Allergo J Int (2020) 29:93–96
https://doi.org/10.1007/s40629-020-00125-7

Dietary implications in acetylsalicylic acid intolerance

Statement by the Food Allergy Working Group of the German Society for Allergology and Clinical Immunology (DGAKI)

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Received: 13 November 2019 / Accepted: 5 December 2019 / Published online: 11 May 2020

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Summary
Background Acetylsalicylic acid (ASA) may cause difficult-to-treat symptoms of the airways, skin, or gastrointestinal tract in hypersensitive patients. Due to the chemical relationship between salicylic acid and ASA, a role of a low-salicylate diet has been discussed.
Methods This review evaluates whether low salicylate diets are meaningful from an allergological or nutritional–physiological perspective.
Results The body's arachidonic acid metabolism plays a crucial role in the pathogenesis of ASA intolerance. Despite their chemical affinity, ASA and salicylic acid affect the arachidonic pathway differently. The intake of salicylic acid with food is low compared to therapeutic doses of ASA. There is increasing evidence that protective effects of a high fruit and vegetables diet is related in part to the intake of salicylates. In salicylate-low diets, fruit and vegetables are reduced, harboring the risk of an insufficient diet and malnutrition.
Conclusion Dietary therapy in ASA-intolerant patients is not recommended.

Keywords Salicylic acid · ASA · COX · Anti-inflammatory diet · Aspirin

Abbreviations

AERD	Aspirin-exacerbated respiratory disease
ASA	Acetylsalicylic acid
COX	Cyclooxygenase
DAMP	Damage-associated molecular pattern molecule
HMGB1	Human high mobility group box 1
NSAID	Non-steroidal anti-inflammatory drugs

Intolerance to acetylsalicylic acid (ASA) is based on a non-IgE-mediated hypersensitivity reaction. In hypersensitive patients, ASA can trigger symptoms of the skin/mucosa as well as the respiratory and gastrointestinal tract. In its most severe form, ASA intolerance can manifest in the airways as Samter's triad. The latter refers to a combined onset of ASA intolerance (intolerance to non-steroidal anti-inflammatory drugs [NSAID]), nasal polyps and bronchial asthma [1, 2]. The term aspirin-exacerbated respiratory disease (AERD) is more recently used for the respiratory form of disease. ASA intolerance is caused by alterations in the arachidonic acid metabolism, followed by an imbalance of eicosanoids formed from arachidonic acid [3].

Oxidative degradation of arachidonic acids takes place through two enzyme systems: the lipoxygenase and the cyclooxygenase (COX) pathway. ASA mainly effects the COX-1 degradation pathway and causes impaired immunological homeostasis with an increased production of pro-inflammatory eiconsoids, primarily leukotrienes and prostaglandin E_2, and can promote an accumulation of immunological effector cells (mast cells and eosinophils among others) [4–6].

ASA is a chemical compound that does not occur naturally. Nevertheless, some foods contain its parent substance, salicylic acid, a phenolic acid belonging to the secondary plant substances and possessing anti-inflammatory properties [7]. The relationship between the two substances has given rise to a discussion on whether the natural salicylic acid content in food should be taken into account for difficult-to-treat ASA intolerance. However, there is no scientific evidence as yet that dietary salicylic acid is relevant in the pathogenesis of ASA intolerance [8].

The main sources of salicylates in foods include alcoholic beverages, herbs, spices, fruit, fruit juice, tomato-based sauces and vegetables. Therefore, a reduction of the dietary intake of salicylates is necessarily associated with a high carbohydrate and protein diet. The increased consumption of cereals and cereal products, milk and milk products, meat, eggs, and fish that often results from this dietary change harbors a clear risk of an insufficient diet.

As such, a reduction in dietary salicylates would have a significant impact on the basic diet, an impact that cannot be justified from the perspective of nutritional science. The salicylate intake in a regular diet is around 3–5 mg/day, which is comparable with the intake of other secondary plant substances [9, 10]. Despite the good bioavailability of dietary salicylates, serum levels are far below the triggering threshold dose shown in studies for ASA [11, 12]. Moreover, even at pharmacological concentrations, salicylic acid has no direct effect on either COX-1 or COX-2, in contrast to ASA [13]. However, by binding to a newly identified protein (human high mobility group box 1 [HMGB1]) belonging to the group of alarmins (damage-associated molecular pattern molecule [DAMP]), salicylic acid and its derivatives can indirectly affect COX-2 and also inhibit the production of pro-inflammatory cytokines [14].

The intake of salicylates as part of a diet high in fruit and vegetables is rather associated with major health benefits. Efforts are underway to include salicylic acid as an essential vitamin: "vitamin S" [13–20].

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Conclusion

The recommendation to reduce dietary salicylates to treat ASA intolerance has no pathophysiological background. In contrast, such a reduction poses the risk of dysnutrition. Nutritional therapy should aim for a diet high in vegetables. This ensures the supply of antioxidants, trace elements, as well as secondary plant and mineral substances. An increased intake of eicosapentaenoic acid and docosahexaenoic acid in fish (oil) at the same time as reducing the intake of arachidonic acid can have a favorable effect on fat intake.

Funding Open Access funding provided by Projekt DEAL.

Conflict of interest J. Kleine-Tebbe has received grants and/or honoraria from AllergenOnline (Nebraska, USA), Allergy Therapeutics, Allergopharma, ALK-Abelló, AstraZeneca, personal fees from Bencard, Dr. Pfleger, GSK, HAL Allergy, InfectoPharm, LETI, Lofarma, Novartis, Merck US, Sanofi Genentech, Stallergenes-Greer, Springer International Publishers, ThermoFisher Scientific, and Thieme Publishers, Germany. He has also received support (non-financial) from the American Academy of Allergy Asthma and Immunology, the European Academy of Allergy and Clinical Immunology, and the WHO/IUIS Allergen nomenclature subcommittee. He has received honoraria and support (non-financial) from the German Society for Allergology and Clinical Immunology—all outside the present work. S. Lau has received honoraria from ALK, DBV, Sanofi Genzyme and Allergopharma, outside the present work. U. Lepp has received honoraria from Chiesi, ALK-Abelló, Bencard Allergie, Novartis Pharma GmbH, Grifols, MedaPharm, and CGC-Cramer, outside the present work. S. Müller has received honoraria from Novartis GmbH and Bencard GmbH, outside the present work. R. Treudler has received grants and/or honoraria from Sanofi-Genzyme, ALK-Abelló, Takeda, Novartis, and the Hautnetz Leipzig. R. Treudler also declares a scientific collaboration with and financial compensation from the Fraunhofer-IZI Leipzig—all outside the present work. M. Worm has received lecture fees, was active as a consultant and member of the advisory board, and has given lectures for the following companies: Mylan Germany, ALK-Abelló Arzneimittel, Allergopharma GmbH & Co. KG, HAL Allergie, Stallergenes GmbH, and Bencard Allergie, outside the present work. T. Zuberbier declares that he is active for the WHO initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA), the German Society for Allergology and Clinical Immunology (DGAKI), the European Centre for Allergy Research Foundation (ECARF), the Global Allergy and Asthma European Network (GA2LEN), the Committee on Allergy Diagnosis and Molecular Allergology, and the World Allergy Organization (WAO). S. Dölle-Bierke, S. Plank-Habibi, C. Schäfer, B. Ahrens, B. Ballmer-Weber, K. Beyer, K. Blümchen, I. Huttegger, U. Jappe, L. Lange, V. Mahler, J. Saloga, S. Schnadt, Z. Szepfalusi, A. Wassmann-Otto, T. Werfel and I. Reese declare that they have no competing interests.

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