, or screening of patients for respiratory symptoms when, for

example, joining a primary care practice could identify patients who need to have further assessment [4].

Malpractice and Barriers to Compliance

Medical malpractice is defined as any deviation from accepted medical guidelines during treatment of a patient caused by physician which can harm the patient [13].

Global and national asthma guidelines were made to guarantee better asthma management and control according to the standards. The 2005 Global Asthma Physician and Patient (GAPP) study described a contrast between recommended GINA guidelines and actual management practice in 16 countries [14].

these guidelines ensure an effective and efficient treatment plan. They also enable the physicians to make the most appropriate therapy decision according to the patient own clinical situation. Noncompliance to guidelines remains a dilemma; in spite of all works to develop and expand them. It would strongly affect healthcare costs and the quality of patients' life [15].

The national review of asthma deaths (2014) identified the lack of knowledge of the UK asthma guidelines as a cause of 25% of asthma deaths in that year. Barriers to asthma guideline adherence can be related to the patient, the health care system, or health practitioners [16]. Recent studies have shown that only a small percentage of asthmatic patients receives appropriate treatment with ICS [17].

In the past, there has been concern that excessive uncontrolled use of beta-2 agonists might have contributed to rise asthma mortality and hospitalization risk [18].

A study performed in the US on more than 16,000 asthmatics aged 12–65 years found that about 40% of patients met the criteria for appropriate prescription of ICS + LABA, and the patients with appropriate prescriptions were significantly more likely treated by pulmonologists and allergists than by GPs [19]. Furthermore, in Northern Ireland a wide use of ICS + LABA has been reported in 67% asthmatic patients without Prior ICS therapy [20].

A considerable overtreatment with ICS in primary care patients has been observed in the Netherlands, where about 43% of asthmatic patients were prescribed ICS without a clear reason [21].

The GINA revealed that primary care settings and developing countries face challenges to implement asthma management recommendations. Mentioned that lack of knowledge is not the only barrier to follow asthma guidelines but insufficient time for control assessment and providing patients with a written asthma plan [22].

Some physicians simply forget to do so. Another important barrier is the lack of experience and confidence. Ignorance about the importance of written asthma plans was obvious with the low referral rate to asthma educators. Surveyed reasons for noncompliance and revealed the same causes, in addition to lack of resources, mentioned by 13.5%. However, lack of awareness remained the most important barrier [23].

One important knowledge related barrier was mentioned by is that physicians who were working for long years seemed to have a low implementation of guidelines explained by their dependence on early gained knowledge which was not guideline adherent, so long years of experience may have a negative impact on guidelines application [24].

Some of the elements mentioned above were stated by the majority of physicians who were not aware and not familiar with the recommendations. The main reasons for that were attributed to them not being included in the development of the guidelines and the guidelines were not circulated well in their facility. Some physicians did not even agree with these guidelines. Some thought they were not applicable to their patients. Assessed the adherence of primary care physicians to the Saudi National Asthma Protocol [25].

A dutch study evaluated self-reported barriers that limit adherence of GPs to clinical practice guidelines; patient related barriers are those mostly reported, suggesting that current guidelines do not always adequately incorporate patient preferences, needs and abilities [26].

The belief that a recommendation could not be successfully implemented by patients likely

makes the physician less adherent. Also in presence of self-reported appropriate knowledge of guidelines, GPs feel that they are limited by the difficulty to reconcile patient preferences with guideline recommendations [27].

At last difficulties in the implementation of guidelines in clinical practice may be caused by different factors such as complexity, poor doctor-patient communication, structural limitations of the health system, lack of incentives, treatment duration, patients' misuse of prescribed medications, low expectations and aspirations about the achievable degree of control [15].

Steps Need to Be Taken

Since GPs often tend to treat patients independently from guidelines, a need for increased physician awareness of GINA guidelines is warranted. Although from the patient's perspective good asthma care is costly, the cost of not treating asthma correctly is even higher [28].

Suggested that the use of electronic medical records might improve guidelines adherence .Although it may not advance the actual delivery of recommendations but serve to achieve better documentation [29]. Pointed to the importance of teamwork and distribution of tasks as a feature of high guidelines adherent practice in the primary care settings. They as well stated that the presence of electronic medical records might enhance guideline compliance. In their study, they argued that teamwork; coordination of care within the health care practice has a greater impact on guidelines implementation than individualized intervention such as improving healthcare professional knowledge and providing resources and time. According to over prescribed short-acting beta-agonists and under prescribed inhaled corticosteroids are the causes of most asthma hospital admission [30]. The introduction of electronic surveillance of the prescription refill system could alert the physicians to facilitate monitoring populations at risk. Computer decision support systems, including electronic alerts, are gaining popularity around the world to raise prescribing safety. They referred to practice policies that

can pick up inappropriate LABA monotherapy and give feedback to physicians [31].

Found that intervention that can support health care workers adherence to asthma guidelines include: Health information technology and paper-based interventions planned to help in decision-making, feedback and audit to deliver information about the performance of health care workers and clinical pharmacy support interventions [32].

Finally, there is a need to further explore why a gap still exists in the provision of evidence-based care for asthma in primary care, and to identify how GPs can be supported to encourage adoption of evidence-based practices. Programs that simplify use of guidelines, based on handier decision support tools and electronic technologies and an expanded medical team involving patient advocates, practice facilitators, school nurses, and pharmacists could improve the quality of asthma care within the primary care setting [28].

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