


FOOD-RELATED NICKEL ALLERGY: AN OVERVIEW

ALERGIA AO NÍQUEL RELACIONADA COM A ALIMENTAÇÃO: UMA VISÃO GERAL

A.R.
ARTIGO DE REVISÃOMarta Carvalho¹  ; Paula Lopes¹  ; Leandro Oliveira^{2*} 

¹ Escola de Ciências e Tecnologias da Saúde da Universidade Lusófona, Campo Grande, n.º 376, 1749-024 Lisboa, Portugal

² CBIOS (Research Center for Biosciences and Health Technologies) da Universidade Lusófona de Humanidades e Tecnologias, Campo Grande, n.º 376, 1749-024 Lisboa, Portugal

*Endereço para correspondência:

Leandro Oliveira
CBIOS (Research Center for Biosciences and Health Technologies) da Universidade Lusófona de Humanidades e Tecnologias,
Campo Grande, n.º 376,
1749-024 Lisboa, Portugal
leandrooliveira.nut@gmail.com

Histórico do artigo:

Recebido a 15 de novembro de 2024
Aceite a 30 de dezembro de 2025

ABSTRACT

INTRODUCTION: Nickel is a widely used metal in industry, found in soil and water, serving as a source of environmental contamination and human exposure, mainly through food. Nickel food allergy/Systemic Nickel Allergy Syndrome affects approximately 10 to 20% of the world population, presenting with dermatological, gastrointestinal, and respiratory symptoms.

OBJECTIVES: This study aims to provide an overview of nickel food allergy, also focusing on its treatment methods (especially dietary).

METHODOLOGY: A scoping review was conducted on PubMed searching for articles published between January 2010 and February 2024. Systemic Nickel Allergy Syndrome can manifest as a skin rash and itching, often triggered by prolonged exposure to items containing nickel, such as jewelry.

RESULTS: The literature emphasizes the need for personalized approaches and multidisciplinary support, particularly in the context of Systemic Nickel Allergy Syndrome. While a low-nickel diet is suggested for certain patients, its effectiveness varies, necessitating personalized interventions. Regional disparities in nickel content of foods further complicate dietary guidance.

CONCLUSIONS: In this regard, nutritionists play a crucial role in personalized nutritional planning and supplementation to detect potential deficiencies and improve patients' quality of life.

KEYWORDS

Allergy, Nickel, Nickel-restricted diet, Systemic Nickel Allergy Syndrome

RESUMO

INTRODUÇÃO: O níquel é um metal amplamente utilizado pela indústria, presente no solo e nas águas, sendo uma fonte de contaminação ambiental e exposição humana, principalmente através da alimentação. A alergia alimentar ao níquel/ Síndrome da Alergia Sistémica ao Níquel, afeta aproximadamente 10 a 20% da população mundial, manifestando-se através de sintomas dermatológicos, gastrointestinais e respiratórios.

OBJETIVOS: Este estudo tem como objetivo fornecer uma visão geral sobre a alergia alimentar ao níquel, focando-se também nas suas formas de tratamento (especialmente alimentar).

METODOLOGIA: Foi realizada uma scoping review na *Pubmed* pesquisando por artigos publicados entre janeiro de 2010 e fevereiro de 2024. A Síndrome da Alergia Sistémica ao Níquel pode manifestar-se por erupção cutânea e comichão, muitas vezes desencadeada pela exposição prolongada a itens que contêm níquel, como joalharia.

RESULTADOS: A literatura aponta para a necessidade de abordagens personalizadas e apoio multidisciplinar, particularmente no contexto da Síndrome da Alergia Sistémica ao Níquel. Embora uma dieta com baixo teor de níquel seja sugerida para determinados pacientes, a sua eficácia varia, exigindo intervenções personalizadas. Disparidades regionais no teor de níquel dos alimentos complicam ainda mais a orientação dietética.

CONCLUSÕES: Neste sentido, os nutricionistas desempenham um papel importante no planeamento nutricional personalizado e na suplementação para detetarem potenciais deficiências, e melhorar a qualidade de vida dos pacientes.

PALAVRAS-CHAVE

Alergia, Níquel, Dieta restrita em níquel, Síndrome da Alergia Sistémica ao Níquel

INTRODUCTION

Nickel (Ni) is a chemical element belonging to the transition metals class, being the 28th element on the periodic table. It is widely distributed in the environment and is the 24th most abundant element in the Earth's crust (1, 2). Together with other elements, nickel is present in soil, meteorites, and can

be emitted by volcanoes, with a significant portion found in seawater (3). It appears in various forms, often bonded to other metals such as iron in nickel steel, and is extremely resistant to corrosion (4). Due to its physical and chemical properties, nickel finds application in diverse metallurgical processes and is present in numerous everyday items like

kitchen utensils, cosmetics, detergents, jewelry, watches, keys, and other metal objects, thus presenting a risk of topical exposure. Additionally, nickel can be found in surgical implants, dental materials, water, and food, leading to systemic exposure to this metal (1, 3, 5).

Nickel has been recognized as an essential nutrient in some microorganisms, plants, and animal species because there are nickel-dependent enzymes in the Archaea kingdom, Bacteria, Algae, primitive eukaryotes, and plants. It is responsible for the normal development of plants and plays a fundamental role in their physiological and morphological functions, such as seed germination (3). In the blood, nickel is mostly bound to albumin, and its primary excretion pathway is through the kidneys (5, 6).

Exposure of the body to this metal can occur through inhalation, ingestion, or absorption at the dermal level, and its concentration in the bloodstream is directly proportional to the degree of exposure to its soluble compounds, unlike its insoluble salts or nickel deposits not absorbed in the lungs (2, 5, 7). The distribution of nickel in organ tissues depends on the duration and type of exposure to this metal (5). The widespread use of nickel increases its concentration in biogeochemical cycles, thereby increasing human exposure to this metal and its components through environmental contamination. At high concentrations, nickel can become toxic and even carcinogenic (2). The primary route of human exposure to nickel is through dietary intake. It is estimated that nickel levels in foods range from 0.1 to 0.5 mg/kg, depending on the amount of the metal in soil, water, industrial production, and food packaging processes (7).

There are data indicating that the body requires approximately 25 to 35 µg of nickel per day (8). However, a typical diet provides around 200 to 350 µg per day, and in some Western countries, it may even reach 600 to 900 µg per day (9-11). With such high exposure to elevated levels of nickel through food, becoming an immunotoxic and carcinogenic agent, nickel can cause a variety of negative health effects in humans. These effects may include allergies, cardiovascular diseases, asthma, pulmonary fibrosis, and even respiratory tract cancer. Nickel exposure can also lead to lesions in various tissues such as the liver, kidneys, spleen, and brain (2, 3).

Nickel allergy affects approximately 10 to 20% of the global population and is increasingly on the rise in various countries (6, 7, 12). In Europe, nickel allergy prevalence varies from approximately 8% to 19% in adults and from 8% to 10% in children and adolescents, being more common among women (13). The most common form of allergy to this metal manifests primarily through contact dermatitis (about 20%), but also through gastrointestinal symptoms (often associated with symptoms of Irritable Bowel Syndrome - IBS), and less commonly, respiratory symptoms and others such as heartburn, canker sores, headaches, and urogenital infections. All of these commonly occur after ingestion of foods with a high nickel concentration (7, 10, 14). These gastrointestinal symptoms combined with cutaneous reactions are referred to as Systemic Nickel Allergy Syndrome (SNAS). This allergy can arise at any stage of life and, once developed, tends to persist throughout life (3, 13).

The literature suggests that patients suffering from SNAS should make dietary changes to reduce the intake of foods with high nickel concentrations for at least 4 weeks as a non-pharmacological alternative to symptom improvement (7, 9, 12, 15-17).

Understanding the various treatment methods, particularly those related to nutrition, is crucial for healthcare professionals to effectively manage and improve the quality of life for individuals with this condition. This study aims to deepen understanding and promote evidence-based practices in allergy and clinical nutrition by providing insights into nickel food allergy and its treatment modalities, such as dietary interventions.

MATERIALS AND METHODS

A scoping review of the scientific literature on nickel food allergy was conceived, and the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) model (18) was used to structure the information. The formulation of the research question was based on the PCC acronym (Population, Context, and Concept): What is known, from the existing literature, about nickel food allergy? The inclusion criteria for the articles are summarized in Table 1 and were defined based on the PCC, study type, language, and date of publication, all related to nickel food allergy.

In the initial phase, an exploratory search was conducted in electronic databases using specific keywords related to nickel food allergy. Relevant articles were identified, and key phrases and search terms were extracted, with Boolean operators for systematic searching defined. English descriptors were identified using MeSH terms from PubMed/MEDLINE.

Combinations of descriptors/MeSH terms, subject headings, and subject terms were then applied to the database, utilizing Boolean operators "OR" and "AND," along with the wildcard tool "*" to generate variations of search terms, namely: "nickel allergy" AND (food* OR diet*) OR "Systemic Nickel Allergy Syndrome."

For original studies addressing the management of nickel food allergy, eligibility criteria included observational studies involving individuals diagnosed with the allergy and studies recommending management strategies. Studies involving participants without confirmed diagnoses or conducted solely on animals were excluded. Additionally, studies not published in Portuguese, English, or Spanish were excluded. Case reports were also not considered.

During the selection process, two independent reviewers were tasked with assessing each study. They meticulously examined the content and evaluated whether each study was suitable for inclusion. If both reviewers concurred on the inclusion of an article, it was selected. In cases where one reviewer advocated for inclusion while the other for exclusion, the article was flagged for further review by a third reviewer, who made the final decision on inclusion or exclusion. However, no study necessitated this classification, and there was no need to appoint a third reviewer. All selected studies included full-text access. Additional articles were added to better explain/complement the results, for example, review articles related to the topic.

After the eligibility selection, pertinent data were extracted from the studies, which were subsequently grouped by themes as presented in the results section of this study.

Table 1

Definition of inclusion criteria

INCLUSION CRITERIA	
POPULATION (P)	Adults aged 18 years and older diagnosed with food-related nickel allergy.
CONTEXT (C)	Studies involving participants diagnosed with food-related nickel allergy.
CONCEPT (C)	Studies addressing various aspects of food-related nickel allergy.
Types of Studies	All primary or secondary, qualitative or quantitative studies.
Language	Studies published in English, Spanish or Portuguese.
Publication date	Studies published between January 2000 and February 2024.

RESULTS AND DISCUSSION

A total of 71 articles were found, with 25 selected according to the inclusion and exclusion criteria mentioned earlier. The results are then presented grouped by themes according to the contents of the selected articles.

Recommended Dietary Allowance of Nickel and Food Sources

There is no established Recommended Dietary Allowance of nickel (19), what makes it uncertain is the amount of nickel in the diet that can reduce SNAS symptoms. Indeed, the only existing Dietary Reference Intake for nickel is the Tolerable Upper Intake Level for adults, which is set at up to 1 mg/day (17). Some studies estimate that individuals who consume about 220-350 micrograms of nickel per day, and therefore a restriction of less than 150 micrograms daily has been suggested for adults suspected of SNAS, while for children the suggestion is less than 100 micrograms daily.

Generally, foods most frequently associated with nickel include legumes, soy, chocolate, nuts, sunflower seeds, oats, and granola (11). In Table 2, a list of some foods grouped according to their nickel content is presented. As can be seen, nickel is present in small amounts in a wide variety of commonly consumed foods, making it difficult to avoid its consumption. Additionally, accurately measuring the nickel content in foods is a challenge due to regional variations in soil and water, as well as differences between plant species, fertilizers, or pesticides used in cultivation (4). Another difficulty is the variety of tests used to measure nickel in foods (4). In some instances, nickel from food processing machinery can contaminate the food. The use of stainless steel utensils for cooking acidic foods, such as tomatoes, vinegar, and citrus fruits, can increase the nickel content (20). Therefore, generally speaking, it is recommended to avoid consuming foods considered to have a high nickel content when following a low-nickel diet (5, 7).

Diet Therapy

Low-nickel Diet

A low-nickel diet is the most commonly recommended treatment approach for patients with sensitivity to this metal. It is an extremely restrictive dietary strategy that requires the avoidance of foods with high nickel content, which are summarised in Table 3 (11). Maintaining this type of diet for an extended period is challenging due to nickel being present in a wide variety of foods (7, 12). The minimum recommended

time to follow this diet to achieve noticeable relief of symptoms is 4 weeks and should not exceed 6 months due to the high nutrient restriction (17). Several studies have been conducted with this approach, and in all of them, patients with nickel sensitivity who exhibited characteristic symptoms showed improvements after adhering to the diet for a period of time. However, all studies also have some limitations due to the fact that many patients were unable to follow the protocol to the end due to the difficulty in maintaining this diet (7, 12).

Mislankar and Zirwas (10) they proposed a point-based dietary strategy, focusing on the nickel content present in various foods, aiming to assist patients in reducing the intake of this metal and consequently reducing associated symptoms. The guidelines for this diet include:

- Be persistent, as it may take up to two months to see significant improvements with the adoption of a low-nickel diet.
- Limit dietary nickel intake to less than 150 µg per day, with the possibility of further reducing this limit to 100 µg per day in cases of children or particularly sensitive patients.
- Adopt a point system, where every 10 µg of nickel consumed corresponds to one point, resulting in a daily limit of 15 points.
- Avoid foods with high nickel content, such as beans, chocolate, soy, nuts, oats, and granola.

Table 3

List of Forbidden foods with high nickel content (11)

FORBIDDEN FOODS		
Almond	Flounder and Plaice	Apricot
Fresh and Dried Fig	Artichoke	Hazelnut
Asparagus	Herring	Avocado
Lentil	Baking Powder	Lettuce
Bean and French Bean	Lobster	Broccoli
Margarine	Buckwheat and Maize	Mushroom
Canned Beverage	Mussel	Canned Foods
Nut	Carrot	Oat
Cauliflower and Cabbage	Onion	Chocolate and Cocoa
Oyster	Stored or Cooked Food in Iron Container	Ni-containing Vitamin/Mineral Supplements
Peanut	Pear	Pea
Plum/Prune	Potato	Raisin
Rhubarb	Shellfish	Spinach
Tea	Tomato	Yeast
Walnut	Whole Wheat Flour	

Table 2

List of foods according to their nickel content

NICKEL CONTENT	100 µG/KG	200 µG/KG	500 µG/KG	>500 µG/KG
Foods	Carrots	Apricot	Artichoke	Almonds
	Fig	Broccoli	Asparagus	Chickpeas
	Lettuce	Corn	Beans	Cocoa and derivatives
	Mushrooms	Eggplant	Cabbage	Lentils
	Codfish	Onions	Cauliflower	Peanuts
	Rhubarb	Peppers	Green bean	Nuts
	Rice	Pears	Wholemeal flour	
	Tea	Raisins	Yeast	
	Liquorice	Courgette	Margarine	
			Mussels	
			Potatoes	
			Peas	
			Plums	
			Spinach	
			Tomato	

- Avoid using stainless steel cookware in the preparation or cooking of acidic foods, such as tomatoes, vinegar, or citrus fruits, to prevent the release of nickel.
- Take vitamin C supplements to prevent nickel absorption in the intestine and avoid taking other types of vitamins or supplements.
- Use bottled or distilled water for drinking and cooking.

Mislankar and Zirwas (10) recommend to patients with nickel allergy or sensitivity a diet that does not exceed 150 µg per day for adults and 100 µg per day for children. According to their guidelines, the sum should not exceed 15 points per day for adults and 10 points per day for children, in order to keep allergic reactions stable. Following a low-nickel diet for 4 to 6 weeks is sufficient to determine if nickel is a cause of SNAS (21).

BraMa-Nickel Diet

Due to the high difficulty faced by patients in adhering to a low-nickel diet in various studies, Braga, Quecchia (12) developed a dietary approach to address this challenge, based on the BraMa-Nickel diet (acronym for Braga and Maccarinelli), aimed at reducing the amount of additives and avoiding foods containing vasoactive amines, which belong to the group of biogenic amines (22). Biogenic amines are compounds originated by microbial decarboxylation of amino acids, such as histamine, tyramine, cadaverine, tryptamine, among others, which are responsible for vasodilation and allergic and inflammatory reactions. These amines are commonly found in foods such as fish, meat, cheese, vegetables, and wines (23).

This approach based on the BraMa-Nickel Diet consisted of developing a balanced dietary plan tailored to the patients' needs. It included foods with low nickel content and was calculated according to the recommended nutrient intake levels for an average-weight adult male and female, with a daily intake of 1932 kcal and 1733 kcal, respectively, and approximately 50 µg/day of nickel.

In this study, one group of patients was subjected to a restricted nickel diet (with a list of prohibited foods), while another followed the BraMa-Nickel diet. Both diets proved effective in improving symptoms for most patients, but the BraMa-Nickel diet achieved greater adherence as it was less restrictive and therefore caused fewer long-term nutritional deficiencies (12). Still regarding the adoption of a patient-tailored diet, a more recent study (24) reveals that telenutrition may enable monitoring of nutritional status, adherence to a balanced low-nickel diet, and positively influence the quality of life in SNAS patients. Furthermore, it confirms the beneficial effect of the low-nickel diet on the quality of life of these patients, as evidenced by improvements in physical domain scales (general health and physical component summary) and mental domain scales (vitality).

Oral Desensitization

Studies have confirmed the efficacy and benefit of oral desensitization with nickel in the treatment of nickel allergy. It has been observed that oral tolerance to nickel sensitivity can be achieved through the ingestion of nickel sulfate by sensitive individuals, which brought a new perspective to the treatment of this condition. The suggested mechanism for oral desensitization in individuals sensitive to nickel involves the stimulation of suppressor T cell production by the excess antigen (25). Oral desensitization involves orally administering low doses of nickel to patients after the minimum period of adherence to a low-nickel diet. It is done through capsules containing nickel sulfate at different dosages, with the dose increasing each week, and can also involve the gradual introduction of foods with higher nickel content (26). In a study conducted by Minelli, Schiavino (26), it was observed that

86% of patients who took nickel sulfate capsules, increasing the dose each week, did not exhibit typical symptoms of nickel sensitivity and were able to gradually reintroduce some foods with higher nickel content without experiencing symptoms.

In another study by Di Gioacchino, Ricciardi (27), patients initially followed the BraMa-Nickel diet for symptom relief for 1 month, after which nickel sulfate capsules were introduced at low doses. The dose of the capsules was gradually increased each week, and after 3 months, foods with a maximum of 100 µg/kg of nickel were reintroduced, increasing to 500 µg/kg after 7 months of treatment. A control group was also established where patients only reintroduced nickel-rich foods without using capsules. The results indicated symptom improvement, particularly gastrointestinal symptoms, in 79% of patients in the group undergoing oral desensitization with nickel sulfate, compared to 54% of patients who showed improvement only with the reintroduction of nickel-rich foods after the BraMa-Nickel diet (27).

In addition to conducting a study with the same parameters, Rizzi, Di Rienzo (14) also assessed psychological symptoms of patients with nickel sensitivity such as depression, anxiety, fear, anger, low self-esteem, etc., before and after treatment with desensitization. Patients also reported improvement in these symptoms 1 year after treatment (14).

Hydroponic Culture: a Hypothesis?

Hydroponic culture presents itself as a soilless cultivation method, meaning the plant roots are suspended in an aqueous solution of nutrients (9). It is used when soil conditions are impractical for cultivation, also reducing environmental impact by not using fertilizers and pollutants. Additionally, it prevents the transmission of diseases and infections from parasites existing in the soil. It is believed that hydroponic culture has contributions to improving the quality of food (9). In a clinical study conducted by Rizzi, Chini (9), tomato in its concentrated form was used, as it is one of the foods with the highest nickel content (around 500 µg/kg). The aim of this study was to compare the impact of consuming concentrated tomato grown in soil versus grown in hydroponic conditions on the symptoms of patients with nickel sensitivity. The patients were subjected to a nickel-restricted diet for at least 4 weeks. Then, one group of patients introduced conventionally grown concentrated tomato into their diet, while another group introduced hydroponically grown concentrated tomato. After 12 months, the two groups of patients exchanged the concentrated tomato introduced in their diet. This trial demonstrated an improvement in symptoms, particularly gastrointestinal and psychological symptoms, in patients who introduced hydroponically grown concentrated tomato into their diet. The authors of this study believe that hydroponic culture may be a future premise for improving the quality of life of people with food allergies.

Food-related Recommendations

In preparing a nickel-restricted diet, some considerations are necessary. The nickel content of foods varies from place to place and even from batch to batch of production of a given food item (21). The seasons of the year can also influence the concentration of nickel in plant-derived foods. It is known that plant tissues have higher nickel content in spring and autumn and lower in summer (4). Indeed, there are even differences in nickel concentration in different parts of the plant. For example, leaves have higher concentrations than the stem and roots. Therefore, each patient may react differently to a nickel-restricted diet depending on where they live and the time of year (4). It is also advisable not to cook food in stainless steel utensils, as they may contain nickel, whose ions can dissociate and increase the concentration of the metal in the food (20).

Other important considerations include the inhibitory effect of vitamin C, orange juice, and milk on nickel absorption(10). Iron deficiency anemia, pregnancy, and breastfeeding can increase nickel absorption, so adequate iron intake is essential to reduce this absorption (4).

Relationship with Other Pathologies

Irritable Bowel Syndrome

The gastrointestinal system plays a crucial role in the immune system, influencing how the body reacts to different substances, either by triggering effector immune responses or promoting tolerance to various antigens. This is achieved through the balance between the activities of anti-inflammatory cytokines produced by Th1 cells, which activate macrophages, and pro-inflammatory cytokines produced by Th2 cells, which activate B lymphocytes responsible for antibody production (13, 28).

In recent years, studies have suggested a potential association between a compromised intestinal barrier function, resulting in a mild inflammatory state, and the development of IBS. Similarly, nickel allergy has been associated with dysregulation of the immune system, characterized by a prevalent immunosuppressive action, with an increased activity of Th2 cytokines and T lymphocytes in the duodenum and intestinal epithelium (17). Rizzi, Nucera (17) showed that there is a high prevalence of nickel allergy in patients with typical IBS symptoms and they reported improvement in gastrointestinal symptoms after the nickel-restricted diet strategy. In this way, a new nutritional strategy is introduced for patients with IBS in addition to the low-FODMAP diet, taking into account that nickel allergy also induces a pro-inflammatory state (17).

Lactose Intolerance

In another study, the prevalence of lactose intolerance was also analyzed in patients with SNAS, compared to a healthy population (29). It was found that 19% of patients with nickel allergy experienced gastrointestinal symptoms, in addition to cutaneous manifestations, after consuming foods rich in nickel, due to its effect on vasodilation of the gastrointestinal mucosa. This study revealed that lactose intolerance is highly prevalent in patients with SNAS, suggesting that the post-inflammatory state caused by nickel ingestion could temporarily impair the intestinal flora, resulting in lactose intolerance. However, additional tests are needed to confirm this relationship.

Endometriosis

There is also a correlation between typical gastrointestinal symptoms of IBS and the presence of endometriosis in women. Exposure to pollutants and heavy metals has been considered a contributing factor to the onset of this condition, with the possibility of heavy metals interfering with estrogenic activity. Since nickel is a heavy metal, the hypothesis that nickel allergy could be responsible for these gastrointestinal symptoms in women with endometriosis has been investigated (7). This pioneering study by Borghini, Porpora (7) shows a prevalence of nickel allergy in 90.3% of women with endometriosis in this trial. A nickel-restricted diet was administered to patients for 3 months, who reported improvement in gastrointestinal symptoms including those most characteristic of endometriosis such as chronic pelvic pain, dysmenorrhea (debilitating menstrual pain), and dyspareunia (pain during sexual intercourse). However, more trials related to this premise are needed, mainly due to the difficulty in gathering a good sample of patients due to reluctance to adhere to the nickel-restricted diet.

The Role of Probiotics in Gastrointestinal Symptoms

Probiotics, live microorganisms that offer health benefits when consumed in adequate amounts, have been marketed with claims based on specific strain characteristics, mainly *Lactobacillus* and *Bifidobacterium*. Clinical studies have shown improvements in gastrointestinal symptoms and intestinal permeability with treatment using *Lactobacillus reuteri* and strains of *Lactobacillus rhamnosus* (30). Dietary nickel intake can affect the composition of the intestinal microbiota. Trials in chickens have shown that nickel intake reduced beneficial bacteria such as *Bifidobacterium* and/or *Lactobacillus*, increasing the presence of harmful species. In this context, probiotics have the potential to positively alter the intestinal microbiota (1).

A pilot study on IBS focused on the intestinal microbial community. Preliminary results suggest that the combination of a low-nickel diet combined with the use of probiotics may reduce the frequency and severity of meal-related symptoms, possibly due to increased microbial diversity in the gut (28). This study is pioneering in proving the effectiveness of combining probiotics with this type of diet in patients with IBS. Despite partial improvement with the diet alone, the introduction of probiotics may not only be beneficial but possibly crucial in treatment (28). These data indicate that, although conditions may have different origins, a dysregulation of intestinal homeostasis may play a fundamental role in both. However, additional studies in larger samples are needed to support this hypothesis (28).

Use of Chelators

The use of a dietary nickel chelator, known as disulfiram, has shown improvements in hand eczema dermatitis in a selected group of patients (31). However, its recommendation should be reserved only for patients with persistent complaints that do not respond to other measures, due to potential significant side effects such as liver toxicity and the need for alcohol abstinence during treatment. The initial dose is 500 mg/day, followed by 125-500 mg/day as maintenance dose (32). Studies have reported response rates of up to 50% with the use of this medication. When combined with nickel avoidance diets, the response rate can reach 90% (31). According to some authors, the occurrence of systemic symptoms such as malaise and myalgias during the first two weeks of treatment with disulfiram may suggest a response to treatment. These symptoms are possibly attributable to the release of nickel from cellular deposits, initiated by chelation therapy (11).

CRITICAL ANALYSIS

Nickel hypersensitivity represents a cause of SNAS, a condition characterized by a rash accompanied by itching. This type of sensitivity occurs when the skin is repeatedly or for prolonged periods exposed to nickel, as commonly seen with jewelry use. In certain cases, suspicion of a nickel food allergy, known as SNAS, may arise when dermatitis is present without known contact with other allergens. Individuals with iron deficiency may absorb more nickel from the diet, as iron and nickel compete for absorption in the body. Therefore, to reduce nickel absorption, it is suggested to consume foods rich in iron and vitamin C, which improves iron absorption, during meals (20). On the other hand, probiotics seem to play an important role in attenuating the negative impact of nickel on the intestinal mucosa (30).

In the literature, the causal relationship between dietary nickel and SNAS remains controversial. This is due to the fact that most studies exhibit inconsistencies in diagnostic procedures, implementation of the diet, doses used in provocation tests, and the type of provocation test applied. In fact, the lack of a uniform and standardized protocol influences this issue.

Therefore, it is crucial to clarify and identify the population that may benefit from these diets and deserves consideration. The widespread application of these measures to all patients with nickel sensitivity is not recommended and is not supported by scientific evidence. The recommendation of an avoidance diet should be made with caution and only in selected cases. Patients who the literature suggests may benefit meet all of the following criteria (33):

- They have proven sensitivity to nickel;
- Other causes of dermatitis have been excluded, especially IgE-mediated pathologies;
- They present chronic dermatitis that does not improve despite the avoidance of cutaneous exposure to nickel, especially if the dermatitis is suggestive of nickel-induced dermatitis, such as vesicular dermatitis on the hands.

If the above criteria are met, then dietary avoidance can be considered for a period of 6 to 8 weeks. Improvement in patients supports the hypothesis of a causal relationship with nickel. However, this relationship can only be confirmed after symptom exacerbation with nickel ingestion in a double-blind, placebo-controlled food challenge. If there is no improvement with the avoidance diet, it should be discontinued (33). There are various guidelines for a low-nickel diet; however, it is crucial to understand that these recommendations should be considered as general guidelines. Studies suggest that the nickel content in foods can vary considerably between different regions within the same country, and that local soil conditions, as well as the use of fungicides, play a significant role in the final amount of nickel present in foods (4, 20). Therefore, it is of utmost importance for patients with this condition to have multidisciplinary support, primarily from a nutritionist, so that they can provide the most balanced nutritional planning possible and compensate for potential nutrient deficiencies with appropriate supplementation tailored to each individual to maintain or improve their quality of life.

Limitations of the Study

The present study has some limitations, so it is necessary to interpret its results with caution. In this study, there may be researcher bias, where subjectivity in the selection and interpretation of studies can influence the conclusions. Additionally, the lack of an explicit protocol may lead to a lack of transparency in the methodology, making it difficult for others to critically evaluate the study. There is also the risk of publication bias, where studies with significant results are more likely to be included, distorting the overall view. Lastly, the generalization of results may be limited due to the descriptive nature of this scoping review. Despite these limitations, this study can provide an overview of nickel food allergy, offering information on the most recent studies on the topic.

CONCLUSIONS

The literature on nickel food allergy, especially related to SNAS, is complex, with ongoing debate about the relationship between dietary nickel and SNAS. Inconsistencies in studies make definitive conclusions difficult, suggesting caution in recommending avoidance diets, which may not benefit all patients. Specific criteria, such as confirmed nickel sensitivity, need to be addressed before considering dietary avoidance. While a low-nickel diet is recommended for some, its effectiveness varies, requiring individualized approaches. Regional disparities in nickel levels in foods further complicate dietary guidelines. Multidisciplinary support, particularly from nutritionists, is crucial for personalized nutritional planning and supplementation to enhance quality of life.

CONFLICTS OF INTEREST

None of the authors reported a conflict of interest.

AUTHORS' CONTRIBUTIONS

MC, PL: Pesquisa e seleção bibliográfica, e redação do artigo; LO: Redação e revisão do artigo. Todos os autores leram e aprovaram a versão final do artigo.

REFERENCES

1. Lombardi F, Fiasca F, Minelli M, Maio D, Mattei A, Vergallo I, et al. The Effects of Low-Nickel Diet Combined with Oral Administration of Selected Probiotics on Patients with Systemic Nickel Allergy Syndrome (SNAS) and Gut Dysbiosis. *Nutrients*. 2020;12(4).
2. Guo H, Liu H, Wu H, Cui H, Fang J, Zuo Z, et al. Nickel Carcinogenesis Mechanism: DNA Damage. *Int J Mol Sci*. 2019;20(19).
3. Genchi G, Carocci A, Lauria G, Sinicropi MS, Catalano A. Nickel: Human Health and Environmental Toxicology. *Int J Environ Res Public Health*. 2020;17(3).
4. Sharma AD. Low nickel diet in dermatology. *Indian J Dermatol*. 2013;58(3):240.
5. Picarelli A, Di Tola M, Vallecoccia A, Libanori V, Magrelli M, Carlesimo M, et al. Oral mucosa patch test: a new tool to recognize and study the adverse effects of dietary nickel exposure. *Biol Trace Elem Res*. 2011;139(2):151-159: <https://doi.org/10.1007/s12011-010-8652-y>.
6. Di Tola M, Amodeo R, Marino M, Tabacco F, Casale R, Bove M, et al. Peripheral blood lymphocyte typing as a useful tool to objectify the oral mucosa patch test in the diagnosis of allergic contact mucositis to nickel. *Biol Trace Elem Res*. 2014;159(1-3):81-86: <https://doi.org/10.1007/s12011-014-9991-x>.
7. Borghini R, Porpora MG, Casale R, Marino M, Palmieri E, Greco N, et al. Irritable Bowel Syndrome-Like Disorders in Endometriosis: Prevalence of Nickel Sensitivity and Effects of a Low-Nickel Diet. An Open-Label Pilot Study. *Nutrients*. 2020;12(2).
8. Nielsen F. Nickel. *Adv Nutr*. 2021;12(1):281-282: <https://doi.org/10.1093/advances/nmaa154>.
9. Rizzi A, Chini R, Porcari S, Settanni CR, Persichetti E, Mora V, et al. Datterino Trial: A Double Blind, Randomized, Controlled, Crossover, Clinical Trial on the Use of Hydroponic Cultivated Tomato Sauce in Systemic Nickel Allergy Syndrome. *J Clin Med*. 2022;11(18).
10. Mislankar M, Zirwas MJ. Low-nickel diet scoring system for systemic nickel allergy. *Dermatitis*. 2013;24(4):190-195: <https://doi.org/10.1097/DER.0b013e3182937e81>.
11. Fabbro SK, Zirwas MJ. Systemic contact dermatitis to foods: nickel, BOP, and more. *Curr Allergy Asthma Rep*. 2014;14(10):463.
12. Braga M, Quecchia C, Perotta C, Timpini A, Maccarinelli K, Di Tommaso L, et al. Systemic nickel allergy syndrome: nosologic framework and usefulness of diet regimen for diagnosis. *Int J Immunopathol Pharmacol*. 2013;26(3):707-716.
13. Ahlström MG, Thyssen JP, Wennervaldt M, Menné T, Johansen JD. Nickel allergy and allergic contact dermatitis: A clinical review of immunology, epidemiology, exposure, and treatment. *Contact Dermatitis*. 2019;81(4):227-241: <https://doi.org/10.1111/cod.13327>.
14. Rizzi A, Di Rienzo A, Buonomo A, Aruanno A, Carusi V, Ricci AG, et al. Impact of nickel oral hyposensitization on quality of life in systemic nickel allergy syndrome. *Int J Immunopathol Pharmacol*. 2020;34:2058738420934629.
15. Di Tola M, Marino M, Amodeo R, Tabacco F, Casale R, Portaro L, et al. Immunological characterization of the allergic contact mucositis related to the ingestion of nickel-rich foods. *Immunobiology*. 2014;219(7):522-530: <https://doi.org/10.1016/j.imbio.2014.03.010>.
16. Randazzo CL, Pino A, Ricciardi L, Romano C, Comito D, Arena E, et al. Probiotic supplementation in systemic nickel allergy syndrome patients: study of its effects on lactic acid bacteria population and on clinical symptoms. *J Appl Microbiol*. 2015;118(1):202-211: <https://doi.org/10.1111/jam.12685>.
17. Rizzi A, Nucera E, Laterza L, Gaetani E, Valenza V, Corbo GM, et al. Irritable Bowel Syndrome and Nickel Allergy: What Is the Role of the Low Nickel Diet? *J Neurogastroenterol Motil*. 2017;23(1):101-108: <https://doi.org/10.5056/jnm16027>.
18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev*. 2021;10(1):89.

19. Institute of Medicine. Nickel. Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. Washington (DC): National Academies Press (US); 2001.
20. Pizzutelli S. Systemic nickel hypersensitivity and diet: myth or reality? *Eur Ann Allergy Clin Immunol.* 2011;43(1):5-18.
21. Cunningham E. What Role Does Diet Play in the Management of Nickel Allergy? *J Acad Nutr Diet.* 2017;117(3):500.
22. Braga M, Maccarinelli K. Una dieta per l'orticaria. *It J Allergy Clin Immunol.* 2003;15:100-103.
23. Doeun D, Davaatseren M, Chung MS. Biogenic amines in foods. *Food Sci Biotechnol.* 2017;26(6):1463-1474.
24. Nucera E, Rizzi A, Chini R, Giangrossi S, Lohmeyer FM, Parrinello G, et al. Diet Intervention Study through Telemedicine Assistance for Systemic Nickel Allergy Syndrome Patients during the COVID-19 Pandemic. *Nutrients.* 2021;13(8).
25. Sharma AD. Relationship between nickel allergy and diet. *Indian J Dermatol Venereol Leprol.* 2007;73(5):307-312: <https://doi.org/10.4103/0378-6323.35733>.
26. Minelli M, Schiavino D, Musca F, Bruno ME, Falagiani P, Mistrello G, et al. Oral hyposensitization to nickel induces clinical improvement and a decrease in TH1 and TH2 cytokines in patients with systemic nickel allergy syndrome. *Int J Immunopathol Pharmacol.* 2010;23(1):193-201.
27. Di Gioacchino M, Ricciardi L, De Pità O, Minelli M, Patella V, Voltolini S, et al. Nickel oral hyposensitization in patients with systemic nickel allergy syndrome. *Ann Med.* 2014;46(1):31-37: <https://doi.org/10.3109/07853890.2013.861158>.
28. Caruso C, Colantuono S, Celi G, Salerno L, De Martino G, Ianiro G, et al. Modulation of gut microbiota in patients with IBS and systemic nickel allergy after diet and probiotic supplementation: a pilot study. *J Biol Regul Homeost Agents.* 2020;34(5):1929-1934: <https://doi.org/10.23812/20-162-L>.
29. Cazzato IA, Vadrucci E, Cammarota G, Minelli M, Gasbarrini A. Lactose intolerance in systemic nickel allergy syndrome. *Int J Immunopathol Pharmacol.* 2011;24(2):535-537: <https://doi.org/10.1177/039463201102400230>.
30. Wieërs G, Belkhir L, Enaud R, Leclercq S, Philippart de Foy JM, Dequenue I, et al. How Probiotics Affect the Microbiota. *Front Cell Infect Microbiol.* 2019;9:454.
31. Sharma AD. Disulfiram and low nickel diet in the management of hand eczema: a clinical study. *Indian J Dermatol Venereol Leprol.* 2006;72(2):113-118: <https://doi.org/10.4103/0378-6323.25635>.
32. Torres F, das Graças M, Melo M, Tosti A. Management of contact dermatitis due to nickel allergy: an update. *Clin Cosmet Investig Dermatol.* 2009;2:39-48.
33. Antico A, Soana R. Nickel sensitization and dietary nickel are a substantial cause of symptoms provocation in patients with chronic allergic-like dermatitis syndromes. *Allergy Rhinol (Providence).* 2015;6(1):56-63.