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Dao blood test

Histamine intolerance can cause symptoms ranging from headaches and digestive issues to skin reactions. A DAO blood test measures diamine oxidase (DAO), an enzyme that breaks down histamine in the gut. Understanding this test and its results can help identify potential histamine metabolism issues affecting health. Role Of DAO In Histamine Breakdown Diamine oxidase (DAO) degrades extracellular histamine, particularly in the digestive tract. This process prevents histamine accumulation, which can lead to intolerance symptoms. DAO is produced in the intestinal mucosa and acts as a defense against dietary histamine from foods like aged cheeses, fermented products, and alcoholic beverages. Without sufficient DAO, histamine enters circulation and triggers adverse reactions. DAO breaks down histamine through oxidative deamination, converting it into imidazole acetaldehyde and then imidazole acetic acid. This prevents histamine from accumulating in the bloodstream. Unlike histamine-N-methyltransferase (HNMT), which works within cells to degrade histamine in tissues, DAO clears histamine from the gut and bloodstream. Insufficient DAO activity allows histamine to cross the intestinal barrier, contributing to symptoms like flushing, headaches, and gastrointestinal distress. Several factors influence DAO production, including genetics, gut health, and nutrient availability. Polymorphisms in the AOC1 gene, which encodes DAO, can reduce enzyme function, increasing susceptibility to histamine intolerance. Conditions such as inflammatory bowel disease (IBD) and celiac disease can impair DAO secretion, worsening symptoms. Nutrients like vitamin B6, copper, and zinc are necessary cofactors for DAO, and deficiencies in these micronutrients may lower enzyme activity. Uses Of A DAO Blood Test A DAO blood test assesses histamine metabolism and helps identify potential intolerance. It is particularly useful for individuals experiencing unexplained symptoms such as migraines, digestive disturbances, skin reactions, or respiratory discomfort that are not linked to allergies or other conditions. By measuring DAO levels, clinicians can determine whether impaired histamine breakdown contributes to symptoms and guide dietary or therapeutic interventions. Research has linked low DAO activity to histamine-related symptoms. A Clinical and Translational Allergy (2018) study found that individuals with chronic migraines often had reduced DAO levels. Similarly, gastrointestinal complaints like bloating, diarrhea, and nausea—often mistaken for irritable bowel syndrome (IBS)—have been associated with insufficient DAO activity. Identifying a deficiency through testing improves diagnostic accuracy and prevents unnecessary treatments. A DAO blood test can also guide dietary modifications. Patients with low DAO levels may benefit from a histamine-restricted diet, avoiding aged cheeses, fermented foods, processed meats, and alcohol. A Nutrients (2020) study found that individuals following a low-histamine diet experienced significant symptom relief. The test can also be used to monitor responses to DAO-enhancing supplementation. Nutrients such as vitamin B6, copper, and zinc support DAO function. A The American Journal of Clinical Nutrition (2021) study reported that patients with histamine intolerance who took these supplements showed increased DAO activity and symptom improvement. Tracking DAO levels before and after interventions helps evaluate their effectiveness. Sample Collection And Laboratory Methods DAO levels are measured through blood samples collected via venipuncture. Serum or plasma is used for analysis, with heparinized plasma preferred to maintain enzymatic activity. EDTA can chelate metal cofactors essential for DAO function, potentially affecting results. Samples must be processed quickly to prevent enzyme degradation. After centrifugation, plasma or serum is stored at -80°C to preserve DAO integrity. Enzyme-linked immunosorbent assays (ELISA) are the primary method for quantifying DAO levels, using antibodies that bind selectively to DAO to produce a measurable signal. Standardized protocols help ensure reliable results. Liquid chromatography-mass spectrometry (LC-MS) has been explored for DAO measurement but is less common due to cost and complexity. Some laboratories assess DAO activity indirectly by measuring histamine degradation rates, though this approach is less standardized. Interpreting Results DAO test results are reported in units of enzymatic activity per milliliter (U/mL). Levels above 10 U/mL indicate sufficient histamine metabolism, while readings below this suggest impaired activity. DAO levels between 3 and 10 U/mL may cause mild to moderate symptoms, while values below 3 U/mL are strongly associated with histamine intolerance. Interpreting results requires considering symptom severity alongside numerical values. Some individuals with borderline-low DAO remain asymptomatic, while others with moderate deficiencies experience pronounced reactions. Factors such as diet, medication use, and systemic inflammation can influence DAO activity, introducing variability. Repeat testing under controlled conditions may be necessary for a definitive assessment. Factors That May Influence DAO Levels DAO activity is affected by genetics, gut health, medications, and diet. Genetic variations in AOC1 can reduce DAO production, increasing histamine intolerance risk. Since DAO is synthesized in the intestinal mucosa, conditions like celiac disease, IBD, and chronic infections can impair production, allowing histamine accumulation. Certain medications, including NSAIDs, antihistamines, and some antidepressants, can inhibit DAO function or alter gut permeability. Alcohol further suppresses DAO activity, explaining why individuals with histamine intolerance often react strongly to red wine or beer. Nutritional deficiencies in vitamin B6, copper, and zinc can also lower DAO efficiency. Addressing these deficiencies through diet or supplementation may improve histamine metabolism. Conditions Linked To DAO Imbalances Low DAO levels are associated with conditions beyond histamine intolerance, affecting multiple systems. Chronic migraines, gastrointestinal disorders, and certain skin and neurological conditions have been linked to reduced DAO activity. Migraine sufferers, particularly those with food-triggered headaches, often have lower DAO activity. A The Journal of Headache and Pain (2017) study found that individuals with chronic migraines had reduced DAO levels. This suggests histamine accumulation may contribute to neurovascular changes involved in migraines. Gastrointestinal conditions such as IBS and small intestinal bacterial overgrowth (SIBO) have been connected to DAO deficiency. Since histamine affects gut motility and permeability, low DAO function can cause bloating, diarrhea, and abdominal pain, often mistaken for other digestive disorders. Skin conditions, including chronic urticaria and atopic dermatitis, may also be linked to impaired histamine breakdown. Patients with persistent skin reactions unresponsive to allergy treatments may benefit from DAO testing. Some neurological conditions, including ADHD and anxiety disorders, have been explored in relation to histamine metabolism. While research is ongoing, preliminary findings suggest histamine imbalances may influence neurotransmitter regulation, affecting mood and cognitive function. As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice . 2023 Oct 2;15(19):4246. doi: 10.3390/nu15194246 Histamine intolerance (HIT) is a clinical condition caused by decreased intestinal degradation of ingested histamine, primarily due to reduced enzyme diamine oxidase (DAO) activity, leading to histamine accumulation and causing various clinical manifestations. The measurement of serum DAO is commonly used as the main diagnostic test for HIT, although its diagnostic use is still uncertain. In this retrospective study, we aimed to assess the validity of DAO determination in patients with clinically suspected HIT. We measured DAO levels in 249 patients with suspected HIT and 50 healthy adult controls without HIT-related problems. Based on five clinical criteria, we divided patients into two groups: high (all five inclusion criteria; 41 patients) and low probability of HIT (≤4 inclusion criteria; 208 patients). Patients with a “high probability of HIT” had the lowest DAO (median: 8 U/mL, IQR: 6–10) in comparison to patients with a “low probability of HIT (median: 10 U/mL, IQR: 7–16, p = 0.0006) and healthy controls (median: 18 U/mL, IQR: 14–22, p < 0.0001). The specificity and sensitivity for DAO levels < 3/< 10 U/mL (manufacturer’s set cut-off) to discriminate between patients with ‘‘high probability of HIT’’ and healthy controls were 100%/92% and 2%/71%. On the other hand, the specificity and sensitivity to discriminate between patients with ‘‘high probability of HIT’’ and ‘‘low probability of HIT’’ were 97%/61% and 2%/71%, respectively. Serum DAO determination represents an additional asset to the diagnosis of HIT based on clinical evaluation and assessment, but the diagnosis should not solely rely on DAO measurements. Keywords: histamine intolerance, diamine oxidase, serum, diagnosis Histamine intolerance (HIT) is caused by decreased intestinal inactivation and degradation of ingested histamine. Histamine is a biogenic amine widely present in the human organism from endogenous and exogenous sources [1]. It is metabolised by two main enzymes: histamine-N-methyl transferase (HNMT) and diamine oxidase (DAO). HNMT is a cytosolic enzyme whose role is the degradation of endogenous histamine [2]. The main enzyme for the degradation of exogenous histamine is DAO, mainly expressed in epithelial cells of the small intestine, the placenta, the kidneys, and the liver [1,3,4,5]. It is a secretory enzyme stored in vesicular structures within epithelial cells and secreted into the bloodstream after a stimulation signal [3]. In normal conditions, DAO is present in the bloodstream in low concentrations; its basal concentration correlates with the level of intestinal integrity. Normal serum DAO concentrations are between 15 and 50 U/mL [6,7]. DAO is not involved only in the degradation of histamine but also in the metabolism of other biogenic amines, for which it has an even greater affinity [4]. Other biogenic amines present in food, such as monoamine tyramine, diamines putrescine and cadaverine, as well as polyamines spermine and spermidine, can affect DAO activity and consequently cause HIT symptoms. Biogenic amines contribute to histamine toxicity due to the saturation of degradation enzymes in the intestinal epithelium; therefore, the proposed diet for HIT consists of foods low in all biogenic amines, not just histamine [8,9]. Inflammatory intestine diseases, such as inflammatory bowel diseases, lactose intolerance, and celiac disease, can also impair DAO activity. Inflammation causes damage to the intestinal mucosa, leading to decreased DAO expression and activity, which can lead to secondary HIT. The severity of epithelium damage correlates with the level of diminished DAO activity [10]. Secondary HIT can also be caused by different medications that disrupt DAO activity, such as antibiotics, antimalarials, antituberculotics, H2 receptor antagonists, antihypertensives, analgesics, mucolytics, antidepressants, antiemetics, and muscle relaxants [1,11]. Decreased DAO activity leads to histamine accumulation, making HIT symptoms and signs appear. Various organic systems are affected due to the ubiquitous distribution of the four histamine receptors in different tissues and organs. We can divide symptoms into six groups: gastrointestinal (diarrhoea, constipation, vomiting, and abdominal pain), cardiovascular (hypotension and arrhythmias—tachycardia), cutaneous (pruritus, urticaria, flushing), respiratory (cough, bronchospasm, rhinitis, and sinusitis), ocular (conjunctivitis), and others (headache, heat waves, swollen joints, oral ulcers, and hand paraesthesia) [1,2,12]. Symptoms appear between 2 h and one day after the consumption of foods rich in biogenic amines [8]. The most frequent foodstuffs rich in biogenic amines are fermented food (sauerkraut), chocolate, alcoholic drinks (red wine and champagne), cheese (aged cheese), meat (cured meat), conserved food (especially fish), vegetables (tomato, aubergine, and spinach), fruits (pineapple, grapefruit, and kiwi), and nuts [12,13]. The concentration of histamine depends on the food preparation process and storage. Bacteria involved in lactic acid fermentation and food spoilage produce additional histamine. Impaired bacterial activity due to added NaCl results in a lower concentration of histamine. Lower pH, higher temperature, and prolonged food exposure to bacteria increase histamine concentration [2]. We can use bacteria that are not producing biogenic amines to prevent histamine accumulation in food fermentation. Another alternative, which is still in the research process, is adding a microorganism that expresses the enzyme DAO to degrade accumulated biogenic amines in food [1,2,14]. The diagnostic work-up of HIT is complex and challenging due to broad clinical manifestations involving multiple organs and a lack of information about in vitro and in vivo diagnostic tests for HIT. Currently, the diagnosis is mainly achieved clinically, consisting of, at the minimum, two typical symptoms: improvement of symptoms while following a low-biogenic amine diet and treatment with antihistamines [12]. The most studied and frequently used diagnostic test for HIT is the determination of serum DAO concentration and activity. Still, there are some doubts about whether the test is suitable for diagnosis. In addition to DAO determination, other tests were proposed for HIT diagnosis, such as the histamine 50-prick test, an intestinal biopsy, the histamine provocation test, or the histamine metabolomics in urine. Still, data about their usefulness as diagnostic tests is lacking [1]. Due to challenges in correctly recognising the disorder, the prevalence of HIT is frequently underestimated, predicted to be between 1 and 3%. The majority of patients (80%) with this condition are middle-aged [1,8,12]. The most efficient measure to control HIT symptoms is following a low-biogenic amine diet, which is beneficial for improving symptoms and increasing serum DAO levels and activity [15]. Exogenous DAO supplementation and treatment with antihistamines might also improve HIT symptoms. With improved serum DAO activity and a lower histamine concentration, patients can be less strict with a low-biogenic amine diet [14]. This retrospective study aimed to assess the validity of DAO determination in patients with clinically suspected HIT. We measured serum DAO levels in patients with suspected HIT with different degrees of symptoms and in healthy control subjects with no HIT-related problems. We assessed the optimal threshold and reference range that were most suitable to distinguish actual patients from controls. A total of 249 patients and 50 healthy adult controls were included in the final analysis of this retrospective study. We enrolled 300 consecutive adult patients with suspected HIT evaluated at the University Clinic of Respiratory and Allergic Diseases Golnik. DAO levels were measured in serum between November 2017 and December 2020. Based on clinical data collected from the hospital information system, we classified patients into distinct groups: ‘‘high probability of HIT’’ (41 patients) and ‘‘low probability of HIT’’ (208 patients). Twenty-one patients were excluded from the research due to insufficient clinical data and 30 due to secondary HIT (lactose intolerance/celiac disease). We enrolled 50 healthy adults without any HIT-related problems who were age- and sex-matched with the included patients. In the healthy adult control group, subjects with a history of food intolerances, IgE-mediated food allergies, celiac disease, and gastric acid hypersecretory states were also excluded. The study was conducted according to the Declaration of Helsinki. It was approved by the Slovenian National Medical Ethics Committee (approval number 0120-155/2021/3), and all patients gave their informed written consent. We classified patients based on five inclusion criteria: typical clinical manifestations (gastrointestinal, cardiovascular, cutaneous, respiratory, ocular, etc.), the appearance of symptoms after consumption of biogenic amine-rich food, the appearance of symptoms within 2 h to 1 day, improvement of symptoms while following a low-biogenic amine diet, and improvement of symptoms through treatment (with antihistamines or exogenous DAO supplementation). Patients who fulfilled all inclusion criteria were classified in the ‘‘high probability of HIT’’ group, and others who fulfilled 4 or fewer were classified in the ‘‘low probability of HIT’’ group. The serum DAO concentration was determined using a quantitative Enzyme-Linked ImmunoSorbent Assay ELISA and a set of reagents IDK DAO ELISA (Immunodiagnostik AG, Germany) in accordance with the manufacturer’s instructions. The reference ranges defined by the assay manufacturer were: 10 U/mL: low HIT probability. Statistical analysis was performed using IBM SPSS Statistics software version 25 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 9 (GraphPad Software, Boston, MA, USA). The distribution of DAO concentration was assessed using the Kolmogorov-Smirnov test of normality. Numeric data were presented with medians and interquartile ranges (IQR). Statistical significance between different groups was determined with the Mann-Whitney, Kruskal-Wallis, and Chi-square tests. Possible correlations between variables were determined with Pearson’s chi-squared test. p-values below 0.05 were considered significant. We evaluated the performance of the IDK DAO ELISA (Immunodiagnostik AG, Bensheim, Germany) test for the diagnosis of HIT using receiver operating characteristic (ROC) curve analysis. Among the 249 patients with suspected HIT (73% female; median age 47 years (IQR 38–61)) included in the final analysis, 41 (16%) were classified as “high probability of HIT” (81% female, median age 51 years (IQR 42–66)) and 208 (84%) as “low probability of HIT” (71% female, median age 47 years (IQR 37–60)) (Table 1). There were no differences in age and sex distribution between different groups (Table 1). Characteristics of the study group. All Patients(N = 249) ‘‘High Probability of HIT’’(N = 41) ‘‘Low Probability of HIT’’(N = 208) Healthy Adults(N = 50) p Value Age (years): median (IQR) 47 (38–61) 51 (42–66) 47 (37–60) 44 (36–55) 0.427 a Women: N (%) 181 (73) 33 (81) 148 (71) 37 (74) 0.672 b Men: N (%) 68 (27) 8 (19) 60 (29) 13 (26) DAO (U/mL): median (IQR) 10 (7–14) 8 (6–10) 10 (7– 16) 18 (14–22)