ANNALES
UNIVERSITATIS MARIAE CURIE-SKŁODOWSKA
LUBLIN-POLONIA
VOL. LIII, 13 SECTIO DD 1998

I Klinika Chirurgii AM w Lublinie oraz Katedra Patofizjologii AR w Lublinie

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Glutathione S-transferase, alcohol dehydrogenase and aldehyde reductase activities in human stomach adenocarcinoma

Aktywność S-transferazy glutanianu, dehydrogenezy alkoholowej i reduktazy aldehydów w gruczolakorakach żołądka u człowieka

4-Hydroxynonenal (4-HNE) is thought to be one of the most important toxic aldehyde products of lipid peroxidation (2). In tumors, there are variations in the production of 4-HNE as well as in other lipid peroxidation products and also variations in enzyme-metabolising aldehydes, derived from lipid peroxidation or from other sources (9, 10).

Lipid peroxidation generally decreases, whereas the activity of some of these enzymes increases. The reason for this behaviour is unknown at present; it could perhaps be due to the tumor cells defense mechanism against toxic agents.

The best-known enzymes which metabolize aldehydes are aldehyde dehydrogenase, aldehyde reductase and glutathione-S-transferase.

In tumors, the behaviour of aldehyde dehydrogenase is well known. It increases in several hepatoma cell lines and during hepatocarcinogenesis (4 , 5). The increase in aldehyde dehydrogenase activity is much more evident in the cytosol fraction than in other cell fractions and seems to be directly correlated to the degree of cell deviation. Less is known about the reductive enzymes and glutathione-S-transferase.

The aim of this paper was to characterize the behaviour of alcohol dehydrogenase, aldehyde reductase and glutathione-S-transferase in human stomach adenocarcinoma.

MATERIALS AND METHODS

The tumor from patients with diagnosed stomach adenocarcinoma and adjacent normal-appeared tissues were obtained during surgery and rinsed in ice-cold medium containing 70 mM sucrose, 220 mM mannitol, and 20 mM Tris - EGTA.

To isolate the cytosol fractions, homogenates from each tissue were prepared in a Potter - Elvehjem homogenizer with four strokes of tightly fitting pestle, in a volume of above mentioned medium corresponding to 2.5 times their weight and diluted to 20% (w/v) with the same medium. The diluted homogenates were centrifuged at 105,000 g for 60 min and the supernatants thus obtained were used as cytosol.

The activities of alcohol dehydrogenase and aldehyde reductase were measured by monitoring changes at 340 nm with a dual Specord UV - VIS spectrophotometer. The assay mixture (1 ml) contained 0.1 mM NADH or NADPH, 200 mM potassium phosphate buffer (pH = 7.0), 0.1 mM benzaldehyde and an appropriate amount of the enzyme.

The activity of glutathione-S-transferase was measured using the method of A l i n et al. (1). Proteins were determined according to L o w r y et al. (7).

The statistical analysis comprised calculation of the standard deviation of the means and variance analysis followed by the t-Student test for unpaired data to determine significant differences from the means.

RESULTS

Figure 1 shows that alcohol dehydrogenase remained unchanged in tumor tissue. Figure 2 refers to the specific activities of aldehyde reductase. It can be seen that the activity of this enzyme increased in malignant tissue about twice as compared

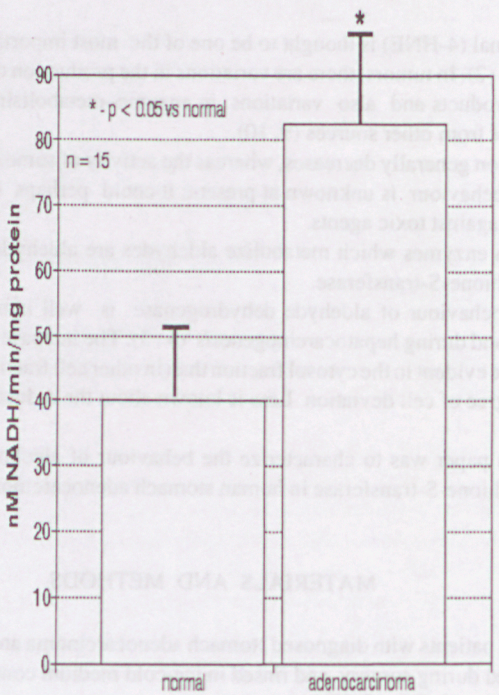

Fig. 1. Alcohol dehydrogenase activity in stomach tissue

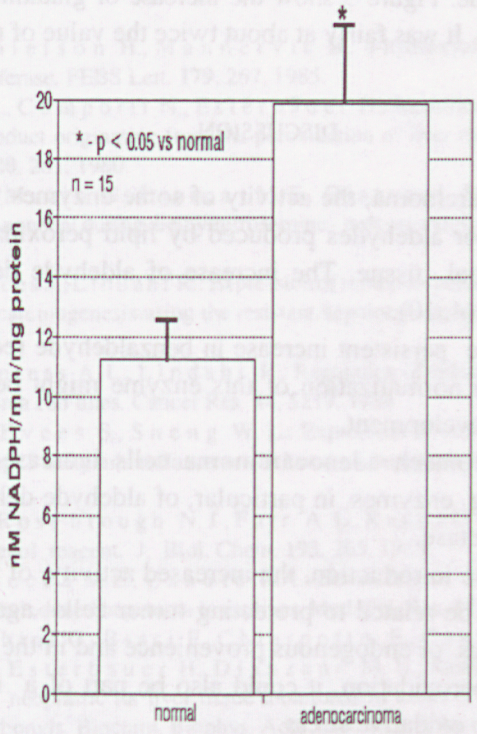

Fig. 2. Aldehyde reductase activity in stomach tissue

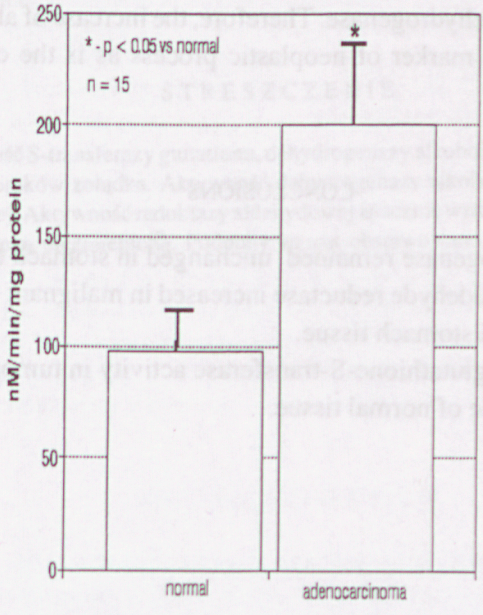

Fig. 3. Glutathione S-transferase activity in stomach tissue

to normal stomach tissue. Figure 3 show the increase of glutathione-S- transferase activity in tumor tissue. It was fairly at about twice the value of normal tissue.

DISCUSSION

In stomach adenocarcinoma, the activity of some enzymes which metabolize exogenous aldehydes or aldehydes produced by lipid peroxidation increases in comparison with normal tissue. The increase of aldehyde dehydrogenase has already been reported (4, 10).

The reason for the persistent increase in benzaldehyde reductase activity is not clear; the delay in normalization of this enzyme might be due to its slight importance in tumor development.

Nevertheless in stomach adenocarcinoma cells increase their content of aldehyde-metabolizing enzymes, in particular, of aldehyde dehydrogenase (6, 8, 10) and aldehyde reductase.

As mentioned in the introduction, the increased activity of aldehyde-metabolizing enzymes might be related to protecting tumor cells against highly toxic aldehydes of exogenous or endogenous provenience and in the case of aldehydes produced from lipid peroxidation, it could also be part of a more generalized response of the cells to oxidative stress.

In conclusion, the increase of aldehyde reductase and glutathione-S-transferase is important in the defense mechanism of stomach adenocarcinoma cells, as is the increase in aldehyde dehydrogenase. Therefore, the increase of aldehyde reductase could be considered a marker of neoplastic process as is the case for aldehyde dehydrogenase (3, 6).

CONCLUSIONS

1. Alcohol dehydrogenase remained unchanged in stomach tumor tissue.
2. The activity of aldehyde reductase increased in malignant tissue about twice as compared to normal stomach tissue.
3. The increase of glutathione-S-transferase activity in tumor tissue was fairly at about twice the value of normal tissue.

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STRESZCZENIE

Badano aktywność S-transferazy glutationu, dehydrogenazy alkoholowej i reduktazy aldehydów w tkance gruczolakoraków żołądka. Aktywność dehydrogenazy alkoholowej nie ulega zmianie w tkance nowotworowej. Aktywność reduktazy aldehydowej znacznie wzrasta w tkance nowotworowej w porównaniu z tkanką niezmienioną. Podobny wzrost obserwowano w przypadku S-transferazy glutationu.