ARTÍCULO ORIGINAL

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Evaluation of the Feasibility and Reliability of Contact Tests in Routine Clinical Practice

Evaluación de la Viabilidad y Fiabilidad de las Pruebas de Contacto en la Práctica Clínica Habitual

Maria Zofia Lisiecka[1]

SUMMARY

Introduction: *This study was conducted to determine the feasibility of using contact tests in routine clinical practice based on the reliability of their results.* **Objective:** *To establish the diagnostic value of patch tests and assess the feasibility of their use in the routine clinical practice of allergists and dermatologists.* **Method:** *Literature review, subject analysis of patient photographs depicting skin reactions, and comparative analysis of the advantages and limitations of contact tests with other diagnostic methods were used.* **Result:** *The results show that among all types of contact tests, the patch test is the most informative. The level of its accuracy is determined by high indicators of sensitivity and specificity due to the principle of operation of the test – the presence of direct prolonged contact of the allergen with the skin, and further improvements: the creation of clear protocols for the procedure, the development of clear criteria for evaluating results, the expansion of the set of allergens, the establishment of optimal exposure time, the use of new hypoallergenic materials. The accuracy of patch test results may substantially decrease under the influence of external and internal factors. External factors include violations of the procedure technique, changes in exposure time, and allergen concentration without considering the allergen's type and seasonality. Internal diseases include individual sensitivity (skin reactivity to an allergen), skin condition, use of local medications, and the presence of concomitant diseases. A comparison of contact and laboratory tests for the diagnosis of contact dermatitis reveals the limited specificity of laboratory tests, indicating that they can be effectively used in combination with patch tests but are not a complete alternative to them. The results allow recommending the use of contact tests, especially patch tests, as a routine procedure for diagnosing contact dermatitis in cases of chronic dermatitis of unknown etiology, occupational dermatitis, eczematous, and non-eczematous dermatoses.*

Keywords: *Patch test, allergology, sensitivity, specificity, dermatitis, gold standard of diagnosis.*

RESUMEN

Introducción: *Este estudio se realiza para determinar la viabilidad del uso de las pruebas de contacto en la práctica clínica habitual en función de la fiabilidad de sus resultados.* **Objetivo:** *Establece el nivel de valor diagnóstico de las pruebas de parche y determinar la viabilidad de su uso en la práctica clínica habitual de alergólogos y dermatólogos.* **Método:** *Se uso la revisión de literatura, el análisis de fotografías de pacientes que mostraban reacciones cutáneas y el análisis comparativo de las ventajas y limitaciones*

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ORCID: 0009-0000-9028-952X

[1]Department of Allergology, National Medical Institute of the Ministry of the Interior and Administration, Warsaw, Poland. E-mail: mariazofialisiecka@gmail.com

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de las pruebas de contacto con otros métodos de diagnóstico. **Resultado:** *Los resultados muestran que, entre todos los tipos de pruebas de contacto, la prueba del parche es la más informativa. El nivel de su exactitud viene determinado por los elevados indicadores de sensibilidad y especificidad debidos al principio de funcionamiento de la prueba -la presencia de un contacto directo prolongado del alérgeno con la piel- y a otras mejoras: la creación de protocolos claros para el procedimiento, el desarrollo de criterios claros para evaluar los resultados, la ampliación del conjunto de alérgenos, el establecimiento de un tiempo de exposición óptimo, el uso de nuevos materiales hipoalergénicos. La precisión de los resultados de las pruebas del parche puede disminuir sustancialmente bajo la influencia de factores externos e internos. Los factores externos son las violaciones de la técnica del procedimiento, los cambios en el tiempo de exposición y la concentración del alérgeno sin tener en cuenta su tipo, y la estacionalidad. Los internos son la sensibilidad individual (reactividad de la piel a un alérgeno), el estado de la piel, el uso de medicamentos locales y la presencia de enfermedades concomitantes. Una comparación de las pruebas de contacto y de laboratorio para el diagnóstico de la dermatitis de contacto identifica una especificidad limitada de las pruebas de laboratorio, lo que indica que pueden utilizarse eficazmente en combinación con las pruebas epicutáneas, pero no son una alternativa completa a estas. Los resultados permiten recomendar el uso de las pruebas de contacto, especialmente las pruebas del parche, como procedimiento rutinario para el diagnóstico de la dermatitis de contacto en casos de dermatitis crónica de etiología desconocida, dermatitis ocupacional, dermatosis eccematosas y no eccematosas.*

Palabras clave: *Prueba del parche, alergología, sensibilidad, especificidad, dermatitis, patrón oro de diagnóstico.*

INTRODUCTION

Provocative tests are the standard of diagnosis in allergology, as they enable the accurate identification of the allergen that causes sensitization and the assessment of the severity of an allergic reaction. One of their types is contact tests, the mechanism of action of which simulates the actual conditions of contact between the allergen and the patient's skin by applying a small amount of potential allergen to a separate area, usually on the back, and monitoring the skin reaction. Contact tests are particularly effective in detecting cell-mediated allergic reactions that manifest as contact dermatitis, allowing for the identification of a wide range of allergens, from metals to cosmetic components. The high specificity of these tests will enable them to be considered an effective method for diagnosing contact dermatitis. However, given the existing limitations, recommendations on the feasibility of using contact tests in routine clinical practice should be made based on an assessment of their reliability.

One of the problems that complicates the examination of the diagnostic value of these tests is the presence of factors that affect their result, including individual variability, concomitant diseases, medication intake, and seasonal factors. Li et al. (1), based on an extensive population-based study, analysed factors influencing the patch test response. They determined that a positive reaction to allergens was more often observed in winter than at other times of the year, and in men, the frequency of reactions was higher. Still, with age, it did not substantially increase; however, in women, a clear age correlation was observed – in the older group (≥50 years), contact tests yielded a reaction 30 % more often than in the younger group (<30 years). The frequency of positive allergic samples in different age groups was also investigated by Heindl et al. (2), based on the analysis of 5 857 positive tests, they determined that the highest frequency of skin reactions to contact with the corresponding allergen was observed in the group of adult women, and it characteristically increased with age. In both studies, factors affecting the results of contact tests are considered rather as risk factors for the development of contact dermatitis, so it is incorrect to assess their level of influence on the results of testing itself in the context of causing false positive or false negative reactions based on the results of these works.

Gupta and Anand (3), studying the diagnostic effectiveness of contact tests, emphasized that for an accurate interpretation of their results, it is important to consider the medical history, general clinical picture, and geographical features of the patient's region of residence. During the lanolin allergenicity study, Jenkins and Belsito (4) noted that the detection of contact dermatitis using patch tests can give false-positive results. The authors attribute this to

the effect of concomitant skin diseases on the manifestation of lanolin allergenicity. Thus, the contact dermatitis provoked by it on diseased skin will not necessarily lead to allergic reactions on healthy skin.

Based on a retrospective analysis of the results of contact tests in 5 446 patients, Comstedt et al. (5) established that testing with Finn Chambers aluminium can give false positive reactions to sodium tetrachloropaladate, palladium chloride, Cain mixture II, and Myroxylon pereirae in patients with contact allergy to aluminium. This result is due to the fact that the material from which Finn Chambers was made could contain aluminium, and under the influence of these compounds, chemical reactions could occur, as a result of which aluminium was released and came into contact with the skin, causing an allergic reaction.

The following works analyse the influence of certain factors on false positive results of contact tests. Still, they do not assess the reliability of the patch testing method, considering possible errors. An important issue related to evaluating the accuracy and reliability of contact tests for allergy diagnosis concerns the interpretation of the results. Reeder et al. (6) analysed data from 4 121 contact tests to identify patterns in the understanding and relevance of questionable responses. The results showed that a third of the patients tested had more than one questionable reaction. Reactions to nickel, neomycin, methylchlorisothiazolinone, and methylisothiazolinone were most often misidentified as contact dermatitis. Difficulties are associated with interpreting the results of patch tests on the coloured skin of patients examined by Burli et al. (7). In patients with a higher Fitzpatrick skin type, contact test reactions were detected due to lichenification and hyperpigmentation, and bright red or pink shades characteristic of light skin looked pale pink or purple. Given these difficulties in interpreting the results of contact tests, Oppermann et al. (8) suggested using dermoscopy as an auxiliary tool in cases where patch tests produce weak or questionable responses. Studies on the problem of correctly interpreting contact test results presented in these works form an understanding of the limitations of this diagnostic method, but do not provide a critical assessment of its reliability.

Although current research has recognised multiple factors affecting contact test outcomes, including seasonal variations, age, gender, and concurrent skin conditions, a substantial gap persists in fully elucidating how these factors specifically lead to false-positive or false-negative reactions. Moreover, while research has identified difficulties in interpreting contact test outcomes, especially in individuals with darker skin tones, there is an absence of standardised methodologies or instruments to enhance the precision and dependability of these interpretations. A comprehensive evaluation of the reliability of contact tests, taking into account these limits and potential inaccuracies, is essential to guide recommendations for their application in standard clinical practice.

The purpose of this literature review is to determine the feasibility of using contact tests in routine clinical practice by evaluating the reliability of test results and analysing factors that affect patients' hypersensitivity to specific contact allergens. Additionally, this study aims to contribute to the existing literature by providing a comprehensive assessment of the limitations and potential errors associated with contact tests, thereby offering insights into areas requiring further standardization and improvement. By critically evaluating the diagnostic accuracy and reliability of contact tests, this research seeks to inform clinical guidelines and enhance the practical application of these tests in diagnosing contact dermatitis, ultimately improving patient outcomes and advancing the field of allergology.

MATERIALS AND METHODS

To assess the feasibility and reliability of contact tests in routine clinical practice, the analysis of scientific sources on allergology, immunology, and dermatology was conducted, which contained up-to-date information on key aspects of the development, diagnosis, and treatment of allergic reactions in general and contact allergies in particular. Determining the validity of contact tests involves two main aspects: assessing their sensitivity and specificity in diagnosing different types of contact allergies and identifying factors that may affect test results.

The search for sources for determining the reliability of contact tests was conducted among publications in the scientific databases PubMed, Google Scholar, Web of Science, and Scopus. Keywords for the search of materials relevant to the task of determining the sensitivity and specificity of contact tests for the diagnosis of various types of contact allergies were: "contact dermatitis", "contact allergy", "patch test", "contact test", "sensitivity of contact tests", "specificity of contact tests", "diagnosis of contact dermatitis", "allergen", "nickel", "cobalt", "chromium", "preservatives", "perfume", "cosmetics", "positive predictive value", "negative predictive value", "accuracy", "reproducibility".

The search query, which was aimed at identifying factors that can affect the results of contact tests, was formed according to the following keywords: "factors that affect the results of contact tests", "false positive results of contact tests", "false negative results of contact tests", "validity of contact tests", "reliability of contact tests", "false results when conducting contact tests", "limitations of contact tests", "interpretation of contact tests". The search was conducted in English and Polish. Sources that met the following inclusion criteria were selected for processing: Relevance of the material (sources published in the period from 2020 to 2024 were considered); Reliability of the results (preference was given to study results that were clinically and logically proven and consistent with the results of other studies); Clinical importance of the results (papers' results of which could be used in clinical practice were evaluated).

The review did not include clinical trials with the absence of a control group, which was explained by the inability to compare and critically evaluate the results, and uncertain criteria for including/excluding participants, which affected the representativeness of the sample. A total of 38 relevant scientific sources were selected for the analysis.

A subject analysis of factors affecting the results of contact tests was conducted based on photos of patients depicting skin reactions to specific allergens and characteristic visual symptoms of certain systemic diseases. When using photos, the necessary legal and ethical standards were observed – patients' informed consent to the use of their images in the study was obtained, and their anonymity was ensured. The advantages and limitations of this diagnostic method and other methods for detecting contact allergies were compared to get a critical assessment of the effectiveness of contact tests. The determination of the feasibility of using contact tests in the routine clinical practice of allergists, dermatologists, professional pathologists, and other doctors who have the skills to conduct the procedure and interpret its results was performed based on a preliminary assessment of the reliability of these tests and the result of their comparison with other methods of diagnosing contact allergies.

RESULTS

Contact tests are diagnostic procedures used to detect allergic skin reactions to various substances. They are an important tool for diagnosing contact dermatitis. There are several types of contact tests, each of which has its own characteristics and purpose: patch tests are used to diagnose contact dermatitis caused by metals, cosmetics, preservatives, dyes; pre-tests – to diagnose allergies to air allergens (pollen, animal hair, house dust); application tests with liquid substances – to diagnose allergies to cosmetics and detergents, perfumes; ocular tests – to diagnose allergies to cosmetics that come into contact with the eye area, in particular, the mucous membrane; inhalation tests – to diagnose allergies to volatile substances; oral – for the diagnosis of allergies to food or medications. The choice of a particular type of test depends on the suspected allergen, the location of the allergic reaction, and the severity of the allergic reaction (9-11).

The most informative and widely used type of contact test is the patch test (12). In the 19th century, doctors noticed the occurrence of skin reactions in some patients after contact with substances used in the textile industry (dyes, wool, silk), agriculture (plant pollen, animal hair, chemicals for processing plants), everyday life (detergents and cosmetics, dust, metals – nickel, cobalt, chromium, which were often part of jewellery and tools). At the beginning of the 20th century, the first experiments on the sensitization of animals

and humans were conducted, which facilitated a better understanding of the mechanisms underlying the development of contact allergic reactions. This contributed to the development of a method for identifying allergens that caused this reaction, which led to the creation of patch tests in the mid-20th century (13).

From the moment of its creation in the 1950s to the present, its technology has undergone substantial changes aimed at improving the accuracy, convenience, and safety of the procedure. This has contributed to the fact that several international allergy communities have recognized the patch test as the gold standard for diagnosing contact dermatitis (14-16). These organizations include the European Academy of Allergy and Clinical Immunology, which regularly publishes recommendations and consensus on the diagnosis and treatment of allergic diseases, in particular, contact dermatitis, in which the patch test is clearly recognized as the main diagnostic method (17); the American Academy of Allergy, Asthma, and Immunology, which sets standards for clinical practice in the field of allergology and immunology and also supports the patch test as the most reliable method for diagnosing contact dermatitis (18); the International Association of Dermatologists, which develops standards for the diagnosis and treatment of skin diseases and confirms the importance of the patch test for diagnosis contact dermatitis (19); an international research group on contact dermatitis, the members of which are actively developing new methods for the diagnosis and treatment of this disease, and use patch tests as one of the main tools of their work (20).

The high sensitivity of patch tests as a diagnostic method for detecting contact dermatitis is mainly explained by the principle of their operation. The patch test provides direct and long-term contact of the allergen with the skin, which allows identifying even mild allergic reactions that may not be detected during the examination using other methods (21). Further improvements in patch tests had a characteristic effect on increasing their sensitivity: the development of protocols to provide standardized conditions for all patients allowed achieving reproducibility of test results and, accordingly, increasing the accuracy of diagnosis; the expansion of the set of potential allergens – detecting even rare forms of sensitization; the establishment of clear criteria for evaluating the results of patch tests increased the level of objectivity and accuracy of diagnosis; the calculation of the optimal exposure time (48-72 hours) – assessing both early and late skin reactions to the allergen (22-24). The list of allergens that cause contact dermatitis is very wide, from metals to plant extracts. Still, the most common of them are nickel, cobalt, chromium, formaldehyde, flavourings, and methyl isocyanate. Contact allergy to nickel is quite common since this substance is found in things that have close and prolonged contact with the skin – in costume jewellery, accessories, coins, stationery, cutlery. The positive reactions of the nickel and methylisocyanate patch test are shown in Figure 1.

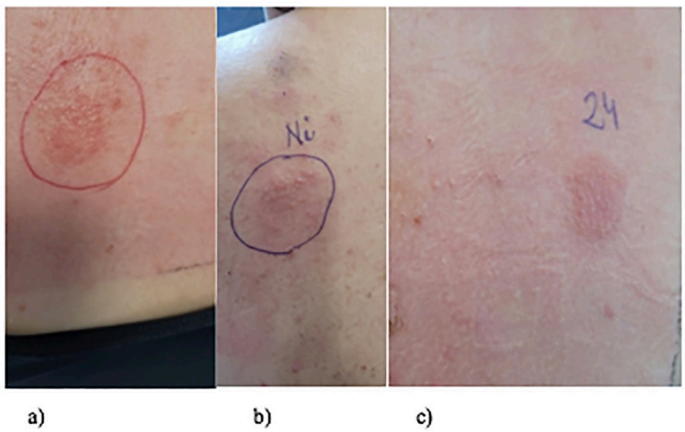

Figure 1. Skin reaction to allergens detected by the patch test: a) nickel, b) nickel (panel position 18), and c) methylisocyanate (panel position 24).

The positive and negative predictive value of the diagnostic method using patch tests was increased by the use of occlusive dressings to create a moist environment that ensures the penetration of allergens into the skin and the development of allergic reactions, and the use of hypoallergenic materials that minimize the risk of false positive reactions (25). This, accordingly, increased the specificity of patch tests as a method for diagnosing contact dermatitis, which allowed prescribing effective treatment, preventing relapses, and improving the quality of life of patients.

Indicators of sensitivity and specificity of patch tests ensure that diagnostic results are obtained with a high confidence probability, but they do not guarantee the avoidance of false reactions. External and internal factors can determine the probability of false results. The main external factors are the technique used in the procedure, the concentration of the allergen, the type of allergen, the duration of exposure, and seasonality (26). Failure to follow the testing technique, such as incorrect fixation of patches, non-compliance with the exposure time, or the use of poor-quality reagents, can distort the result and lead to an erroneous diagnosis. An excessively high or low allergen concentration in the test can also lead to false results. Depending on the type, some allergens may cause a more pronounced reaction than others, which can lead to misinterpretation and erroneous conclusions. The duration of contact between the allergen and the skin also influences the intensity of the reaction. At certain times of the year, the skin may be more sensitive, causing an increased reaction to the allergen. Increased sun activity in summer can lead to photodermatitis, an inflammation of the skin caused by simultaneous exposure to ultraviolet radiation and certain substances (27). Some components of sunscreens (oxybenzone, avobenzone, zinc oxide, titanium dioxide, flavourings, and preservatives) can cause an allergic contact reaction. Increased skin sensitivity to allergens during the cold season is primarily associated with a weakened immune system and dry skin, which develops due to low temperatures and humidity outside, as well as exposure to indoor heaters. An effective way to reduce or eliminate the influence of external factors is strict adherence to standardized protocols for conducting the testing procedure (28), the use of a comprehensive set of allergens, and the use of modern patch tests based on hypoallergenic materials (Figure 2).

It is more challenging to mitigate the impact of internal factors than external ones, so it is more appropriate to accurately assess their impact and consider it when analyzing the results of the patch test. Such factors are individual sensitivity, the patient's skin condition, the use of topical medications, and the presence of

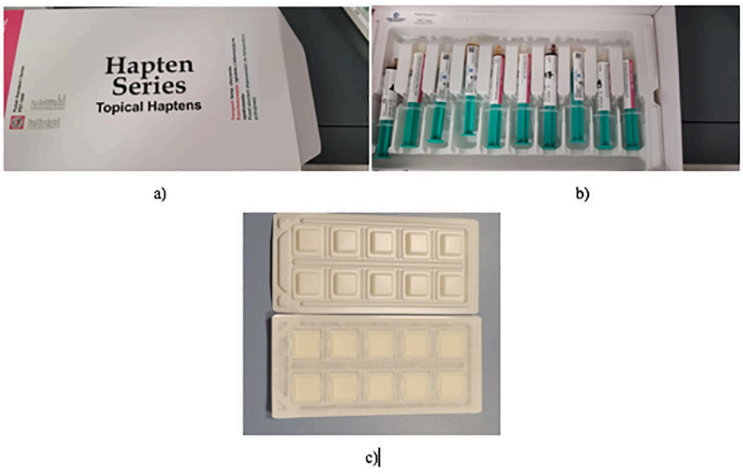

Figure 2. Modern contact tests using a series of haptens: a) packaging, b) container where the substance is placed and sealed on the back, c) substance tested in contact tests. Source: compiled by the author.

concomitant diseases. Individual sensitivity, or skin reactivity to allergens, is an important factor that affects the results of a patch test. This indicator is highly variable and depends on several factors, particularly age, genetic predisposition, the state of the immune system, and overall health. Depending on individual sensitivity, patch tests can yield false-positive or false-negative results (29). Hypersensitivity can provoke more pronounced reactions to allergens, even to very low concentrations, which leads to more pronounced reactions on the skin and, accordingly, more positive test results (30). In some cases, individual sensitivity can lead to cross-reactivity with related allergens – for example, a person with a nickel allergy may also exhibit increased sensitivity to cobalt (31). People with reduced sensitivity often exhibit less pronounced or absent reactions to allergens, even if they are sensitized to them, which can lead to false-negative patch test results. A factor in the absence of a reaction in such patients may be an insufficient concentration of the allergen in the patch (32). When interpreting the results of patch tests, considering individual sensitivity, it is essential to take into account the patient's overall clinical picture and medical history. In addition, it is important to use control tests to assess the overall reactivity of the skin.

The condition of the skin can substantially affect the accuracy of the results of the patch test and, in some cases (the presence of open wounds, burns, abrasions, and other lesions), even become a contraindication to its implementation. Inflammation can increase the skin's sensitivity to irritants and cause a false positive patch test response (33,34). Against this background, a strong inflammatory process can make it difficult to distinguish a true allergic reaction, leading to false-negative test results (35). Dry skin increases its tendency to irritation, which can cause false positive reactions. The presence of skin infections affects the change in the immune response, leading to distortion of the results of the diagnosis of contact allergies. Some skin diseases, such as psoriasis, ichthyosis, and atopic dermatitis, can alter the skin's reactivity to allergens, thereby reducing the reliability of patch tests (36). During the procedure using these tests, it is important to adhere to the mandatory requirements for the skin condition, which will reduce the risk of false results: the skin should be clean and dry; the day before the procedure, it is worth avoiding usage of cosmetics and perfumes on the site where the test will be performed; a few days before testing, it is important to avoid contact with known irritants. The skin as an external protective barrier of the body is subject to damage and injuries that affect its condition, and, accordingly, the result of allergy testing but since it is the largest human organ, the doctor can choose the most optimal area for conducting a patch test, considering the protocol of the procedure.

The intensity of the patch test reaction can be substantially affected by the use of topical medications. Many of them have an anti-inflammatory effect, which suppresses the development of allergic reactions, leading to false negative test results. The main types of these drugs are corticosteroids, antihistamines, and immunomodulators (37). Corticosteroids are the most well-known group of drugs that have an anti-inflammatory effect, and they are widely used to treat various skin diseases, including eczema and dermatitis. They reduce inflammation, redness, and itching by suppressing the skin's immune response, thereby masking allergic reactions during the patch test. Topical antihistamines have a direct effect on the response of patch tests, as they are designed to eliminate itching, redness, and other allergy symptoms, which are used to interpret the result. Immunomodulators also affect the immune system and can alter its response to allergens, masking an allergic reaction.

Some local medications can increase the skin's sensitivity to allergens, leading to false-positive test results. Among them, some antibiotics are distinguished (for example, neomycin, which is often added to ointments and creams, can cause contact dermatitis and increase skin sensitivity to other allergens), preservatives that are part of cosmetics (parabens, formaldehyde), perfumes, or their components (synthetic to natural flavours, essential oils) (38). Certain substances or medications can cause skin irritation (redness, blisters), which may visually be confused with an allergic reaction. Their use before the procedure complicates the diagnostic process and increases the possibility of obtaining a false positive result. Most often, antiseptics (alcohol, iodine, chlorhexidine) and active ingredients in external

products (salicylic acid, benzoyl peroxide) cause irritation (39). It is necessary to stop using topical medications at the site where the test will be performed 1-2 weeks before the procedure to avoid false test results.

The effect of concomitant diseases on the results of the patch test is conducted by changing the reactivity of the skin or masking an allergic reaction. The vast majority of skin diseases can alter the skin's sensitivity to various irritants. For example, in eczema, inflamed skin can react to allergens more or less than healthy, and in psoriasis, the inflammatory process can hide a weak allergic reaction (40). Changes in skin reactivity and masking an allergic reaction can also trigger infectious diseases. In addition, damage to the skin barrier caused by infections contributes to increased allergen permeability and increased response to them (41). Validity patch test results can be affected by bacterial (boils, carbuncles, impetigo, streptoderma), viral (herpes, chickenpox, viral warts), fungal (mycosis, candidiasis), and parasitic skin infections (Sarcoptes scabiei, trichomonas).

Systemic diseases substantially affect the immune system, and this can lead to changes in the skin's response to various stimuli, including allergens (42,43). Depending on the strengthening or weakening of the immune response, the intensity of the allergic reaction also changes. By analogy with the effects of infections, some systemic diseases can disrupt the barrier functions of the skin, increasing the permeability of allergens. The response of patch tests may be affected by the general weakening of the body characteristic of these diseases, and the effect of therapy, which may include corticosteroids and other anti-inflammatory drugs. Most often, the results of patch tests are affected by autoimmune diseases (Sjogren's syndrome, systemic lupus erythematosus, Crohn's disease, ulcerative colitis, rheumatoid arthritis), endocrine diseases (diabetes mellitus, thyroid diseases), oncological diseases (tumours of the blood and lymphatic system), connective tissue diseases (scleroderma, dermatomyositis, polymyositis) (44).

Since the immune system plays a key role in both autoimmune diseases and allergic reactions, conducting allergy tests in such patients requires special care and additional measures. Before allergological tests, such as a patch test, it is recommended to conduct a general and biochemical blood test to analyse the general condition of the body, detect inflammatory processes, assess the function of the kidneys, liver and other organs; immunological studies – to assess the activity of the autoimmune process, the level of immunoglobulins and other indicators of the immune system; consultation with a rheumatologist – to assess the activity of the main autoimmune disease. In addition to these measures, it is important to individually select allergens for testing, considering the clinical picture of the disease, and conduct dynamic monitoring of the patient after allergy tests. Considering all these factors that may affect the test result, and strict compliance with the procedure protocols and criteria for evaluating the skin reaction, will increase the reliability of patch tests as a method for diagnosing contact dermatitis.

An important step to assess the feasibility of contact tests in routine clinical practice is to determine the optimal patient screening strategy based on comparing the effectiveness of different methods for diagnosing contact allergies. Although laboratory tests cannot be called an alternative to contact tests, they can also be used to diagnose allergies. Determination of allergen-specific immunoglobulin E (IgE) can detect elevated levels of antibodies to specific allergens in the blood (45). However, this method may give false-positive results in patients with atopic dermatitis. Cytological examination of skin rashes identifies characteristic changes in skin cells in contact allergies. Histological examination of the skin biopsy allows confirming the diagnosis of contact dermatitis and excludes other skin diseases (46). The advantages of laboratory tests are safety since they do not carry the risk of allergic reactions during the procedure, the ability to detect allergies to volatile substances that are difficult to investigate with patch tests, and the absence of the need for special equipment, given that these tests can be performed in most medical laboratories. Disadvantages of laboratory tests include a limited number of allergens, the possibility of false-positive and false-negative results, and the lack of mandatory correlation with the clinical manifestations of the disease.

Considering the advantages and disadvantages, laboratory tests can be methods for diagnosing contact allergies in clinical practice in cases of contraindications to the patch test, the need to confirm the results of the patch test, or to detect allergies to volatile substances or medications. Compared to contact tests, laboratory tests for detecting contact allergies have a lower specificity index since the antibodies used in the study can react not only to a specific allergen but also to related substances, provoking false-positive results. In general, contact tests have a higher level of reliability, given that the sensitivity and specificity indicators analysed are higher than those of laboratory tests. Still, both methods can be used in combination to obtain a more accurate diagnosis. In a comprehensive assessment of the feasibility of contact testing, in addition to the theoretical analysis of the aspects that influence it, it is important to consider several clinical cases that demonstrate the value of patch testing in clinical practice.

A 50-year-old female patient presented with severe allergic reactions on the skin of both arms, neck, and décolleté, manifested by large, well-demarcated blisters, severe itching, and swelling. A long-term medical history indicated a chronic course of the allergic process. The contact test revealed pronounced positive reactions to nickel – 17 mm diameter swelling, numerous blisters and severe itching; epoxy resins – 15 mm diameter swelling; formaldehyde – 12 mm diameter swelling and numerous blisters; fragrance mixture – 15 mm diameter swelling and numerous blisters; palladium – 23 mm diameter swelling, numerous blisters, severe itching (Figure 3).

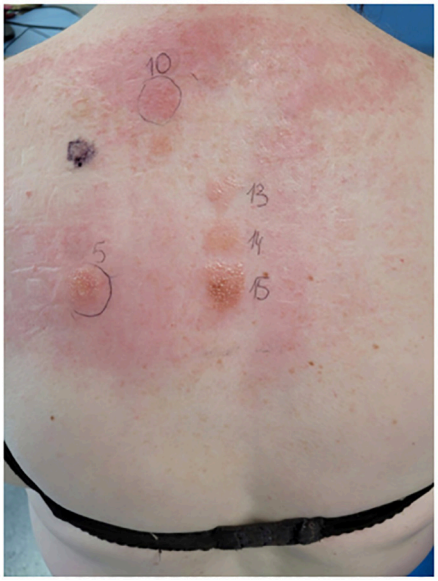

Figure 3. Results of the patient's contact test for nickel, epoxies, formaldehyde, fragrance mixture and palladium. Notes: reaction to nickel – position 5; epoxy resins – 10; formaldehyde – 13; fragrance mixture – 14; palladium – 15. Source: compiled by the author

The pronounced positive reactions to nickel, epoxy resins, formaldehyde, fragrance mixture and palladium confirm the patient's sensitization to these allergens, and their size and nature (blisters, swelling, itching) correlate with the severity of this sensitization. Positive reactions to several allergens indicate multiple allergies. The diagnosis is contact dermatitis sensitized to several allergens.

A 15-year-old female patient complained of eczema on both hands. Over the past 2 years, the skin condition had been constantly deteriorating, and the use of corticosteroid-based creams periodically improved the situation. According to the patient's anamnesis, an allergic reaction occurred during the use of hair shampoo. Patch test results revealed a pronounced positive reaction to methyl chloroisothiazolinone and methylisothiazolinone, which are common preservatives added to various cosmetic products, including shampoos (Figure 4).

The pronounced positive reaction to methyl chloroisothiazolinone and methylisothiazolinone confirms the patient's sensitization to these preservatives. The diagnosis was contact dermatitis sensitized to methyl chloroisothiazolinone and methylisothiazolinone. A similar clinical picture to the previous one was observed in a thirteen-year-old patient. External manifestations of eczema were found on both hands and around the mouth. The results of the patch test revealed a pronounced positive reaction to methylisothiazolinone – a significant 30×15 mm oedema that crossed the 5×5 mm boundaries of the applied allergen, erythema, and severe pruritus (Figure 5).

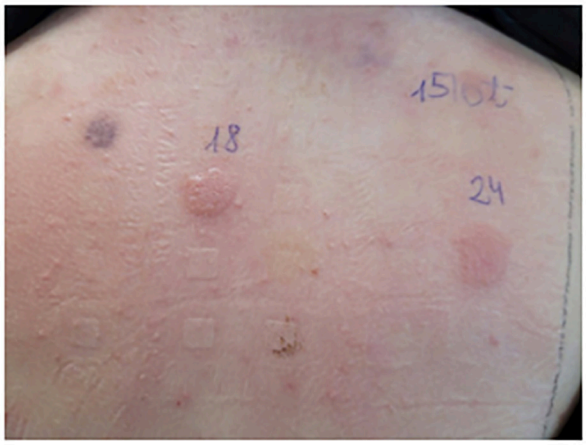

Figure 4. Results of the patient's contact test for methylchloroisothiazolinone and methylisothiazolinone. Notes: reaction to methylchloroisothiazolinone – position 18; methylisothiazolinone – 24.

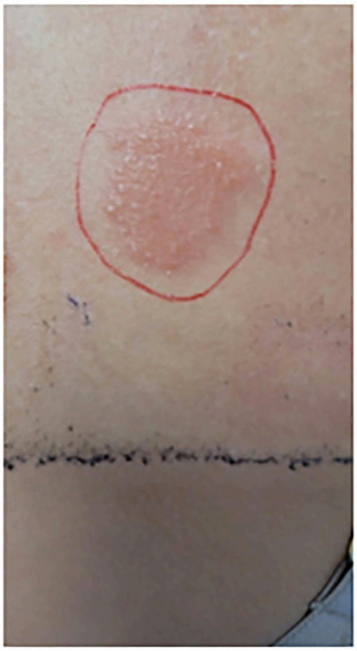

Figure 5. Results of a patient's contact test for methylisothiazolinone. Source: compiled by the author.

During further follow-up, it was found that the reaction to the patch test persisted for two weeks, indicating persistent sensitization to the allergen. The large size of the oedema and the duration of the reaction indicate severe sensitization to the allergen. The diagnosis was made – contact dermatitis sensitized to methylisothiazolinone. It is important to add that in clinical practice, allergic reactions to contact with methylchloroisothiazolinone and methylisothiazolinone in children were relatively rare. However, an increase in the number of cases with clinical features similar to the above case histories of underage patients indicates a trend that allergists should take into account when compiling a list of potential allergens for patients of a certain age, and manufacturers should review the composition of products to replace potentially allergenic components with hypoallergenic ones.

Proper preparation of the patient is crucial for the accuracy and reliability of patch test results. Before testing, patients should be advised to avoid using topical corticosteroids, antihistamines, and other anti-inflammatory medications on the test area for at least one to two weeks, as these can suppress skin reactions and lead to false-negative results. Additionally, patients should refrain from applying lotions, creams, or cosmetics to the test site for a few days before the procedure to prevent potential interference with the test results. It is also important to inform patients about the necessity of keeping the test area dry and avoiding activities that may cause excessive sweating during the testing period. Clear communication regarding these preparatory steps ensures that the skin is in an optimal state for accurate allergen exposure and reaction assessment.

In the event of severe reactions during patch testing, medical professionals need to follow a clear and structured action algorithm to ensure patient safety and effective management. Initially, the allergen patches should be immediately removed, and the affected skin area should be gently cleaned with water to eliminate any residual allergen. Topical corticosteroids can be applied to reduce inflammation and alleviate symptoms. For severe systemic reactions, such as anaphylaxis, prompt administration of epinephrine and emergency medical intervention may be required. Patients should be closely monitored for any signs of respiratory distress or cardiovascular compromise. Having a well-defined protocol in place, including access to emergency medications and equipment, ensures that healthcare providers can respond swiftly

and effectively to any adverse reactions, thereby minimizing risks and enhancing patient care.

Understanding the differences between allergic and irritant reactions is fundamental for accurate diagnosis and treatment. Allergic reactions are immune-mediated responses that occur when the skin comes into contact with a specific allergen, leading to sensitization and subsequent reactions upon re-exposure (47). These reactions typically manifest as erythema, oedema, and vesicles, and are characterized by a delayed onset, usually appearing 48 to 72 hours after exposure. In contrast, irritant reactions result from direct damage to the skin by substances such as acids, solvents, or detergents, and do not involve the immune system. Irritant contact dermatitis often presents with dryness, redness, and cracking of the skin, and can occur immediately after exposure. Differentiating between these types of reactions is crucial for determining the appropriate treatment and preventive measures.

The rather pronounced results of patch tests in all clinical situations are associated with prolonged exposure of patients to allergens. Firstly, this indicates the high sensitivity and specificity of this diagnostic method for determining the cause of chronic dermatitis. Contact tests, in particular, patch tests, are a highly specific method for diagnosing contact dermatitis, which proves the feasibility of their use as a routine procedure for examining patients with chronic dermatitis of unknown aetiology, occupational dermatitis, eczematous and non-eczematous dermatoses. It is important to use modern sets of allergens, adhere to standard test protocols, and consider possible limitations of the method associated with the influence of external and internal factors to improve the accuracy of diagnostics.

While patch testing is a valuable tool for diagnosing contact dermatitis, it is important to acknowledge the limitations of the studies and the method itself. One significant limitation is the potential for false-positive and false-negative results, which can be influenced by various factors such as the concentration of allergens, the duration of exposure, and individual patient characteristics. Additionally, the relevance of positive patch test results must be carefully interpreted in the context of the patient's clinical history and current symptoms. Another limitation is the inability of patch tests to identify all possible allergens, particularly those that are not included in standard test panels. Furthermore, the variability in test procedures and interpretation criteria among different healthcare providers can affect the consistency and reliability of the results. Recognizing these limitations is essential for a balanced and informed approach to diagnosis and treatment.

When evaluating the reliability and accuracy of patch tests for diagnosing contact dermatitis, it is essential to consider both external and internal factors that can significantly influence test results. External factors include the technique used during the procedure, where improper application or removal of patches can lead to false results; the concentration of the allergen, as both excessively high and low concentrations can cause misleading reactions; and environmental conditions, such as seasonality, which may affect skin sensitivity and reactivity. Internal factors encompass the patient's skin condition, as pre-existing skin diseases or damage can alter the skin's response to allergens, potentially leading to false positives or negatives. Additionally, the use of medications, particularly topical corticosteroids, antihistamines, and immunomodulators, can suppress or enhance skin reactions, thereby impacting the accuracy of the test results. Understanding and mitigating these factors are crucial for optimizing the diagnostic value of patch tests in clinical practice.

Contact tests, particularly patch tests, play a pivotal role in the diagnosis of contact dermatitis by identifying specific allergens responsible for skin reactions. Over the years, significant improvements have been made to enhance the accuracy, sensitivity, and safety of these tests. Modern patch tests utilize standardized allergen panels, hypoallergenic materials, and occlusive dressings to ensure consistent and reliable results. Advances in technology have also led to the development of more sophisticated test systems that can detect a broader range of allergens and provide more precise measurements of skin reactions. These improvements have solidified the patch test as the gold standard for diagnosing contact dermatitis, offering healthcare providers a powerful tool for accurate diagnosis

and effective management of this condition. The continuous refinement of contact testing methods underscores their relevance and practical significance in clinical practice.

A precise and timely diagnosis of contact dermatitis significantly enhances the quality of life for affected individuals. By identifying specific allergens through patch testing, patients can avoid exposure to these substances, thereby preventing recurrent allergic reactions and chronic skin inflammation. This proactive approach not only alleviates physical symptoms, such as itching, pain, and discomfort, but also reduces the psychological burden associated with chronic skin conditions. Furthermore, an accurate diagnosis enables targeted treatment strategies, including the use of appropriate topical or systemic therapies, which can lead to better disease management and improved overall well-being. Educating patients about their condition and how to manage it empowers them to take control of their health, fostering a sense of confidence and reducing anxiety related to their skin condition.

DISCUSSION

The criteria that determine the feasibility of any diagnostic method for use in clinical practice are the accuracy, safety, and relative availability of the procedure. The accuracy of contact tests is determined by sensitivity and specificity indicators, a high level of which was analyzed in the study. Conducting these tests is generally a safe procedure, but like any medical intervention, they have a certain percentage of risk. The most common side effect is slight redness and itching at the test site, which is a normal skin reaction to the allergen concentration needed to detect an allergy. Such symptoms usually disappear within a few hours or days and do not cause substantial discomfort to patients or concern doctors. However, there is a small risk of developing more severe allergic reactions, such as prolonged allergic reactions, extended skin reactions, and systemic allergic reactions (including anaphylactic shock).

The frequency of long-term allergic reactions to the patch test was determined by Mancuso (48), who showed that the reactions caused by the test, which persist for several days or even weeks after removing the patches, are characteristic of many allergens and occur at a frequency of 17.9 % of the total number of reactions, with most being caused by gold salts. The exact mechanism of long-term reactions is not clear, but there are hypotheses about the influence of constant antigenic stimulation and a defect in cell-mediated regulation of immunity. Uchida et al. (49) and Ophaug and Schwarzenberger (50) described reactions that persisted in the patch test site for several months. Analyzing the factors that affect the duration of the reaction, they identified a strong initial reaction to the allergen, the elderly age of patients, and the body's tendency to allergic reactions. In this study, there are some doubts about the accuracy of the indicator of the frequency of long-term reactions since it was determined based on a literature review, and the methodology of systematic review is considered more accurate for such an analysis.

An extended skin reaction after a patch test is a situation where an allergic reaction to an allergen applied to the skin during the test extends beyond the site of direct contact with the allergen (51). It can manifest as large, itchy spots that appear on different parts of the body, not necessarily at the test site, small or large blisters, sometimes with fluid inside, and swelling of the face, limbs, or even the entire body. Such an abnormal reaction may be associated with severe sensitization, individual characteristics of the body, and the type of allergen. Anaphylactic shock during a patch test is a rare but possible complication. In some cases, an allergen applied to the skin during a patch test can be quickly absorbed into the bloodstream through damaged or sensitive skin, which can lead to an instant systemic allergic reaction. Such a reaction can be triggered by individual hypersensitivity, when even a small amount of allergen can provoke a strong reaction in the patient. The risk of developing an anaphylactic reaction may increase due to the presence of other allergic diseases, in particular, asthma or atopic dermatitis (52). A violation of the test procedure, such as using too much allergen or damaging the skin when removing patches, may increase the risk of a systemic reaction or other complications.

Daftary et al. (53) studied the incidence of anaphylaxis during patch testing, conducting a

review of the literature describing cases of this reaction and a survey among dermatologists-experts in contact testing. In total, 3 cases of anaphylaxis were found, and according to the results of a survey of doctors – 2 cases for 201 720 tests. General calculations showed that the frequency of anaphylactic reactions during patch tests was 1 case per 100 860 tests performed. The likelihood of this reaction increased in patients with a history of anaphylaxis. The authors' calculations confirmed the fact that anaphylaxis caused by a contact test is quite rare, which should still be considered when conducting testing. In agreement with the authors, it is worth stating that, in addition to ensuring the availability of emergency medications in the medical institution for anaphylactic shock (adrenalin, antihistamines, glucocorticoids), it is worth continuing to monitor the patient for some time after the test to avoid unpredictable reactions of the body to the allergen.

An additional argument in favor of the safety of patch tests can be considered the similarity of the principle of contact tests and allergy tests before using cosmetics, which manufacturers recommend conducting at home. Both procedures have a common goal – to determine the presence of an allergic reaction to a particular substance, a similar technique – applying the substance to a small area of the skin and monitoring the reaction, and aim to minimize the risk, helping to avoid the development of a full-fledged allergic reaction, which can occur when using the substance on a large area of the skin. A substantial difference between both tests is the use of numerous allergens when performing a patch test, while cosmetics contain one or more potential allergens. Patch tests, as well as tests for cosmetics, have a high level of safety, and conducting them in a medical institution allows identifying even the slightest sensitivity to allergens and professionally responding to possible complications.

Evaluating the availability of patch testing includes the cost of the procedure, the complexity of interpretation, and the need for specialized equipment. Conducting a patch test involves certain costs, both for the patient and for the medical institution. If health insurance does not cover all costs, the cost of the procedure for some patients may be too high. Interpretation of the results of patch tests requires a highly qualified allergist, and special sets of allergens are required for their implementation. However, given that not all patients who seek medical help with dermatological problems have the need for a contact test, it is advisable to consider this method as a routine procedure in cases where: the patient has skin rashes, itching, and other symptoms for a long time, and traditional methods of treatment do not give an effect; their professional activity is associated with contact with various substances that are included in the list of potential allergens; in the presence or exacerbation of atopic dermatitis or other eczematous dermatoses in the patient as an aid in identifying additional allergens that complicate the course of the disease. In other cases, the patch test can be used as a differential diagnostic tool to distinguish contact dermatitis from other skin diseases (eczema, psoriasis).

Foti et al. (54) recommend performing patch tests in all cases of eczematous dermatoses and in exacerbation of other dermatoses, when contact allergies are suspected, caused, for example, by substances from the composition of drugs for local treatment. This is due to the fact that in many eczematous dermatoses (atopic dermatitis, discoid eczema, nummular eczema), contact allergies can be one of the provoking factors, and patch tests will help to establish an accurate diagnosis and prescribe appropriate treatment. The authors' arguments and recommendations correlate with the conclusions of this study regarding the feasibility of using patch tests as a routine procedure in certain cases. However, it is worth adding that their use is not limited only to cases of eczematous and non-eczematous contact dermatitis, but can be conducted if a skin allergy is suspected to confirm or exclude contact dermatitis. The reliability and relative safety of contact tests make them a valuable diagnostic tool for detecting contact dermatitis. Their use in the case of suspected skin allergies is an appropriate, and in some cases mandatory, measure.

In comparing the findings of this study with existing literature, it is evident that the accuracy, safety, and availability of patch tests are consistently highlighted as critical factors in determining their feasibility for routine clinical practice. The high sensitivity and specificity of patch tests align with numerous other investigations that underscore their reliability in diagnosing contact dermatitis. Studies have reported high accuracy rates but also caution about

the potential for long-term allergic reactions, which necessitate careful monitoring and patient follow-up. Safety concerns, particularly the risk of severe allergic reactions such as anaphylaxis, have been documented in the literature, albeit as rare occurrences. Research indicates that such reactions are infrequent but require preparedness and post-test observation. The similarity between clinical patch tests and at-home cosmetic allergy tests further supports the safety profile of patch tests, as both methods aim to minimize risk through controlled exposure to potential allergens.

Regarding availability, the cost and need for specialised equipment and expertise are common themes in the literature. While patch tests are advocated for use in cases of eczematous dermatoses and suspected contact allergies, the financial and logistical barriers to widespread use cannot be overlooked. Although patch tests are not universally accessible, their targeted use in specific clinical scenarios, such as chronic dermatological conditions unresponsive to conventional treatments or occupational dermatitis, can optimize their diagnostic value. Overall, the results of this study are consistent with the broader scientific community's view that patch tests are a valuable diagnostic tool in allergology and dermatology. The emphasis on their judicious use, considering both their strengths and limitations, reflects a balanced approach that maximizes their clinical utility while mitigating potential risks. Future research could further enhance the accessibility and safety of patch tests, ensuring they remain a cornerstone in the diagnosis of contact dermatitis.

CONCLUSIONS

This study has comprehensively evaluated the feasibility of using contact tests, particularly patch tests, in routine clinical practice for diagnosing contact dermatitis. The findings underscore the high sensitivity and specificity of patch tests, affirming their status as the gold standard in diagnosing contact dermatitis. Various external and internal factors, including procedural techniques, allergen concentration, skin condition, and medication use, influence the accuracy of these tests. Despite the potential for false-positive and false-negative results, patch tests remain a reliable and valuable diagnostic tool when used judiciously.

Internal factors that affect the result of the patch test include individual sensitivity, skin condition, the use of topical medications, and the presence of concomitant diseases. Depending on the genetic predisposition, age, and state of the immune system, the patient may experience increased or decreased sensitivity to a particular allergen, which will affect the result of the patch test. The presence of skin infections, inflammation, and dry skin can change its reactivity to allergens and provoke false test results. Depending on the composition of local drugs, their effect can both suppress and increase the intensity of allergic reactions, which will also affect the results of diagnosis. Skin, infectious, and systemic diseases can affect the patch test response in two main ways – by changing the skin's reactivity and masking the true allergic reaction. A comparative analysis of contact tests and laboratory tests revealed that laboratory tests cannot be considered as an alternative to contact tests, due to their limited specificity. Still, the combined application of both methods can give a more accurate result.

However, the study acknowledges several limitations. The potential for false reactions due to external factors such as seasonal variations and improper test techniques highlights the need for standardized protocols and further research to mitigate these issues. Additionally, the variability in interpreting test results, particularly in patients with darker skin tones, calls for the development of more objective assessment tools and criteria. The financial and logistical barriers to widespread use of patch tests also pose challenges, necessitating a balanced approach to their application in clinical practice. For future research, it is recommended to focus on the standardization of patch test procedures to minimize variability and enhance reliability. Further studies should explore the development of advanced materials and techniques to reduce the risk of false reactions and improve the accuracy of test results. Additionally, investigating the cost-effectiveness and accessibility of patch tests could provide insights into optimizing their use in various clinical settings.

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