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Clinical study of the relationship between histamine intolerance and variants in the AOC1-ABP1 Gene

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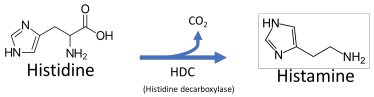
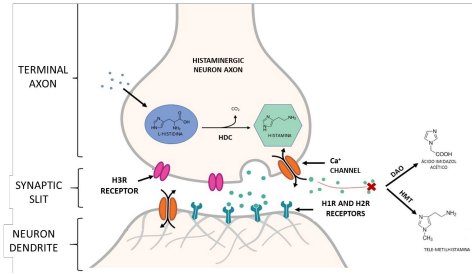
Introduction

Histamine is a biogenic amine with many essential physiological activities. However, its deregulation and accumulation can cause a multitude of pathologies such as histamine intolerance [(1)].



There are two enzymes involved in the metabolism of histamine: histamine N-methyltransferase (HNMT) is responsible for degrading histamine inside cells [(2)]. **Diamine-oxidase (DAO)** is the other enzyme involved in the degradation of histamine, mainly exogenous histamine, ingested with the diet.



Histamine synthesis and release in the axons of histaminergic neurons.

H1R, H2R and H3R: histamine receptors. DAO: diamino oxidase. HMT: histamine methyl transfersa. HDC: Lhistidine decarboxylase. Modified from [(2)]Diez-García & Garzón 2017.

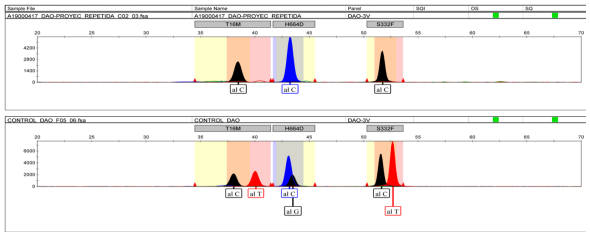
The deficiency of DAO activity could be one of the main causes of **histamine intolerance**, an alteration in homeostasis that is caused by a reduced intestinal degradation of histamine, with the consequent increase in its plasma levels. **Variants in AOC1/ABP1** gene, coding DAO enzyme, have been associated with a **reduction in DAO activity** and accumulation of histamine [(3)].

Objective

The present study aims to demonstrate the negative effect that the variants **rs10156191, rs1049742 and rs1049793** have on DAO plasma activity in Caucasian male patients with clinical manifestations associated with histamine intolerance.

Methods

We analyzed **78 white male patients with a clinical manifestation associated with histamine intolerance.** Variants analyzed were genotyped by multiplex SNPE (Single Nucleotide Primer Extension).

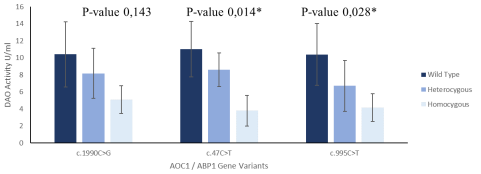


Electropherogram resulting from the capillary electrophoresis of the multiplex SNPE reaction.

Visualized using the GeneMapper® 5 v3.2.1 software. Sample A corresponds to a triple homozygous patient for the 3 variants analyzed. Sample B corresponds to a triple heterozygous patient for the three variants analyzed. T16M is named to variant c.47C> T, H664D to c.1990C> G and S332F to c.995C> T.

Results

The variants rs10156191 and rs1049742 reduce significantly DAO plasma activity.



Average DAO activity in plasma.

Analiced in 78 patients presenting clinical symptoms associated with Histaminosis for each variant studied in the AOC1 gene. Error bars indicate standard deviation.

Factors such as worsening symptoms after eating a diet rich in histamine or NSAID-type drugs (non-steroidal anti-inflammatory) are associated with a greater number of alternative alleles in the SNVs analyzed, and reduced DAO plasma activity.

Conclusions

These results show **the predictive value** of this genetic study in patients who have a clinical manifestation associated with histamine intolerance.

References

[(1)] Ohtsu H. Pathophysiologic role of histamine: evidence clarified by histidine decarboxylasegene knockout mice. Int Arch Allergy Immunol. 2012; 158: 2-6

[(2)] Díez-García A & Garzón M. Regulación de las fases del ciclo vigilia-sueño por la histamina. Rev Neurol 2017; 64: 267-277.

[(3)] Mauro-Martin S, Brachero S, Garicano-Vilar E. Histamine intolerance and dietary management: A complete Review. Allergologia et Immunopathologia 2016; 44 (5): 475-483.

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