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Review Article

Management of Allergies in Primary Care

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Abstract

Introduction: In the majority of countries in Europe, most patients who ask for medical advice for allergic medical conditions are first observed in primary care settings, likely due to the relative simplicity of access but also due to the paucity of expert allergists to be able meet the largely increasing need

Aim of Work: In this review, we will discuss the most recent evidence regarding Management of Allergies in primary care.

Methodology: We did a systematic search for Management of Allergies in primary care. using PubMed search engine and Google Scholar search engine. All relevant studies were retrieved and discussed. We only included full articles.

Conclusions: The diagnosis of allergic medical conditions usually involves obtaining a detailed clinical history, that will further be supported by *in-vivo* or *in-vitro* investigations. Additional procedures like challenge tests are required to confirm the accurate diagnosis. In accordance with the significant workload in a primary care setting, simplified protocols for detection and management of allergic diseases are suggested, that must be further altered based on local (national) conditions.

Keywords: *Allergy; IgE; Management Pathways; Primary Care*

Introduction

In the majority of countries in Europe, most patients who ask for medical advice for allergic medical conditions are first observed in primary care settings, likely due to the relative simplicity of access but also due to the paucity of expert allergists to be able meet the largely increasing need [1]. Accurate diagnosis with detection of all causing allergens is an important prerequisite for proper treatment

of allergic condition by the clinician. One of the goals of the EAACI Task Force for Allergy Management in Primary Care settings was to critically evaluate the diagnostic investigations and to give treatment guidelines for the most common allergic medical conditions encountered and managed by general practitioners. In this review, we will discuss the most recent evidence regarding Management of Allergies in primary care.

Methodology

We did a systematic search for Management of Allergies in primary care. using PubMed search engine (http://www.ncbi.nlm.nih.gov/) and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles.

The terms used in the search were: allergy; IgE; management pathways; primary care.

Skin prick testing

Skin prick tests (SPT) are considered to be the oldest and, to a large extent, the most clear investigations to confirm or rule out the suspicion of the presence of an IgE-mediated allergic medical condition. Skin prick tests create the allergic response locally: a drop of the suspected allergen extract is put on the skin and the skin barrier is then disrupted using a lancet. If an IgE allergy against the allergen is present on local skin mast cells, a wheal and flare allergic reaction is created, seen macroscopically and recorded to make the diagnosis of IgE-mediated allergy.

Skin prick tests are generally used in any case where a clinical suspicion of IgE-mediated allergy is present [2]. In relation with a relevant past history, results of the skin prick tests could aid in the confirmation or exclusion of the presence of specific allergen triggers in any individual who has allergic rhinitis, atopic dermatitis, asthma, or food allergy. There are no clear age limits for allergy, despite that skin reactivity is relatively less among young children and likely older individuals. The number of investigations must be guided by clinical manifestations and economic concerns [3]. The sensitizations of IgE is altered through relatively longer durations, thus investigations must be only redone less commonly [3].

The presence of any underlying systemic inflammation and/or respiratory infections might elevate the severity of skin reactivity influencing the outcomes and the possibility of developing systemic reactions [4]. After the development of an anaphylaxis, there could be a period of non-reactivity, thus Skin prick tests are advised not to be done before at least a few weeks after [3]. The skin must be intact in order to perform an accurate Skin prick test. In patients who have severe eczema or dermographism Skin prick tests are generally challenging to perform and interpret.

The development of systemic reactions and/or severe anaphylaxis reactions following Skin prick tests are extremely rare and, in most cases, are linked to testing to foods, usually fish-related, but can also be with nuts or milk [5]. A previous study concluded the presence of a relatively higher rate among infants, with 6 cases among more than one thousand cases evaluated over a duration of three years, all linked to food testing, on the other hand, this rate was later questioned by other studies during the same duration that concluded no presence of systemic reactions among more than 10,000 children evaluated [6]. All patients recovered promptly following proper management. In another series of surveys reporting deaths related to skin testing or immunotherapy in the US between 1945 and 2001, two cases attributed to Skin prick tests were included. Intradermal testing, usually used during the assessment of drug or venom allergies, and less in respiratory-related allergies, carries a relatively increased risk for the development of systemic reactions and will not be detailed in this current review as these tests are only done by specialists. To improve the consequences of the development of a serious side effect, it is advised that Skin prick tests are only done within professional settings where there is emergency equipment, enough adrenaline and trained personnel for its use, so any developing systemic reaction could be immediately managed. Food allergen testing and/or the presence of an active or severe asthma must be considered as important predisposing factors. On the other hand, Skin prick tests using commercial aeroallergen extracts must generally be considered to be relatively safe.

Parameters that are considered include the presence of drug interference, other underlying co-morbidities, site, extracts, controls, panel, prick device, time period, interpretation of results, determination of cut-off values, recording and reporting of results [7]. The details of different protocols of Skin prick tests are not relevant to the scope of this review. Briefly, multiple drugs, most usually anti-histamines, could influence the outcomes of the test and must be asked for and stopped prior to performing Skin prick tests [7]. The presence of any contraindications to Skin prick tests must be also ruled out. The forearm and the back are usually the preferred sites. The drops must be placed at least two centimeters apart, as there may be an existing interference in highly positive cases. Manufacturers standardizes available extracts in varying methods thus outcomes cannot be not directly compared. Non-commercial extracts are usually considered to be of a less value, on the other hand, they might be beneficial when standardized extracts are not readily available, or in the case of foods, where fresh products could be more sensitive. The diluent (which is often sodium chloride) must always be used as a negative control and histamine at ten mg/ml, as a positive control. The allergen panel must reflect the local sensitization map, on the other hand, GA2LEN has recently suggested another European panel that might improve testing harmonization and give more comparative data [3]. Multiple prick devices are generally available. A new lancet must be used for each used allergen to prevent any cross-contamination. The solution used could be dried off immediately when the prick is done, considering avoiding spill-over to adjacent prick sites. Outcomes could be read 150 later (100 in cases with histamine positive control). The negative control is generally expected not to give any wheal, whereas the positive must produce a wheal that is larger than three millimeters in diameter. With applying such controls, an arbitrary cut-off of three millimeters is most commonly used in clinical settings to confirm a positive reaction; whereas, the presence of smaller wheals could still possess clinical importance. Wheals are usually marked using a pen and transferred to another piece of paper that has scotch-tape for archiving. The maximum wheal diameter is enough to report [8].

When interpreting results of Skin prick tests, the variations between allergic medical conditions and different allergen extracts must always be considered. Regarding other methods that evaluate IgE sensitization, a positive result does not prove the presence of an underlying allergy. Generally, Skin prick tests are considered to be more sensitive than being specific tests [9]; this might reflect the fact that a significant rate of the general population, varying among different countries, might actually have asymptomatic sensitization. Taking this into consideration, Skin prick tests are considered to be stronger for excluding a hypothesized correlation between an allergen and a patient's clinical manifestations, rather than confirming its presence. however, the latter could be most usually done in association with the clinical signs and symptoms. In cases of food allergy, cut-off values, commonly close to seven or eight millimeters, have been demonstrated to have a relatively high predictive value in association with positive challenges [9]. These cut-off limits have not been confirmed for cases of respiratory allergy, despite that generally the larger the response of Skin prick tests, the higher the likelihood for the presence of a clinically significant evaluation.

Usefulness of skin prick tests in primary care

Generally, there is no consensus on the simplicity of general practitioners performing Skin prick tests, taking into consideration the differences of access to education and regulations around different countries in Europe and in the world. General practitioners who are well-trained to do and interpret the results of Skin prick tests and working in different settings where the development of any possible serious systemic adverse event could be well-managed, could facilitate the diagnosis and treatment of allergy and mild-to-moderate asthma. Additional caution must be considered in cases of food allergy or severe/uncontrolled asthma, where general practitioners might prefer to refer to secondary care to perform Skin prick tests [7].

In vitro allergy diagnosis

Allergen-specific IgE assessment in blood is considered to be an essential tool that aids in diagnosing cases of allergy. nowadays, the *in vitro* diagnostics market is generally diverse with a relatively huge number of present options. The task force assessed which assays can be most beneficial in any given clinical condition and how to ideally compare between variable options. The general indications for the use of *in-vitro* diagnostic investigations are usually the same indications of Skin prick tests. *In-vitro* diagnostic investigations often demonstrate relatively more sensitivity but less specificity and thus are used whenever Skin prick tests do not produce reliable outcomes. In fact, in

some countries in Europe, some health insurance companies ask for *in-vitro* IgE investigation prior to an allergen-specific immunotherapy is given.

Similar to results of Skin prick tests, similar considerations that refer to the presence of an asymptomatic sensitization are valid. The interpretation of allergen-specific IgE assays is based on the cut-off values. Several comparative studies [10] demonstrated that, even in cases where outcomes obtained with different systems link and are observed in the same or similar type of units, they are not considered to be inter-changeable. thus, critical and clinically significant cut-off values must be determined and assessed for any allergen and system is used.

The choice of the test

Regardless of which investigations is used to detect the presence of IgE-mediated allergy, the general practitioner must know that the assay be done with enough accuracy. General practitioners have a choice of either evaluating the samples on site or sending the samples to an external laboratory. If practitioners testing is present, it might be used as a standard assessment. Taking into consideration that the panels in some cases provide the summarized picture of IgE against a number of several allergens without further distinguishing. Doctor's office investigations are not as well studied as the more conventional lab assays assessed in auto analyzers. The general impression of is that they have relatively lower sensitivity, and thus ruling out the presence of an allergy requires more confirmation using a laboratory assay. however, doctor's office investigations make it possible to get feedback while the patient is still present at the office, with taking advantage of the fact that the decision on the later management should not be delayed. The outcomes from using these assays could be interpreted qualitatively or semi quantitatively without the need of an aid of any special reading devices.

Different investigations from different manufacturers might give unreliable results. For biological concerns, the quantity of allergens that are used for the production of the investigations significantly differs among different sources and preparations, therefore affecting the variability between different test systems. nowadays, no source material quality or quantity description is present for most allergy investigations, therefore comparing allergen content as a quality parameter among different producers is not possible.

To produce reliable guidelines [11] many companies in European countries have been making *in vitro* allergy investigations were identified. Available websites were assessed for assay methods, products and cited publications. Most investigations use a reference curve that is calibrated against the WHO 75/502 reference IgE standard concentrations. The concentrations of detected IgE antibodies are frequently reported using IU/ml or KIU/l units. Multiple Several studies [12,13] assessing correlation, accuracy, reliability, and precision of IgE investigations demonstrated that there is significant variability in measured IgE concentrations. The present variation between different assay systems has also been found to be allergen dependent.

Factors affecting test results

Tests result usually depend on the way the sample is handled, the quality and contents of the allergen parts, the sensitivity of the detection test, the determination of the cut-off values, and the unit in which the outcomes are expressed. The price by test could limit the number of allergen extracts that are used for evaluation and therefore influence the final diagnosis.

Allergen-specific IgE assays done with multiple testing systems display outcomes that are not interchangeable. It is thus important that the method used is mentioned clearly. A choice between different producers is considered to be rather difficult. There is in fact, a wide range of cost per test within and between different countries because of differences in culture, government policies (including reimbursement), size of laboratories, staffing, number of investigations needed, company-supported placement of equipment. Comparison of pricing from a general practitioners' perspective is hampered by the situation that only a few, usually only one, diagnostic test is provided by laboratories in close vicinity to general practitioners.

Management pathways for allergic diseases in a primary care setting

Management pathways were constructed for the allergic conditions detected as most commonly encountered and management in a primary care setting: allergic rhinitis, asthma, food allergy, urticaria and contact dermatitis.

Past medical history is the most important factor in the diagnosis of allergic rhinitis, as it makes it possible to evaluate the presence, severity and longevity of nasal clinical manifestations. Allergic rhinitis is usually known as having at least 2 of the known manifestations for more than one hour a day for more than two weeks [14]. Often, these clinical manifestations follow allergen exposure, whereas, non-allergic factors (like cigarette smoke, drugs, alcohol intake, spices) might be the only triggering factor [14]. Past medical history must include certain questions associated with timing and severity of clinical manifestations, predisposing factors, seasonal variations, and indicators of atopy in different organs. Allergic rhinitis and asthma commonly co-exist, therefore bronchial clinical manifestations must be assessed.

Physical examination consists mainly of internal and external nasal examination, revealing mucosal pathology without the presence of signs of infection and without the presence of major structural abnormalities. In primary care, anterior rhinoscopy is considered to be the first step as it makes it possible to inspect the first part of the endonasal cavity. Mucosal pathology in allergic rhinitis can consist of mucosal congestion and/or transparent secretions but might be normal among managed patients. In cases of unilateral pathology, major crusting or bleeding, headache, smell disorder or suspicion of rhinosinusitis, patients must be referred for nasal assessment by an expert specialist [15].

The diagnosis is made on the concordance between a classical history, physical examination and demonstrating sensitizations [16]. The demonstration of sensitization is not always required in primary care settings, especially when clinical manifestations occur in conjunction with seasonal variations or in cases where there is a relatively good response to management.

Asthma

Similar to other allergy-related medical conditions, obtaining a thorough medical history is a crucial factor to make an accurate diagnosis. Frequently, asthma is classified by clinical manifestations of dyspnea, wheezing, cough, and the presence of chest tightness. The use of a short acting beta2 agonist (SABA) might show reversible airflow obstruction [17]. In specialist care, the most commonly used ways for diagnosing asthma are spirometry and bronchial challenge. In countries of western Europe, spirometry is being largely performed in primary care settings, but the quality is relatively questionable [18]. In a published report, twenty-two percent of spirometric investigations performed in primary care setting demonstrated no adherence to the ERS/ATS guidelines, although practitioners were intensively trained [19].

Objective investigations that measure airway obstruction are advised as the association between pulmonary clinical manifestations and lung functions is poor [20]. Assessing LF in primary care is required to confirm a diagnosis of asthma and for helping later treatment plans. This could be done mainly by PEF assessment. Showing reversibility might be quite simple with a significant improvement in lung functions following a small dose of a SABA. On the other hand, patients presenting in the late afternoon might have optimal lung functions and not show reversibility, because of the exaggerated diurnal rhythm witnessed in poorly controlled asthma. In this situation, several (two or more usually) PEF readings might help the diagnosis. Spirometers are considered to be much more accurate when compared to PEF assessment (three percent vs ten percent) and FEV1 is less effort-dependent, therefore, PEF assessment is less recommended nowadays [19], but might be beneficial when spirometry is not readily available, in occupational asthma, and/or for monitoring of asthma at home.

There are no contraindications for spirometry assessment. Patients should respect the bronchodilators washout criteria for diagnosing asthma, but not for assessing the response towards management. The technical requirements of spirometry devices are standardized. It is essential that the spirometer gives the possibility of seeing the flow-volume (FV) loop and the volume-time curve together as the first one allows the analysis of the initial effort and the second checks if the expiratory effort is long enough for the VC method. Guidelines recommend 3 technically acceptable measurements and no more than 8 trials [21].

Conclusions

The diagnosis of allergic medical conditions usually involves obtaining a detailed clinical history, that will further be supported by *in-vivo* or *in-vitro* investigations. Additional procedures like challenge tests are required to confirm the accurate diagnosis. In accordance with the significant workload in a primary care setting, simplified protocols for detection and management of allergic diseases are suggested, that must be further altered based on local (national) conditions.

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