REVIEW ARTICLE

Therapeutic management in histamine intolerance: an integrative review

Manejo terapêutico na intolerância à histamina: uma revisão integrativa

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Abstract

Objective: we conducted a literature survey on nutritional strategies for the management of histamine intolerance to produce an integrative literature review in databases. **Methodology**: After removing all duplicates, relevant articles were selected in three distinct phases. These phases consist of a gradual process of article selection and verification and narrowing of the inclusion criteria until reaching the proposed result. Original articles published in the last five years focusing on strategies for the treatment of histamine intolerance were included. **Results:** After research and tabulation of data, it was demonstrated that a low-histamine diet effectively reduces gastrointestinal and systemic symptoms in more than 70% of patients with histamine intolerance. Furthermore, DAO supplementation proved to be a complementary alternative for patients with refractory symptoms. **Conclusion**: The study is of great relevance in clinical practice and a guide for patients. On the other hand, additional studies are needed to validate diagnostic biomarkers, consolidate clinical guidelines and explore personalized approaches that promote intestinal health and overall well-being of patients.

Keywords: diet; strategies; diamine oxidase; supplementation; treatment.

Resumo

Objetivo: Nós realizamos um levantamento bibliográfico sobre estratégias nutricionais para o manejo da intolerância à histamina para a produção de uma revisão integrativa da literatura em bases de dados. **Metodologia**: Após a remoção de todas as duplicatas, os artigos relevantes foram selecionados em três fases distintas. Essas fases consistem em um processo gradual de seleção de artigos e verificação e estreitamento dos critérios de inclusão até chegar ao resultado proposto. Foram incluídos artigos originais publicados nos últimos cinco anos com foco em estratégias para tratamento de intolerância à histamina. **Resultados:** Após pesquisa e tabulação de dados, foi demonstrado que a dieta com baixo teor de histamina reduz efetivamente os sintomas gastrointestinais e sistêmicos em mais de 70% dos pacientes com intolerância à histamina. Além disso, a suplementação de DAO provou ser uma alternativa complementar para pacientes com sintomas refratários. **Conclusão**: O estudo é de grande relevância na prática clínica e um guia para pacientes. Por outro lado, é necessário realizar estudos adicionais para validar biomarcadores diagnósticos, consolidar diretrizes clínicas e explorar abordagens personalizadas que promovam a saúde intestinal e o bem-estar geral dos pacientes.

Palavras-chave: dieta; estratégias; diamina oxidase; suplementação; tratamento.

INTRODUCTION

Food intolerance is a widespread condition impacting approximately 15-20% of individuals globally, manifesting through a range of symptoms that primarily affect the gastrointestinal system, although extra gastrointestinal manifestations are also noted[1,2]. The pathophysiology of food intolerance is multifactorial and varies significantly among individuals, often complicated by coexisting gastrointestinal disorders such as Irritable Bowel Syndrome (IBS)[3,4]. Food intolerances are generally considered non-immunological in nature, distinguished from food allergies, which typically invoke an immune-mediated response. Common forms of food intolerance include lactose malabsorption, fructose malabsorption, and sensitivity to food additives or naturally occurring vasoactive compounds in foods[5].

Histamine intolerance (HIT) is an emerging dietary dysfunction characterized by an impaired capacity to degrade histamine, leading to the accumulation of this biogenic amine in the body. It is associated with gastrointestinal and systemic symptoms. Estimates suggest that approximately 1% of the global population is affected by histamine intolerance6. However, other studies indicate that the prevalence may be higher due to a lack of standardized diagnostic criteria and awareness among healthcare providers[7]. It has led to an ongoing debate regarding how many individuals may experience histamine-related issues without receiving a proper diagnosis. Typical presentations may include gastrointestinal symptoms such as diarrhea and abdominal pain, as well as systemic reactions like headaches, flushing, and respiratory issues[8,9]. Symptoms can vary widely among individuals, complicating diagnosis and management[2]. Research indicates a significant overlap between histamine intolerance and other food intolerances, such as lactose and fructose intolerances, with studies reporting the co-occurrence

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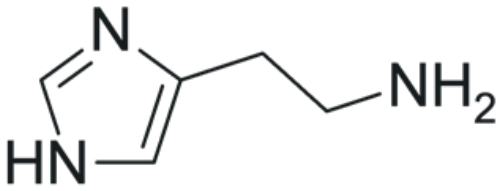
of these conditions in many patients presenting with unclear gastrointestinal discomfort[10,11].

Recent advancements in understanding HIT have highlighted the need for better diagnostic tools and strategies. The HIT results from a deficiency of the diamine oxidase (DAO) enzyme, which is essential for the breakdown of histamine obtained through dietary sources. Investigations utilizing DAO activity measurements have shown a notable association between low serum DAO levels and symptom severity in individuals diagnosed with HIT[12]. Moreover, dietary modifications, including histamine-reduced diets and DAO supplementation, have been subjects of research and have shown promise in alleviating symptoms for many patients[13,14]. Despite these therapeutic approaches, compliance with dietary restrictions remains a challenge for many patients, partly due to the lack of clear guidance regarding histamine levels in various foods[9].

Histamine (2(1 H-Imidazol-4-yl)ethanamine), CAS 51-45-6, see Figure 1. Its chemical structure consists of a five-membered aromatic ring containing two nitrogen atoms and a two-carbon ethylamine side chain with a terminal amine (-NH_2) group.

Figure 1. Chemical structure of histamine (2(1 H-Imidazol-4-yl) ethanamine).

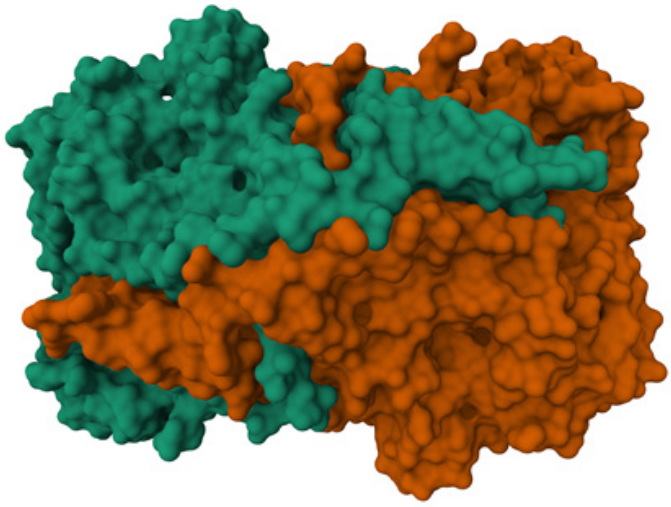


Histamine is a biogenic amine that plays a crucial role in various physiological processes, including immune response, gastric acid secretion, and neurotransmission. It exerts its effects through four distinct G-protein-coupled receptors, designated as H1, H2, H3, and H4 receptors[15]. The H1 receptor is primarily involved in mediating allergic responses and inflammation, as it causes vasodilation and increases vascular permeability when activated[16]. Alternatively, the H2 receptor is chiefly responsible for regulating gastric acid secretion and is found prominently in the stomach's parietal cells[17]. The H3 receptor functions mainly as an inhibitory autoreceptor in the central nervous system, moderating the release of neurotransmitters, while the H4 receptor is implicated in immune responses and is predominantly expressed in hematopoietic cells[18]. Recent studies have expanded the understanding of histamine receptors, revealing their involvement in complex signaling pathways that may influence several disease processes, including allergies and neurodegenerative conditions[19].

In terms of dietary sources, histamine is produced through the decarboxylation of histidine, an amino acid commonly found in many foods. Foods rich in histidine, such as aged cheeses, fermented alcoholic beverages, cured meats, and some fish (like tuna and mackerel), can lead to the accumulation of histamine when they spoil[20,21]. Moreover, histamine can also be present in lesser amounts in fresh fruits and vegetables, though these instances are generally considered less concerning with respect to food intolerance[22]. The burden of histamine intake, particularly from high-histamine foods, is of great concern for individuals with histamine intolerance, where the body's ability to metabolize histamine - primarily through the DAO enzyme diamine - is compromised[23].

Diamine oxidase (DAO), also known as histaminase, is a copper-containing enzyme primarily responsible for the oxidative deamination of histamine and other polyamines, such as putrescine and spermidine. This process results in the production of the corresponding aldehydes, ammonia, and hydrogen peroxide[24]. Its structure has been elucidated through X-ray crystallography, revealing detailed insights into its configuration[25]. DAO functions as a homodimer, meaning it consists of two identical subunits. Each subunit contributes to the enzyme's overall activity (Figure 2). Each subunit houses an active site characterized by a copper ion, which is essential for the enzyme's catalytic activity, beyond the topaquinone cofactor derived from the post-translational modification of a tyrosine residue. This cofactor plays a pivotal role in the enzyme's function[25].

Figure 2. Surface representation of Diamine oxidase (DAO) dimer with PDB code 3HI7.



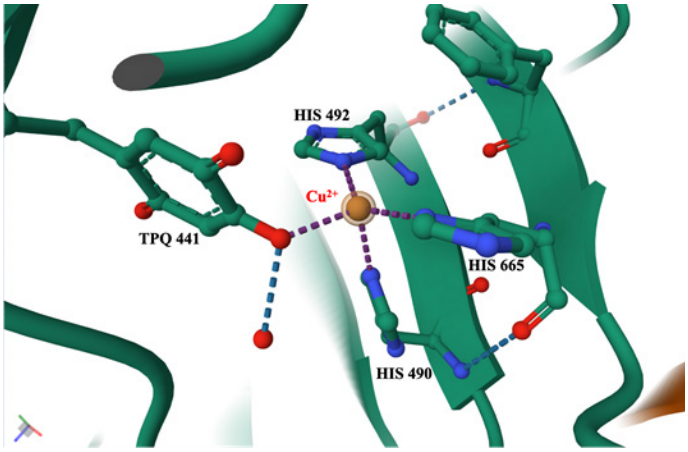
HIT can lead to a variety of symptoms, including headaches, skin flushes, gastrointestinal disturbances, and respiratory issues[26]. This condition is not universally recognized, which complicates both diagnosis and management and is increasingly acknowledged in clinical nutrition and gastroenterology[27]. Dietary management often involves a low-histamine diet, aiming to alleviate symptoms while preventing the intake of foods with high histamine levels[22].

Due to the variety of symptoms, HIT is often not properly recognized, or its symptoms are misinterpreted. Several disorders affecting the gastrointestinal tract, such as food intolerances, IBS, or celiac disease, can be controlled by following

restrictive diets. Restrictive diets for the treatment of different gastrointestinal disorders alter the composition of the intestinal microbiota of the patients undergoing them. Recently, it has been proposed that individuals with HIT suffer from intestinal dysbiosis, having an overabundance of histamine-secreting bacteria, but it is still unknown how this condition is affected by the usual dietary treatment of HIT, i.e. a low-histamine diet and supplementation with DAO enzyme[28].

In general, it is difficult for health professionals to provide nutritional advice and guidance on a low-histamine diet. In fact, this difference exists in the list of foods declared excluded from various low-histamine diets22. In addition, there is disagreement among professionals about the length of exclusion in the diets. Thus, it is proven once again how the work of nutritionists in the treatment of HIT is so important[29].

Figure 3. Cartoon representation of Diamine oxidase (DAO) active site (PDB code 3HI7). Histidine (HIS 490, HIS 492 and HIS 665) residues, topaquinone (TPQ 441) cofactor and copper ion (Cu2+) are represented in ball-and-stick model.



In this work, the main objective is to carry out a bibliographical survey on nutritional strategies for managing HIT. This study is expected to support future research in the development of protocols or guidelines for nutritional care in patients with HIT, broadening the view on effective nutritional strategies for the management of this condition while providing guidance for health professionals and patients.

METHODOLOGY

To gather pertinent research and articles in English, an in-depth search was conducted in online databases, including MEDLINE-Pubmed and ScienceDirect. The selected articles included health assessment studies and studies seeking to identify nutritional strategies for the therapeutic management of histamine intolerance, differentiating them and comparing them with each other.

Duplicate data sources were also identified through a comparison of similar studies and articles, and study sources with more valid details were selected and used. For the literature search, descriptors such as “histamine intolerance”, “histamine intolerance and nutrition”, “histamine intolerance and diet”, and “low histamine diets” were used, which included low histamine diets, treatment for histamine intolerance, the impact of histamine intolerance on daily life and histamine level in foods.

After all duplicates were removed, relevant articles were selected in three distinct phases. The initial phase involved screening the titles and abstracts of the articles, while the second phase involved excluding articles considered irrelevant. The final phase involved an in-depth exploration of the full text of the recruited articles with the aim of selecting only articles that met the inclusion criteria.

Inclusion criteria included original studies, randomized clinical trials, crossover studies, and cohort studies that met the following criteria: Studies that focused on the treatment and nutritional management of histamine intolerance in patients with a diagnosis or possible diagnostic hypothesis of histamine intolerance who were treated with low-histamine diets during their treatments. In addition, only articles that are available online, in English, and published in the last 05 (five) years were selected. Opinion articles, clinical trials on animals, secondary studies, scoping reviews, or any other types of research that did not address the proposed topic were excluded.

RESULTS

As a result of the first selection of articles, 1.462 studies were found. After preliminary analysis, 1.443 articles were excluded, and 19 articles were selected for full reading. Next, a careful analysis of the methodology and results explored was carried out. Thus, 14 articles were excluded, and five (5) articles that met the inclusion criteria were used to compose the results presented in the integrative review. The complete article selection process is presented in the Flowchart in Figure 4.

The five (5) articles were organized and described according to author/year/country/type of study, intervention, period, diagnostic criteria, population, and main results (Table 1).

Figure 4. Flowchart demonstrating the steps of the inclusion and exclusion analysis of the articles selected in this research. Source: Author's own.

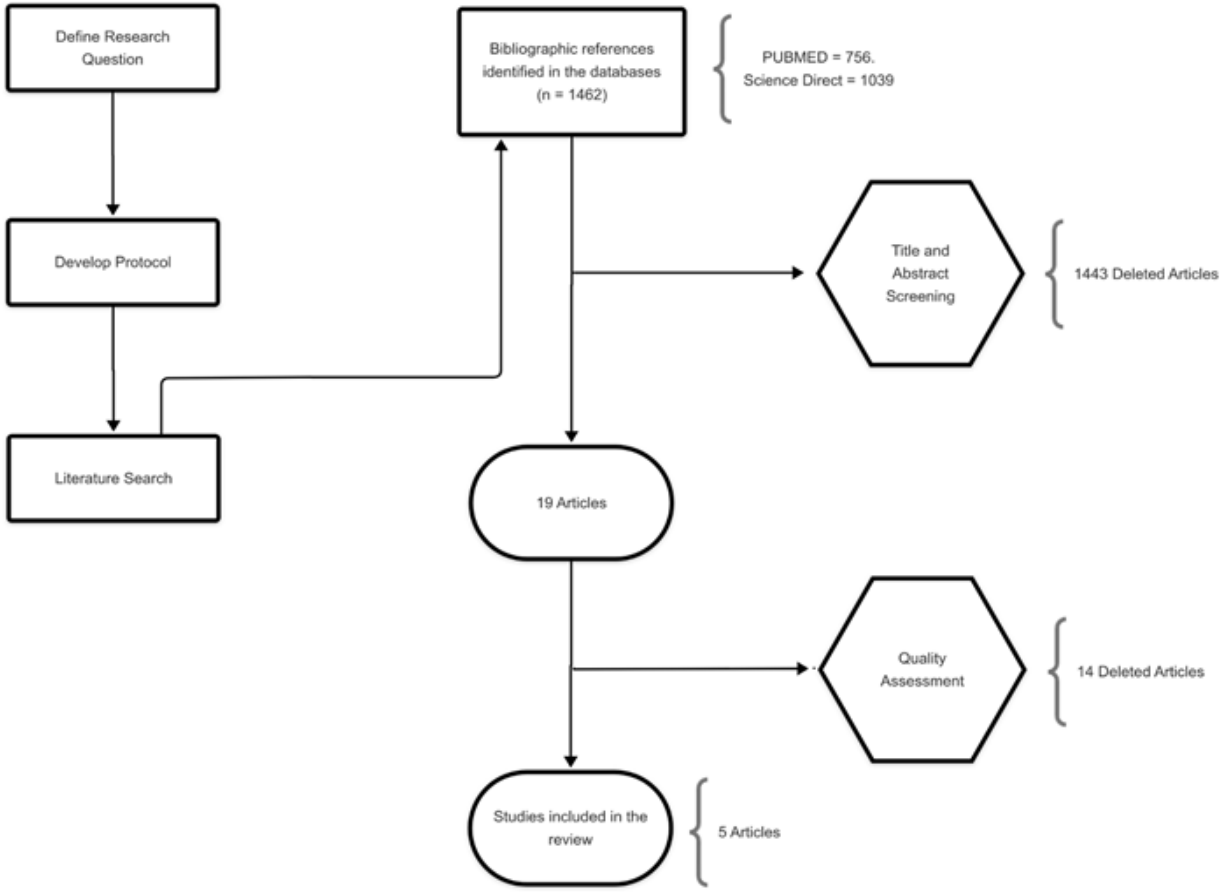


Table 1. The table below indicates the list of studies included in this review, showing the authors' names, study titles, period, diagnostic criteria, sample size, and study results.

Intervention	Period	Diagnostic criteria	Population	Main results	Refs.
Patients were given a histamine-rich meal to assess serum histamine (DAO) enzyme response.	DAO measurements were performed before and up to 4 hours after the food challenge.	The diagnosis of HIT was based on clinical history, exclusion of IgE-mediated allergies, and elimination diet followed by reintroduction to confirm symptoms.	Seven patients with suspected HIT and 10 healthy control individuals participated.	There was no significant change in mean DAO levels in patients after the histamine-rich meal. Only 1 of 10 control subjects reported symptoms, while 6 of 7 patients reported typical symptoms such as headache and gastrointestinal symptoms.	Clinical case study[30].
The study involved two dietary regimens: a low-histamine diet (LHD) and a conventional mixed diet (MXD). The main intervention was switching between these two diets, during which patients' serum DAO levels were measured. Patients also reported their symptoms throughout the study, with a focus on gastrointestinal and skin manifestations.	The study was conducted over six weeks. Patients were randomly assigned to start on one of the diets for three weeks, followed by a switch to the other diet for another three weeks.	The diagnosis of HIT was made based on the exclusion of IgE-mediated allergies, use of an elimination diet followed by reintroduction to confirm symptoms, and measurement of serum levels of (DAO).	The study population consisted of 18 patients diagnosed with (HIT) and 9 healthy control individuals. All participants were monitored throughout the dietary interventions, with DAO measurements and symptom records.	No significant differences in DAO levels were observed between the LHD and MXD diets. However, patients reported a significant reduction in gastrointestinal and skin symptoms during the LHD diet compared with the mixed diet, suggesting that a low-histamine diet may alleviate symptoms in patients with HIT, although DAO levels were not measurably altered.	Randomized clinical trial with crossover design[31].
The primary intervention was to measure histamine-rich enzyme levels (DAO) in a cohort of 1051 individuals to explore its association with HIT and other factors such as age, BMI, and food allergies. The study also involved assessing self-reported symptoms associated with the consumption of histamine-rich foods.	The study was based on data from the West Sweden Asthma Study, a longitudinal study that began in 2008. However, this particular study used data collected over 15 years, looking at cross-sectional associations between factors over that period.	The diagnosis of histamine intolerance was made based on clinical history for food hypersensitivity.	The sample consisted of 1051 individuals from various age groups, between 16 and 75 years old. A portion of the participants reported symptoms associated with the consumption of histamine-rich foods.	The study demonstrated that 44% of the individuals had DAO levels below the cutoff value considered normal (10 U/mL). Factors such as age and BMI showed a significant correlation with DAO activity: lower DAO levels were found in people with a BMI below 20 and in younger individuals. However, there was no direct correlation between DAO levels and symptoms reported after consumption of histamine-rich foods, suggesting that the use of DAO as a diagnostic marker should be reevaluated.	Cohort study based on a large random population sample[30].

Intervention	Period	Diagnostic criteria	Population	Main results	Refs.
Dietary treatment for HIT, which included a restrictive low-histamine diet and supplementation with the enzyme DAO. The goal was to reduce the levels of histamine-producing intestinal bacteria.	The study was conducted over 9 months. During this period, stool samples were collected at four time points: at the beginning (baseline), and after 2, 6 and 9 months of treatment.	The diagnosis of HIT was based on clinical criteria, considering the presence of at least two typical symptoms and negative results for specific food allergies by IgE.	Five women with iHIT participated, all with gastrointestinal symptoms and low levels of serum DAO activity. They were followed in a center specialized in the dietary management of iHIT.	Dietary treatment resulted in a significant reduction in the abundance of histamine-secreting bacteria, such as Proteus mirabilis, Raoultella, and the Morganella ceae family, after 2 and 6 months. In addition, there was an increase in the presence of beneficial bacteria, such as Roseburia spp., associated with intestinal health. Despite the overall improvement in symptoms, no patient achieved complete remission of symptoms.	Pilot study of original research[28].
Patients diagnosed with HIT took (DAO) capsules, which contained 0.3 mg of DAO, before meals, up to three times a day, for four weeks.	The study lasted a total of eight weeks, with the first four dedicated to DAO supplementation and the last four to monitoring without the use of the enzyme.	The diagnosis of HIT was made based on serum diamine oxidase (DAO) values less than 10 U/mL and the presence of at least two recurrent symptoms associated with the condition.	Twenty-eight patients (7 men and 21 women), with a mean age of 47.5 years, who presented with recurrent symptoms of HIT and serum DAO levels below 10 U/mL, were included.	During the DAO supplementation phase, all symptoms associated with HIT, including gastrointestinal, cardiovascular, respiratory and skin symptoms, showed significant improvement. At the end of the DAO-free follow-up period, some symptoms increased again, but were still at a lower level than at baseline.	Open intervention pilot study14.

DISCUSSION

HIT is a condition that was only discovered and defined in this century. Due to its nonspecific clinical manifestations (itching, rash, edema, abdominal distension after meals, abdominal pain and constipation, diarrhea, and others), HIT has often been misdiagnosed as other diseases in the past (e.g., food allergies, irritable bowel syndrome, other food intolerances, celiac disease, and urticaria)[14,32]. Furthermore, the presence of HIT is often underestimated, or its symptoms are misunderstood[28].

The diagnosis of HIT requires a detailed history and investigation with the available parameters. Tests such as the oral provocation test with liquid histamine have been proposed by some authors with contradictory results. However, this procedure is not common in clinical practice due to safety issues and the lack of standardized doses of histamine to be administered. In addition to the above, the test to assess fecal histamine levels is not highly recommended, as its accuracy is inconclusive due to interference from the intestinal microbiota, which produces histamine. Another available test is the measurement of DAO in the blood; however, there is no valid, fully accepted, specific, and sensitive measurement sufficient to serve as a diagnostic criterion. In addition, it is a very expensive test and is not covered by health insurance. Therefore, the diagnosis of HIT is currently achieved mainly clinically by excluding other conditions and by a beneficial response to a low-histamine diet. The latter is the main line of treatment for patients with HIT[33].

Furthermore, the use of antihistamines and exogenous DAO supplements have been

suggested as adjunctive treatments in patients who do not respond to a low-histamine diet. The goal of this treatment is to improve the digestion of dietary histamine in patients with HIT, as well as to prevent symptoms and resolve clinical manifestations associated with the disease. Therefore, individualized treatment of each patient should be conducted with individualized nutritional intervention, using a histamine-reducing diet and/or oral DAO supplementation[34].

Conceptually, a low-histamine diet should be based on the elimination of foods that contain histamine. Designing a diet with such characteristics is a challenge due to several disadvantages. One of them is the lack of consensus regarding histamine levels in foods, which can generate triggers in patients. These levels can vary between 5 to 50 mg/kg of body weight[22].

Therefore, different studies are being carried out to demonstrate the effectiveness of such treatments. A good example is the study by Georgios Rentzos and co-workers[33], where participants were subjected to two types of diets: a low-histamine diet (LHD) and a mixed-histamine diet (MXD). The LHD was structured to eliminate or reduce foods known to be high in histamine, such as fermented items, cured meats, aged cheeses, and canned foods. The LHD does not rigorously quantify the histamine content excluded in numerical terms, as histamine in foods varies widely. This approach was based on the guidelines of the European Food Safety Authority (EFSA), which identifies high-histamine foods, aiming to minimize the intake of the amine. The MXD, on the other hand, did not exclude these foods; instead, it required participants to consume at least two histamine-rich foods per day to ensure moderate exposure. In this way, it was possible to directly compare the response of symptoms to the reduction versus the inclusion of foods rich in histamine in a model that controlled nutritional and environmental variables throughout the weeks of intervention. This study confirms that a low-histamine diet is an effective strategy for reducing typical HIT symptoms, such as gastrointestinal discomfort and skin reactions. Although serum DAO levels did not show significant changes during LHD, patients reported significant improvement in symptoms. This finding suggests that, from a clinical perspective, LHD may be a practical and effective intervention to alleviate symptoms, even if the measurement of biomarkers such as DAO does not reflect this improvement. On the other hand, the article highlights that, although LHD is effective in reducing symptoms, the variation in DAO levels was not significant. It points to the need to investigate other approaches, such as DAO enzyme supplementation or probiotic use, which could be compared to LHD in future studies. It also reinforces the importance of a personalized approach, as the impact of diets can vary between patients, depending on comorbidities or individual sensitivity to histamine.

Furthermore, previous research has identified links between self-reported food intolerances and psychological symptoms, as well as their impact on quality of life. It is why approaches such as dietary restriction, while they may work for some patients, are not sufficient to solve the problem for all patients since they do not address the underlying causes of the disease, and treatments that offer greater long-term safety are needed. It is further complicated by the inadequate understanding of histamine interactions within broader pathological networks, hampering efforts to develop a targeted therapy for this disease alone[33].

The search for complementary treatment options is very necessary. The study of Odijk and co-workers34 raises questions about the efficacy of endogenous DAO in degrading dietary histamine in people with HIT since the intake of histamine-rich foods did not significantly increase serum DAO levels. In individuals with low levels of this enzyme, the inability to adequately process histamine leads to the accumulation of the compound and the emergence of clinical symptoms. These findings suggest that exogenous DAO supplementation may be a necessary intervention since the body's natural enzymatic response is not sufficient to deal with the histamine load in people with HIT. The research reinforces the importance of detailed anamnesis and symptom monitoring for the effective management of HIT since the isolated quantification of DAO does not reflect the symptomatology of patients. In the nutritional context, the study supports the use of histamine elimination diets and proposes DAO supplementation as a possible adjuvant, reducing the need for strict dietary restrictions and promoting a more flexible treatment. Future controlled and randomized studies are recommended to confirm these findings and better evaluate the role of DAO in improving the quality of life of patients, offering a more personalized and sustainable dietary approach for the treatment of HIT.

Studies have shown that diamine oxidase (DAO) supplementation is effective in reducing symptoms of histamine intolerance (HIT), including gastrointestinal, cardiovascular, respiratory, and dermatological symptoms35. This study revealed a significant improvement in the 22 symptoms analyzed during supplementation, although some returned shortly after treatment was discontinued. In addition to alleviating symptoms, DAO can aid in the recovery of the intestinal mucosa and reduce inflammation. This study reinforces the importance of combining a low-histamine diet and DAO supplementation as a safe and personalized therapeutic strategy for patients with HIT.

Another study that very well summarizes the two most widespread forms of treatment is the pilot study by Sánchez-Pérez and co-workers22, which indicates a significant improvement in the symptoms of women with HIT after implementing a low-histamine diet and diamine oxidase (DAO) supplementation. Over the 9 months, all participants reported a reduction in gastrointestinal symptoms, such as bloating, flatulence, and diarrhea, as well as improvements in symptoms, such as headache and dermatological discomfort. This reduction in symptoms was observed as early as the second month of dietary treatment. This study also demonstrated important changes in the composition of the intestinal microbiota.

There was a reduction in histamine-producing bacteria and an increase in beneficial bacteria associated with intestinal health. These microbial changes suggest that the low-histamine diet, combined with DAO supplementation, not only reduces the symptoms of HIT but may also promote a healthier intestinal environment, potentially reducing inflammation and improving mucosal integrity. Additionally, changes in the gut microbiota were observed, including a reduction in histamine-producing bacteria and an increase in beneficial microorganisms, suggesting that this approach not only alleviates symptoms but also improves gut health and reduces inflammation.

Therefore, it is understood that the treatment of HIT goes beyond drug therapy and is necessary in all spheres of life, such as adopting healthier habits, increasing fruit consumption, increasing fiber consumption, using specific probiotics to help modulate the intestinal microbiota and an anti-inflammatory dietary pattern that promotes the health of the intestinal barrier, in addition to a low-histamine diet and DAO supplementation. Understanding the pathophysiological mechanisms and treatment of HIT is essential to support future research in the area of nutrition on effective nutritional strategies for the management of this condition.

CONCLUSION

Based on the evidence analyzed in this integrative review, it is concluded that nutritional management of histamine intolerance (HIT) is a promising and indispensable strategy for alleviating symptoms associated with the condition. Low-histamine diets, diamine oxidase (DAO) supplementation, and individualized approaches are effective in improving gastrointestinal, dermatological, and systemic symptoms. Additionally, the relevance of interventions that consider the composition of the intestinal microbiota and promote the health of the intestinal barrier as adjuvants to traditional treatment is highlighted.

REFERENCES

1. Lomer MC. Review article: the aetiology, diagnosis, mechanisms and clinical evidence for food intolerance. Aliment Pharmacol Ther. 2015 Feb; 41(3): 262–275. doi: https://doi.org/10.1111/apt.13041.

2. Tuck CJ, Biesiekierski JR, Schmid-Grendelmeier P, Pohl D. Food Intolerances. Nutrients. 2019 Jul; 11(7): 1684. doi: https://doi.org/10.3390/nu11071684.

3. Silva CJ, Leite ID, Rodrigues JW, Almeida SP, Nóbrega BP, Sampaio JDR Filho. Analysis of lactose intolerance in students with suggestive symptoms of irritable bowel syndrome. Arq. Gastroenterol. 2019 Sep; 56(3): 304–311. doi: https://doi.org/10.1590/S0004-2803.201900000-57.

4. Soares RLS. Irritable bowel syndrome, food intolerance and non- celiac gluten sensitivity. a new clinical challenge. Arq. Gastroenterol. 2018 Oct-Dec. 55(4): 417–422. doi: https://doi.org/10.1590/S0004-2803.201800000-88.

5. Pasta A, Formisano E, Calabrese F, Torres, MC, Bodini G, Marabotto E, et al. Food intolerances, food allergies and IBS: Lights and shadows. Nutrients. 2024 Jan; 16(2):, 265. doi: https://doi.org/10.3390/nu16020265.

6. Kettner L,Seitl I, Fischer L. Evaluation of porcine diamine oxidase for the conversion of histamine in food-relevant amounts. J Food Sci. 2020 Mar; 85(3): 843–852. doi: https://doi.org/10.1111/1750-3841.15069.

7. Malsagova K, Stepanov A, Sinitsyna AA, Izotov A, Klyuchnikov MS, Kopylov AT, et al. Determination of specific igg to identify possible food intolerance in athletes using ELISA. Data. 2021, 6(11): 122. doi: https://doi.org/10.3390/data6110122.

8. Smolinska S, Jutel M, Crameri R, O'Mahony L. Histamine and Gut Mucosal immune regulation. Allergy. 2014; 69(3): 273–281. doi: https://doi.org/10.1111/all.12330.

9. Díaz-Reixa JP, Rodriguez MA, Breijo SM, Hernández JS, Casares ER, Alcalde TP, et al. Lower Urinary Tract Symptoms (LUTS) as a new clinical presentation of histamine intolerance: a prevalence study of genetic diamine oxidase deficiency. J Clin Med. 2023 Oct; 12 (21): 6870. doi: https://doi.org/10.3390/jcm12216870.

10. Enko D, Meinitzer A, Mangge H, Kriegshäuser G, Halwachs-Baumann G, Reininghaus EZ, et al. Concomitant prevalence of low serum diamine oxidase activity and carbohydrate malabsorption. Can J Gastroenterol Hepatol. 2016; 2016(1): 4893501. doi: https://doi.org/10.1155/2016/4893501.

11. Pinzer TC, Tietz E, Waldmann E, Schink M, Neurath MF, Zopf Y. Circadian profiling reveals higher histamine plasma levels and lower diamine oxidase serum activities in 24% of patients with suspected histamine intolerance compared to food allergy and controls. Allergy. 2018 Apr; 73(4): 949–957. doi: https://doi.org/10.1111/all.13361.

12. Manzotti G, Breda D, Di Gioacchino M, Burastero SE. serum diamine oxidase activity in patients with histamine intolerance. Int J Immunopathol Pharmacol. 2016 Mar; 29(1): 105–111. doi: https://doi.org/10.1177/0394632015617170.

13. Izquierdo-Casas J, Comas-Basté O, Latorre- Moratall ML. Lorente-Gascón M, Duelo A, et al. Diamine oxidase (DAO) supplement reduces headache in episodic migraine patients with DAO deficiency: a randomized double-blind trial. Clin Nutr. 2019 Feb; 38(1): 152–158. doi: https://doi.org/10.1016/j.clnu.2018.01.013.

14. Schnedl WJ, Schenk M, Lackner S, Enko D, Mangge H, Forster F. Diamine oxidase supplementation improves symptoms in patients with histamine intolerance. Food Sci Biotechnol. 2019 May; 28(6): 1779–1784. doi: https://doi.org/10.1007/s10068-019-00627-3.

15. Nebreda AD, Zappia CD, González AR, Sahores A, Sosa M, Burghi Vet al. Involvement of histamine H1 and H2 receptor inverse agonists in receptor's crossregulation. Eur J Pharmacol. 2019 Mar; 847: 42–52. doi: https://doi.org/10.1016/j.ejphar.2019.01.026.

16. Jutel M, Klunker S, Akdis M, Małolepszy J, Thomet OA, Żak-Nejmark T, et al. Histamine upregulates Th1 and downregulates Th2 responses due to different patterns of surface histamine 1 and 2 receptor expression. Int Arch Allergy. 2001 Jan-Mar; 124 (1–3): 190–192. doi: https://doi.org/10.1159/000053707.

17. Sim Y-B, Park S-H, Kim S-S, Kim C-H, Kim S-J, et al. The Modulatory Role of Spinally Located Histamine Receptors in the Regulation of the Blood Glucose Level in D-Glucose-Fed Mice. Korean J Physiol Pharmacol. 2014 Feb; 18(1): 41–46. doi: https://doi.org/10.4196/kjpp.2014.18.1.41.

18. Hasala, H.; Giembycz, M. A.; Janka-Junttila, M.; Moilanen, E.; Kankaanranta, H. Histamine reverses il-5-afforded human eosinophil survival by inducing apoptosis: pharmacological evidence for a novel mechanism of action of histamine. Pulm Pharmacol Ther. 2008; 21(1): 222–233. doi: https://doi.org/10.1016/j.pupt.2007.03.002.

19. Nguyen T, Shapiro DA, George SR, Setola V, Lee DK, Cheng R, et al. Discovery of a novel member of the histamine receptor family. Mol Pharmacol. 2001 Mar; 59(3): 427–433. doi: https://doi.org/10.1016/S0026-895X(24)12231-6.

20. Peng X, Wang S, Su K, Sun Y, Xu Z. Direct competitive immunoassay method for sensitive detection of the histamine in foods based on a MI-Cu-GMP nanozyme marker and molecularly imprinted biomimetic antibody. J Sci Food Agric. 2025 Jan; 105(2): 791–797. doi: https://doi.org/10.1002/jsfa.13869.

21. Young JA, Jiang X, Kirchhoff JR. Amperometric Detection of histamine with a pyrroloquinoline-quinone modified electrode. Electroanalysis. 2013 Jun; 25(7): 1589–1593. doi: https://doi.org/10.1002/elan.201300114.

22. Sánchez-Pérez S, Comas-Basté O, Veciana-Nogués MT, Latorre-Moratalla ML, Vidal-Carou MC. Low-histamine diets: is the exclusion of foods justified by their histamine content? Nutrients 2021 Apr; 13(5): 1395. doi: https://doi.org/10.3390/nu13051395.

23. Chung BY, Park SY, Byun YS, Son JH, Choi YW, Cho YS, et al. Effect of different cooking methods on histamine levels in selected foods. Ann Dermatol. 2017 Dec; 29(6): 706–714. doi: https://doi.org/10.5021/ad.2017.29.6.706.

24. Elmore BO, Bollinger JA, Dooley DM. Human kidney diamine oxidase: heterologous expression, purification, and characterization. J Biol Inorg Chem. 2002. 7(6): 565–579. doi: https://doi.org/10.1007/s00775-001-0331-1.

25. McGrath AP, Hilmer KM, Collyer CA, Shepard EM, Elmore BO, Brown DE, et al. Structure and Inhibition of Human Diamine Oxidase. Biochemistry. 2009 Oct; 48(41): 9810–9822. doi: https://doi.org/10.1021/bi9014192.

26. Schnedl WJ, Lackner S, Enko D, Schenk M, Holasek SJ, Mangge H. Evaluation of Symptoms and symptom combinations in histamine intolerance. Intest Res. 2019 Jul; 17(3): 427-433. doi: https://doi.org/10.5217/ir.2018.00152.

27. Biosse-Duplan M, Baroukh B, Dy M, Vernejoul M-C, Saffar J.-L. Histamine promotes osteoclastogenesis through the differential expression of histamine receptors on osteoclasts and osteoblasts. Am J Pathol. 2009 Apr; 174(4): 1426–1434. doi: https://doi.org/10.2353/ajpath.2009.080871.

28. Sánchez-Pérez S, Comas-Basté O, Duelo A, Veciana-Nogués MT, Berlanga M, Latorre-Moratalla ML, et al. Intestinal dysbiosis in patients with histamine intolerance. Nutrients. 2022 Apr; 14(9): 1774. doi: https://doi.org/10.3390/nu14091774.

29. Martin IS, Brachero S, Vilar EG. Histamine Intolerance and dietary management: a complete review. Allergol Immunopathol. 2016 Sep-Oct; 44(5): 475–483. doi: https://doi.org/10.1016/j.aller.2016.04.015.

30. Jochum C. Histamine intolerance: symptoms, diagnosis, and beyond. Nutrients. 2024 Apr; 16(8): 1219. doi: https://doi.org/10.3390/nu16081219.

31. Comas-Basté O, Sánchez-Pérez S, Veciana-Nogués MT, Latorre-Moratalla M, Vidal-Carou MC. Histamine intolerance: the current state of the art. Biomolecules 2020 Aug; 10(8): 1181. doi: https://doi.org/10.3390/biom10081181.

32. Arih K.; Đorđević N, Košnik M, Rijavec M. Evaluation of serum diamine oxidase as a diagnostic test for histamine intolerance. Nutrients. 2023 Oct; 15(19): 4246. doi: https://doi.org/10.3390/nu15194246.

33. Rentzos G, Weisheit A, Ekerljung L, van Odijk J. Measurement of diamine oxidase (DAO) during low-histamine or ordinary diet in patients with histamine intolerance. Eur J Clin Nutr. 2024 Aug; 78(8): 726–731. doi: https://doi.org/10.1038/s41430-024-01448-2.

34. van Odijk J, Weisheit A, Arvidsson M, Miron N, Nwaru B, Ekerljung L. The Use of DAO as a marker for histamine intolerance: measurements and determinants in a large random population-based survey. Nutrients. 2023. 15(13): 2887. doi: https://doi.org/10.3390/nu15132887.

35. Schnedl WJ, Enko D. Histamine intolerance originates in the gut. Nutrients. 2021 Apr; 13(4): 1262. doi: https://doi.org/10.3390/nu13041262.

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