

Lowered Glutathione-Peroxidase Activity in Asthmatic Patients with Food and Aspirin Intolerance

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In analogy with findings from animal experiments, people with low glutathione-peroxidase (GSH-Px) activity could be expected to have altered sensitivities to effects of drugs, chemicals and possibly food. We have investigated GSH-Px activity in 12 patients with intrinsic asthma and food and aspirin intolerance. Ten of the 12 patients had very low or low GSH-Px activity and the frequency of low GSH-Px activity in this group was statistically significant ($P < 0.001$) compared with the control material of age- and sex-matched healthy individuals. Our finding of lowered GSH-Px activity in patients with aspirin intolerance may indicate the involvement of hitherto unknown mechanisms in the pathogenesis of asthmatic disorders.

Key words: aspirin intolerance; GSH-Px.

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The asthmatic reaction is brought about by an initial release of mediators, several of which are arachidonic acid metabolites (2, 3, 4). The cellular metabolism of arachidonic acid involves the generation of free radicals in the step-wise production of endoperoxides with bronchoconstrictive properties (5, 11). The healthy cell is protected from the hazards of oxidative stress by several factors functioning as active, free radical scavengers and among which glutathione peroxidase (GSH-Px) may be one of the most important (1). GSH-Px apparently also exerts a regulating influence on the cyclooxygenase enzyme in the arachidonate pathway.

Acetylsalicylic acid (ASA) irreversibly inhibits the platelet cyclooxygenase (10). We have earlier found that platelets from asthmatic patients with aspirin-intolerance have a significantly lowered capacity to accumulate and retain serotonin (9). The present pilot study of the GSH-Px activity in blood was part of an

ongoing investigation of the platelet function in asthmatic patients with symptoms of food intolerance.

MATERIAL AND METHODS

Twelve patients who had experienced reactions of food intolerance participated in the study. In three of the patients, low titers of specific allergens were found. These were considered to be without any major importance for their asthma. Eleven of the patients were ASA-intolerant (Table 1). The patients and control subjects had taken no drugs for 10 days prior to the investigation. The GSH-Px activity was determined with a modified semi-quantitative method previously described by Kelly (6). Briefly, the assay was performed as follows:

Capillary blood (25 µl) was placed on a filter paper (Munktel 3 A 390 700), and the blood spots allowed to dry for 1 h. (Pending analyses the paper analyses spots can be stored at 4-8°C

for up to 4 weeks). Discs of 5 mm were punched from the spots with a plexiglas instrument. The discs were put in a plastic tray and soaked in 0.20 ml of phosphatecyanide buffer (10 ml 1 M potassiumdihydrogen phosphate + 2 M potassiumhydroxide pH 7.0, 2 ml 0.2 mM EDTA, 1 ml 0.4 M sodiumazide, 2 ml 0.91 mM tri-potassiumferricyanide + 2.0 mM sodiumcyanide and 14 ml demineralized water). The redox reaction was started by the addition of excess amounts of glutathione reductase (GSSG-R, 100 mg), and nicotineamide adenine dinucleotide phosphate (NADPH, 1.0 ml 2 mM) and 25 μ l 5 mM hydrogen peroxide. Aliquots of 2 μ l were removed from the reaction mixture after 1, 3, 6, 9 and 12 min and applied on filter paper. The spots were dried at 60°C and the intensity of the fluorescence was observed in a longwave UV-light. A filter paper disc soaked in buffer-redox reaction mixture without blood was used as control. A measure of the peroxidase activity was achieved by denoting the defluorescence time. A short defluorescence time < 1 min thus indicates a very high GSH-Px activity, while a very low GSH-Px activity is indicated by a defluorescence time of > 6 min.

RESULTS

The frequency and distribution of very low, low, medium, high and very high GSH-Px

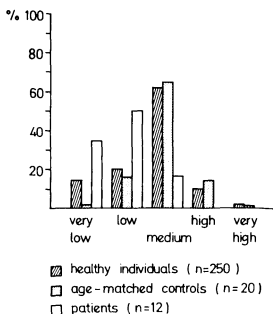


Fig. 1. The frequency and distribution of different degrees of GSH-Px activity in healthy individuals, age-matched controls and asthmatic patients with ASA intolerance. (The statistical significance of the frequency and distribution of GSH-Px activity in patients were assayed with Fisher's exact 2×2 table, $P < 0.001$).

activity in blood in 250 healthy individuals and 20 age- and sex-matched controls, randomly selected from this material, are shown in Fig. 1. As can be seen, the frequency of very low and low GSH-Px activity in blood in the patient group was significantly higher ($P < 0.001$, Fisher's exact test for 2×2 table).

DISCUSSION

GSH-Px is a selenoenzyme and normal GSH-Px activity requires selenium. Low GSH-Px activity may thus reflect a general selenium deficiency. Animal studies have shown that low selenium status is associated with decreased activity of drug metabolizing enzymes, altered responses to chemical stresses, and poor food utilization (1). In analogy with animal responses to selenium deficiency, people with low selenium status, and consequently low GSH-Px activity, could be expected to have altered sensitivities to effects of drugs, chemicals

Table 1

Age, sex, aspirin intolerance and degree of GSH-Px activity in 12 patients with intrinsic asthma

Age (years)	Sex	Aspirin intolerance	GSH-Px activity
27	F	+	low
30	F	-	very low
48	F	+	medium
45	F	+	very low
44	F	+	very low
53	F	+	low
43	M	+	low
34	F	+	very low
29	M	+	medium
35	F	+	low
54	M	+	low
31	F	+	low

and possibly food. The frequency of aspirin hypersensitivity is much higher in asthmatic subjects than in the healthy population, and the probability of an asthmatic patient developing aspirin hypersensitivity is high (12).

The maintenance of an adequate cellular level of GSH-Px activity is probably of importance. Very low levels of selenium intake and subsequent decreased GSH-Px activity have been shown to cause Keshan and Kaschin-Bec disease (7, 8). In what way the arachidonic acid metabolism is affected at low levels of GSH-Px activity is largely unknown. Our finding of lowered GSH-Px activity in asthmatic patients with food intolerance and aspirin-induced asthma may indicate, however, an involvement of hitherto unknown mechanisms in the pathogenesis of asthmatic disorders.

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