Histamine Intolerance

The clinical pattern of histamine intolerance (HIT) is defined as the exceeding of the individual histamine tolerance limit. Usually, this is caused by a lack of the histamine-degrading enzyme diamine oxidase (DAO). A decrease in activity of the second histamine-degrading enzyme histamine N-methyltransferase (HNMT) may lead to a worsening of symptoms. HIT may also manifest clinically if the organism is currently exposed to more histamine than it can degrade, despite normal DAO activity. Both a lack of DAO and an excessive exposure to histamine, can be detected with the help of laboratory diagnostic measures. In the case of proven lack of DAO, DNA testing is used to differentiate between primary and secondary causes. Furthermore, an activity-decreasing genetic HNMT variant can be detected.

Histamine – the most important vasoactive mediator.

Histamine is a biogenic amine, which is released by activated mast cells. Being a vasoactive mediator, it plays a dominating role in allergic diseases, such as Rhinitis allergica (hay fever), allergic bronchial asthma and urticaria (hives). Moreover, histamine is released in cases of pseudoallergies originating from food and histamine occurring during allergic reactions intermittently. This explains why, next to the main symptoms nausea, headache, hot flushes, and shortness of breath, primarily diarrhoea also occurs. Furthermore, eczema, rhinitis, episodes of urticaria, hypertension, colitis, and asthma have been observed. A lack of HNMT, on the contrary, rather has an impact on the breakdown of the comparably constant occurrence of intracellular endogenous histamine. Hence, a lack of HNMT leads rather to chronic forms of HIT, often affecting the nervous system. Main symptoms would be unrest, myoclonic twitches, insomnia, fatigue, vertigo, and states of anxiety.

HIT can induce food intolerances.

Histamine in food is formed primarily due to bacterial enzymes transforming histidine to histamine. Therefore, the longer the storage period, the higher the histamine concentration. Because of its stability, histamine can be destroyed through neither freezing nor heating. Due to bacteria being responsible for histamine formation, large concentrations of histamine can be found in微生物ally produced or fermented foods (cheese, sauerkraut, wine), as well as in protein-rich foods such as fish and meat, depending on the respective storage period. In the case of a decreased DAO activity, the consumption of foods that contain high concentrations of histamine can lead to the aforementioned intestinal and systemic reactions.

There are two histamine-degrading enzymes.

Diamine oxidase (DAO) is histamine’s most important degrading enzyme. DAO breaks down extracellular [free] histamine and is primarily produced by intestinal epithelial cells. If the activity of DAO is inhibited, histamine will accumulate in the blood. Histamine N-methyltransferase (HNMT), the second histamine-degrading enzyme, in contrast only breaks down intracellular histamine (primarily in liver, kidneys, bronchial mucosa and central nervous system). Due to this spatial and functional separation, a lack of these enzymes may lead to various symptoms or clinical pictures.

HIT Symptoms vary.

Since histamine receptors can be found throughout the entire body’s organ systems, HIT symptoms are very heterogeneous. Generally speaking, a histaminosis is caused by a lack of DAO. DAO breaks down both histamine originating from food and histamine occurring during allergic reactions intermittently. This explains why, next to the main symptoms nausea, headache, hot flushes, and shortness of breath, primarily diarrhoea also occurs. Furthermore, eczema, rhinitis, episodes of urticaria, hypertension, colitis, and asthma have been observed. A lack of HNMT, on the contrary, rather has an impact on the breakdown of the comparably constant occurrence of intracellular endogenous histamine. Hence, a lack of HNMT leads rather to chronic forms of HIT, often affecting the nervous system. Main symptoms would be unrest, myoclonic twitches, insomnia, fatigue, vertigo, and states of anxiety.

DAO activity and histamine concentration in blood are measurable.

DAO is continuously released into the bloodstream, and hence the activity of DAO in blood serum is a suitable marker for HIT diagnoses. Measuring the intracellular HNMT, which occurs primarily in the liver, is, on the contrary, not possible. Here, the detection of an activity-decreasing genetic HNMT variant is available. HIT is nevertheless not only caused by the insufficient breakdown of histamine. It may also manifest clinically when there is a histamine surplus that is currently not broken down sufficiently, even under normal DOA activity. Allergic diseases, such as hay fever, sensitisation towards mould, and elevated levels of mast cell activity are sources of additional histamine that accumulates with ingested histamine. In order to diagnose this type of transgression of the individual histamine tolerance limit, DAO activity should be analysed together with the histamine total in blood.

Do you have questions? Our serviceteam will be happy to support you: +49 (0)30 7701 01-220.
Genetic testing differs between primary and secondary lack of DAO

In order to avoid unnecessary lifelong dieting, whether the existing lack of DAO is caused by a genetic primary, or a secondary condition, must be analysed. The result will then have an impact on the treatment. A primary lack of DAO is accompanied by decreased DAO activity, due to genetic variations (polymorphisms). Patients with proven decreased DAO activity in blood and corresponding clinical symptoms ought to receive genetic screening, in order to differentiate between a genetic or secondary, and therefore causally treatable and reversible, form of histamine intolerance.

Therapeutic consequences of reduced DAO activity

When decreased DAO activity or significantly elevated histamine levels are proven, foods rich in histamine have to be avoided. In the case of a secondary HIT, meaning a lack of DAO in an individual who is otherwise healthy, treatment differs according to the cause. When it is identified that dietary intolerance is due to DAO deficiency, a mere symptomatic therapy through the prescription of H1 receptor antagonists should only be a temporary measure.

Known DAO-inhibiting drugs:

- Acetylsalicylic acid
- Cimetidine
- Morphine
- Alcuronium
- Clavulanic acid
- Pancuroniumbromide
- Alprenolol
- Cyclophosphamide
- Pentamidine
- Ambroxol
- Dihydralachazine
- Pethidine
- Amiloride
- Dobutamine
- Prilocaine
- Aminophylline
- Isoniazid
- Propafenone
- Amitriptyline
- Metamizole
- Sodiumthiopental
- Cefotiam
- Metoclopramide
- Thiamine
- Cefuroxime
- Meronidazole
- Verapamil
- Chloroquine

HNMT can have genetic causes or show decreased activity due to environmental exposures.

While Symptoms of a lack of DAO are often periodical, symptoms of HNMT deficiency occur immediately after meals, for example. In the case of dysfunctional HNMT, especially the brain, bronchial mucosa and liver are affected. Patients with normal DAO levels, who experience only slow deterioration (days) of symptoms after dietary errors and in which after dieting properly symptoms abate only slowly, may suffer from HNMT deficiency. Testing the activity of this intracellular enzyme is not possible. Diagnostics are done via testing for a genetic variant (C314T) that decreases HNMT activity by 30-50%. This genetic variant is associated with histamine-related diseases, such as asthma and atopic dermatitis. Additionally, drugs are known to be HNMT inhibitors. Amodiaquine, Metoprine, Tacrine and Diphenhydramine (H1-antihistamine!) block HNMT’s histamine binding sites. Carriers of C314T-polymorphisms should hence avoid HNMT blockers as well as histamine liberators.

Material

- DAO activity: 2 ml whole blood or serum
- Histamine tot.: in blood: 10 ml heparin blood

For both tests, postal dispatch over 24 hrs at room temperature is possible, but courier dispatch is recommended.

DAO genetic testing and/or HNMT genetic testing:

2 ml EDTA blood

For genetic testing, the patient’s declaration of consent is mandatory. Transport to the laboratory is not time-sensitive and can be sent by mail.

Billing

With corresponding indication, tests are billable to statutory and private health insurance companies.