



Clinical nutrition

Histamine-reduced diet and increase of serum diamine oxidase correlating to diet compliance in histamine intolerance

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Abstract

Diagnosis of histamine intolerance (HIT) has been based on low serum diamine oxidase (DAO) values, functional gastrointestinal disorders and improvement of symptoms with a histamine-reduced diet (HRD). In a retrospective analysis of outpatients' charts we identified 101 patients with HIT. After a median of 13 months, a questionnaire was distributed to the patients so that they could be classified into four diet-compliance groups. Calculated with all 101 patients we found an increase of serum DAO values due to a HRD. In the 63 patients that completed the questionnaire, we found that 50 patients had improvement of symptoms or no continuing symptoms. A significant increase of serum DAO levels was found in the patients with strict and occasional diet compliance. Therefore, we demonstrate that a HRD is not only improving symptoms in HIT, but is causing an increase in serum DAO values that correlates with the degree of diet compliance.

Introduction

The diagnosis of histamine intolerance (HIT) is clinically challenging because HIT is causing various clinical symptoms mainly after ingestion of histamine-rich food and, HIT is thought to be due to a reduced activity of the enzyme diamine oxidase (DAO) [1]. Although serum DAO values are not established to reflect gastrointestinal DAO activity, the diagnosis of HIT can be supported with measurements of serum DAO [2]. We demonstrate that a histamine-reduced diet (HRD) is not only improving symptoms, but is increasing serum DAO correlating with the degree of diet compliance.

Methods

In an analysis of outpatients' charts at a follow-up visit after a median of 13 months (range: 2–44) we identified 101 white patients, who presented with functional abdominal complaints and a serum DAO value < 10 U/mL at the first visit (male/female = 34/67, median age = 53, and range: 20–81 years). They received written information about HIT and a registered dietician helped to develop an individually tailored HRD according to the literature [3–5].

At the follow-up visit a questionnaire was distributed to patients so that they could be classified into four diet-compliance groups, which were determined as strict (HRD every day), occasional (HRD 3 days a week), rare (HRD once a week), and no diet (Fig. 1). Seventy-two patients (71.3%) returned their anonymous information and, 29 patients (28.7%) did not answer the questionnaire. Additionally, they were asked about the development of symptoms and 2 groups were created: 50 patients with an improvement or who were free of symptoms and 13 patients with unchanged symptoms since diagnosis (Fig. 2).

Determinations of DAO in serum were made with a radio extraction assay (Sciotec Diagnostic Technologies, Tulln, Austria). For individual diagnosis of single or combined food intolerance/malabsorption, all of the patients were examined for and did not show lactose intolerance, fructose malabsorption, *Helicobacter pylori* infection or celiac disease [6]. All patients >50 years old presented no pathology

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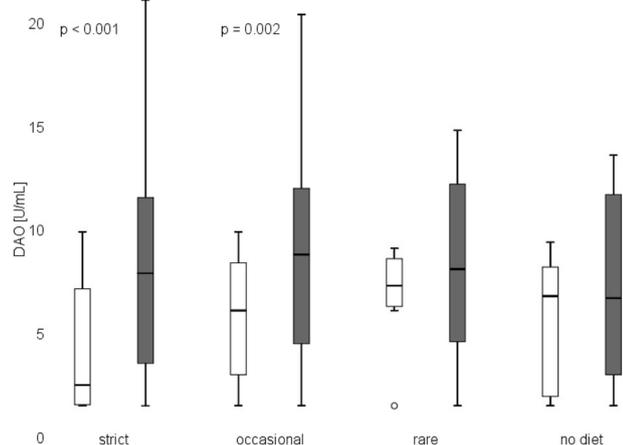


Fig. 1 Boxplots of serum DAO values at first visit and at follow-up visit after a HRD, divided into diet compliance groups. □ at first visit ■ at the follow-up visit

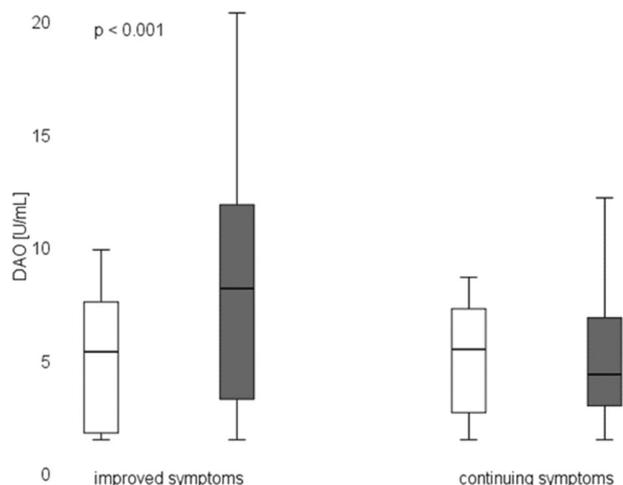


Fig. 2 Boxplots of serum DAO values of 63 patients at first visit and at the follow-up visit after following a HRD with improved and with continuing symptoms. None of the patients with strict diet compliance indicated continuing symptoms. The diet compliance groups occasional, rare and no diet are contained in both symptom groups. □ at first visit ■ at the follow-up visit

in screening by colonoscopy. Body mass index and routine laboratory data did not change from first to control visits.

Statistical analysis was performed with SPSS version 23.0 (IBM, Paris, France). Shapiro–Wilk test revealed that the data were not normally distributed. Data analysis were performed with the nonparametric Wilcoxon signed-rank test for related samples. The Kruskal–Wallis test for the duration of histamine-reduced dieting time was used. To compare the distribution of the compliance groups over the observation period four time groups were created and the chi-squared test was performed. The study was approved by the Ethical Committee of the Johannes Kepler University in Linz, Austria.

Results

In all, 101 included patients the median of serum DAO values increased significantly from 5.8 U/mL (range: 1.5–9.9) to 7.5 U/mL (range: 1.5–25.3) after initiating the HRD ($p < 0.001$). Of the 101 patients 66 demonstrated an increase in DAO values (65%), 8 had unchanged DAO (8%) and 27 had a decrease in DAO (27%). A significant increase of DAO was found in the 27 with strict and 29 patients with occasional compliance (Fig. 1). The groups with rare and no compliance (9 and 7 patients, respectively) did not show significant changes in DAO ($p = 0.401$ and $p = 0.345$). The patients with strict compliance had the highest increase in DAO from a median of 2.5 to 7.9 U/mL. Subgroup analysis of 29 patients, who did not return their questionnaires, showed an increase of median DAO from 5.6 to 6.3 U/mL ($p = 0.022$).

Sixty-three patients reported their symptomatology after initiating a HRD, 50 of these indicated improvement of symptoms (79%). Of these 50 patients, 33 also had an increase in DAO (52%), 6 reported improved symptoms even though their DAO was the same in the first and the follow-up visits (10%), and 11 reported improved symptoms but their DAO decreased (17%).

Combining the DAO values of all 50 patients reporting symptom improvement after following the HRD, there was a significant increase of DAO from median 5.4 U/mL (range: 1.5–9.9) to 8.2 U/mL (range: 1.5–20.4), whereas DAO in 13 patients with continuing symptoms slightly decreased ($p = 0.701$) (Fig. 2). Of the 27 patients with strict diet compliance, 21 reported their symptomatology, 12 of these patients were symptom-free and nine reported symptom improvement due to following the HRD.

Evaluating the DAO values of 101 patients based on time periods following the HRD, all except the time group >18 months, showed a significant increase of serum DAO (<7 months $p < 0.023$, from 8 to 12 months $p < 0.020$, 13–18 months $p < 0.001$, and >18 months $p < 0.067$). However, this time group >18 months had the highest DAO at the first visit.

The Kruskal–Wallis test did not reveal significant differences in dieting time duration between the compliance groups. Comparing the distribution of diet compliance groups within the time periods using the chi-squared test, no difference was found.

Discussion

The clinical diagnosis of HIT is challenging due to complex symptoms and the involvement of numerous organs [7]. However, DAO is the primary enzyme required for the degradation of ingested histamine and is synthesized by apical enterocytes located in the intestinal villi [8].

Based on the diagnosis of HIT a HRD may be developed to treat to the individual symptomatology by reducing the ingestion of histamine-containing foods [2, 9]. This aims to exclude sources that are high in histamine, which include aged, fermented foods and beverages. The list of foods with high histamine content is long and contains a variety of foods, including fruits, vegetables, seasonings, and fish, many of which may have high histamine content as fresh and/or frozen, smoked, and canned products [4]. Additionally, the histamine content in food varies considerably depending on storage time and processing [5]. Certain foods, food additives, preservatives, and medications may support the release of histamine or inhibit enzymes needed to metabolize histamine [6]. Additionally, diet recommendations should take into account the foods that are locally available [10]. A HRD is useful, simple and inexpensive to reduce HIT related symptoms [9] and we here show symptom improvement in 79% and an increase of DAO in 52% of patients with HIT.

Conclusions

We demonstrate that a HRD is not only improving symptoms but is causing an increase in serum DAO values that correlates with the degree of diet compliance. Parts of this study were used by Dr. Verena Malcher to fulfill the requirements for obtaining the degree “Dr. med.” at Medical University in Graz, Austria.

Compliance with ethical standards

Conflict of interest Wolfgang J. Schnedl received speaking honoraria from Sciotec. Remaining authors declare no conflict of interest.

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