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Mini Review

Nickel Allergy: Epidemiology, Sources of Exposure, Risk Factors, Clinic and Diagnosis, Prevention and Treatment, Occupational Disease

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Abstract

Nickel allergy is one of the most common forms of Allergic Contact Dermatitis (ACD) worldwide, affecting between 8 to 9% of adults and 8 to 10% of children and adolescents, with a higher prevalence among women. This study reviews the literature on the epidemiology, sources of exposure, risk factors, diagnosis, prevention and treatment of this dermatitis. There are several sources of contact with nickel, including jewelry, medical devices, dental materials, household utensils and food. Occupational exposure continues to be a relevant factor, particularly in industry, construction and the health sector, and is recognized as an occupational disease in some situations. Diagnosis is based on clinical history and epicutaneous testing. Prevention essentially involves physical barriers, regulation of the use of nickel in industry and education on avoidance. Following the introduction of the European Union Nickel Directive in 2001, there has been a decrease in prevalence in Europe, but nickel allergy continues to have a significant impact on quality of life and the professional context. This review highlights the continuing need for regulation and effective strategies to minimize exposure and adverse effects of nickel in and outside the occupational context.

Keywords: Contact dermatitis; Occupational dermatitis; Nickel; Allergen

Introduction

Nickel allergy is one of the most common forms of contact dermatitis, affecting a significant portion of the world's population. Nickel is the fifth most abundant element on Earth and, due to its corrosion-resistant properties, high ductility and low cost, it is widely used in various industries. This metal is also widely present in everyday objects such as jewelry, dental material, implantable medical devices and even food. It has a high allergenic capacity, making it a challenge for both affected individuals and health professionals [1-3].

Exposure to nickel can occur in various ways, with skin exposure being the most relevant for the development of allergy. Factors such as accumulated dose, skin condition and duration of contact play a crucial role in the development of metal sensitization [2,3].

Nickel allergy not only affects individuals' quality of life, but can also have significant occupational implications. Professionals working in the metal industry, construction and the health sector are particularly at risk, and ACD to nickel has already been recognized as an occupational disease in some cases [4]. In fact, allergic contact dermatitis in an occupational context is associated with a worse prognosis and a lower cure rate [1]. The regulation of nickel exposure, such as the introduction of the European Directive in 2001, and the development of other preventive strategies, such as the use of protective barriers, are essential to minimize the impact of this condition [2].

Given its clinical and occupational relevance, understanding the mechanisms of nickel allergy, as well as prevention and treatment strategies, is key to reducing its incidence and improving the quality of life of affected individuals.

Results

Epidemiology

The epidemiology of nickel allergy reveals a significant global prevalence, ranging from 8 to 19% in adults and 8 to 10% in children and adolescents. Rates are higher in women, reflecting frequent exposure to nickel-containing products such as jewel-

ry and accessories [2]. In Europe, a reduction in prevalence has been observed following the implementation of more restrictive regulations, such as the European Nickel Directive, which limits the concentration of nickel in certain objects. However, in regions such as Asia and North America, rates remain high [5].

Historically, nickel contact dermatitis was identified as an occupational disease at the end of the 19th century, especially in workers who handled the metal. Over the following decades, exposure expanded to various industries, including construction and the health sector. Today, nickel is still present in many every day and professional objects, such as tools, keys, coins and medical equipment [3].

Sources of Exposure

Nickel is ubiquitous in our environment and the population will inevitably continue to be exposed to it. Topical exposure to nickel occurs from metal items, household products and cosmetics, while systemic exposure is possible from food, water, surgical implants and dental materials. The sources of nickel allergy have changed over time as a result of industrialization, changes in fashion and the implementation of regulations. While between the 1930s and the 1960s nickel allergy was most often caused by contact with watches or spectacle frames. In the 1970s it was more associated with jeans buttons and in the 1980s an epidemic broke out associated with the increased use of earrings [2].

Food

Nickel is naturally present in drinking water and in various foods, such as vegetables (cabbage, onions, spinach, tomatoes), fruit (pineapple, figs, strawberries), whole grains (oats, whole wheat, rye), shellfish and certain fish such as cod and salmon which are rich in nickel. However, foods such as rice, pasta, white bread and tuna are low in nickel. In addition, kitchen utensils can contribute to increased nickel intake. Although the different concentrations of nickel in food are known and the European Food Safety Authority has established a tolerable daily intake of 13 µg/kg, the level of nickel in food is not regulated [6,7].

Implantable Devices and Dental Materials

Orthopedic, cardiac and endovascular surgeries can be sources of nickel exposure. Although its use in orthopaedics is currently rare, studies point to a possible relationship between the presence of nickel in coronary stents and complications such as in-stent restenosis in cardiology. In the field of dentistry, nickel-chromium alloys are common in orthodontic brackets and dental prostheses and, although the release of nickel in these materials is low, prolonged exposure to the corrosive environment of the oral cavity can increase its release [2,8].

Consumer objects

Everyday objects such as jewelry, watches, eyeglass frames and trouser buttons have historically been sources of nickel. In the 1980s, the increased use of earrings led to an epidemic of nickel allergies. Currently, some regulations limit the release of this metal in products with prolonged contact with the skin, notably the European Union Directive which prohibits the use of piercings containing nickel in wound epithelialization [2].

Occupational

The relevance of nickel as an occupational allergen is often difficult to demonstrate due to the simultaneous presence of irritants or short time repeated exposure to nickel, possibly from various sources.

A wide variety of occupational exposures to nickel have been found, including industrial machinery, work tools, keys, electrical components, coins, sewing needles, dental alloys, crochet needles, dermatoscopes, guitar strings and computers, among others [2,3].

Risk Factors

The main risk factor for contact allergy to nickel is the accumulated dose on the skin.

In addition to this accumulated dose, the type of exposure, which can be cutaneous, piercing or systemic, is also a risk factor. Individuals with damaged skin or pre-existing dermatitis are more susceptible, as the skin barrier is compromised, making it easier for nickel to penetrate and trigger an allergic response.

The area of skin exposed also influences the risk, with prolonged contact and the high bioavailability of the metal increasing sensitization. In addition, exposure combined with other irritants can potentiate the allergic reaction. The presence of genetics factors may also play a role in the predisposition to nickel allergy, although the exact mechanisms of tolerance are not yet fully understood [2,9].

Clinic and Diagnosis

Nickel allergy, characterized by a type IV hypersensitivity reaction, manifests itself predominantly as contact dermatitis of the skin at the site of contact with the metal. Historically, the anatomical location of the lesions has evolved over time, accompanying changes in the habits and products used by the population. For example, dermatitis caused by stocking suspenders was first described by Bonnevie.

The clinical presentation can be acute with erythema, papules, vesicles and exudation, or chronic with lichenification and skin xerosis [2].

Nickel ACD is suspected clinically and the gold standard for diagnosis is epicutaneous testing [10]. The nickel sulphate contact test is part of the basic series of the Portuguese Contact Dermatitis Study Group. The test is read on the second day (D2) and then on the third or fourth day (D3/D4). Studies indicate that a single reading on D2 can result in up to 29% fewer identified reactions compared to adding an extra reading [2,10,11].

Prevention and Treatment

The prevention of nickel allergy is fundamental in both personal and occupational contexts, given the high prevalence of this condition and the impact it can have on the quality of life of affected individuals. The pillar of prevention consists of avoiding this allergen as much as possible, where preventive strategies then aim to reduce or eliminate exposure to nickel, the main trigger for allergic contact dermatitis. In this context, it is difficult to separate the terms prevention and treatment, since the mainstay of both is allergen avoidance [6].

One of the most effective measures to prevent contact allergy to nickel was the implementation of the European Union (EU) Nickel Directive in 2001. This regulation limited the amount of nickel released by objects intended for direct and prolonged

contact with the skin. Among the requirements are:
- A ban on the use of piercings containing more than 0.05% nickel during the skin healing process;
- Limiting the release of nickel to less than 0.5 µg/cm²/week in items such as jewelry, watches, buttons and buckles;
- Mandatory durable coating on articles containing nickel, ensuring that they do not exceed migration levels for at least two years of normal use.
After the directive was introduced, a number of amendments were later made to further restrict the limits and exposure to nickel. Thus, the restriction on the use of piercings with more than 0.05% nickel during the healing process now covers any piercing. Also, the limitation of nickel release to less than 0.5 µg/cm²/week in certain objects was reduced to 0.2 µg/cm²/week [12].

A consistent pattern of decreasing prevalence of nickel allergy has been observed in some EU countries following the introduction of the nickel directive, although prevalence among young women remains high [13].

In addition to regulation, other forms of prevention include:
- Use of physical barriers, such as protective gloves and barrier creams, especially in occupational environments with a known risk of exposure;
- Surface coating of metal objects, reducing direct contact with nickel;
- Education and sensitization of workers and the general population on the importance of avoidance;
- Early recognition of symptoms in work environment enabling measures to be taken before chronic sensitization occurs.

It is important to note that although gloves are a recommended protective measure, nickel can in some cases, penetrate certain materials due to local conditions such as temperature and humidity, requiring a careful choice of the type of personal protective equipment.
In addition to these measures, the symptomatic treatment itself is similar to contact dermatitis from another cause, such as the use of emollients, topical corticosteroids or calcineurin inhibitors [14].

Occupational Disease
Although ACD to nickel is a relatively easy condition to diagnose using epicutaneous tests, it is not always simple to establish the causal relationship with work activity, which makes its characterization as an occupational disease a clinical and legal challenge.

A study carried out in Germany published three cases of recognized occupational disease, some of which were attributed permanent partial disability. One of the cases involved a 30-year-old woman who worked as an assistant in a chemical laboratory where her main activity consisted of removing objects plated with nickel, cobalt and gold. After three years of work, she developed pruritus, erythema and vesicles on all the fingers of both hands, which improved at home but did not cease completely. The patch test was positive for nickel and cobalt, and the occupational disease was recognized as ACD to nickel and cobalt [15].

According to Decree-Law no. 503/99, of November 20, any doctor is obliged to notify a suspected occupational disease, using the appropriate forms (GDP-12 for the application and GDP-13 for the medical opinion). This notification is essential to ensure that the worker has access to the legal protection and benefits arising from the recognition of the pathology as occupational. Thus, it not only allows access to compensatory and protective measures, but also reinforces the importance of prevention and vigilance in the workplace.

Discussion
Nickel allergy continues to be one of the main challenges in the field of occupational dermatology, with a high prevalence and significant impact on patients' lives. Despite the important legislative measures implemented, such as the European Union's Nickel Directive, exposure to this metal persists in various everyday contexts and also in work environment.
A detailed personal and occupational medical history, epicutaneous testing and mandatory reporting are essential pillars in the process of diagnosing and managing the disease.

However, there are still many gaps in knowledge about the mechanisms of nickel tolerance, associations that have not been fully clarified and data suggesting that not all exposure necessarily results in sensitization, which could open the door to new therapeutic or desensitization approaches in the future.

The ideal approach should be multidisciplinary, involving occupational physicians, dermatologists, employers and the workers themselves, promoting safer environments and reducing exposure to the sensitizing agent. In addition, it is essential to continue investing in education, research and innovation in order to better understand the mechanisms of the disease and develop more effective preventive strategies.

Conclusion
Nickel allergy is a common problem in the general population, with social and economic impact leading to a reduction in quality of life due to the chronicity of the condition [2].
Recognizing nickel ACD as an occupational disease is fundamental to guarantee workers' right to social protection, as well as promoting more effective prevention policies in the workplace. The causal relationship between type IV nickel sensitization and the occupational context needs to be clarified on a case-by-case basis [15].
Therefore, the prevention of nickel allergy is multidimensional, involving legal regulation, individual protection, changes in product design and continuing education, with the aim of minimizing exposure and the consequent adverse effects on health.

Author Contributions
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Rita Gil Duarte - acquisition of data/ articles
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Nuno Augusto Saldanha – critical review; final approval of the version to be published
Leonor Cunha - critical review; final approval of the version to be published
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