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High consumption of Nickel-containing foods and IBS-like disorders: late events in a gluten-free diet

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ABSTRACT

As reported in the recent literature, Nickel has become an important part of our daily life since the last decades. We can find it in skincare products, occupational exposures and foods. Only recently, research has started to show a link between Nickel and many health disorders, including adverse reactions to food containing nickel. Nowadays, the relationship between nickel-containing foods and well-being is becoming a topic of growing interest in clinical practice and will play an even larger role in the future. The use of foods with a high nickel content, largely present in a gluten free diet, could explain the lack of clinical remission in celiac patients and dispel a diagnosis of refractory celiac disease.

In Europe, almost 20% of the population is sensitized to Nickel (Ni) and can develop Allergic Contact Dermatitis (ACD) (Nielsen and Menné, 1994). ESSCA (European Surveillance System on Contact Allergies) showed that the highest Nickel Allergy's prevalence in Europe is in Italy (32.2% of patients who undergo patch test) (ESSCA Writing Group, 2008).

Nickel is a widespread metal that is present in the air, water and soil and it is essential in many plants and bacteria metabolism (Campanale et al., 2014). In humans, sensitization to Nickel occurs primarily through skin contact but also after Nickel-containing food ingestion.

Allergic Contact Dermatitis is a skin-localized inflammatory reaction induced by different haptens, including Ni. ACD is caused by a type IV Delayed Hypersensitivity Reaction mediated by CD4 + and CD8 + lymphocytes that occurs after keratinocytes release IL-1 α , IL-1 β , TNF- α , GM-CSF, IL-8. Ni sulfate can also cause ACD by interacting with TLR-4 specific histidine residues, able to stimulate pro-inflammatory pathways (Ward et al., 2019).

In addition to the better known Ni-ACD, there is also a clinical condition defined Nickel Allergic Contact Mucositis (Ni-ACM) (Borghini et al., 2017) that can affect sensitized subjects after the ingestion of Ni-containing foods. Tomatoes, mushrooms, cocoa, coffee, legumes, corn, soy, onion and many other foods are rich in Ni (Picarelli et al., 2011). Bloating, abdominal pain, diarrhea and heartburn frequently characterize this clinical entity (Braga et al., 2013). Extra-intestinal symptoms such as foggy-mind, headache, malaise, fever, arthralgia, chronic fatigue and motor coordination impairment are also frequently observable in these patients.

Ni-ACM causes hyperemia and edema of the oral mucosa (Picarelli et al., 2011) that can be revealed by laser doppler perfusion imaging techniques showing a significant increase in mucosal perfusion (Borghini et al., 2016).

Ni-induced clinical manifestations observed in the general

population are also frequent among Celiac Disease patients after prolonged gluten-free diet. These patients are often wrongly labeled as Gluten-free Diet Non Responders or affected by Refractory Celiac Disease. Corn-based flours and various legumes high consumption, in fact, leads to greater Nickel sensitivity and symptoms characteristically improve after a low-Ni diet (Borghini et al., 2020).

The attention to this new clinical entity and its dietary and pharmacological treatment is today assuming an important role in Western countries.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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