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Plasma Content Variation and Correlation of Plasmalogen and GIS, TC, and TPL in Gastric Carcinoma Patients: A Comparative Study

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Statistical Analysis C
Data Interpretation D
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Background: We studied the variation in plasma content of plasmalogen and ganglioside, total cholesterol (TC), and total phospholipid (TPL) in gastric carcinoma patients. The plasma plasmalogen levels were determined according to the vinyl ester bond method.

Material/Methods: Plasma ganglioside level was determined according to the method of Sevennerholm. The total cholesterol and total phospholipid were determined by routine methods.

Results: The plasma plasmalogen level of gastric carcinoma patients was significantly higher than in the control (normal) group, and the difference was markedly significant ($p < 0.01$). The plasma total sialic acid (TSA) and lipid-bound sialic acid (LSA) of gastric carcinoma patients were higher than those of the normal control group ($p < 0.05$). The total cholesterol content was higher than those in the normal control group ($p < 0.02$), but the total phospholipid content was lower than in the normal control group and the difference was markedly significant ($p < 0.05$). In the gastric carcinoma patients group, the plasmalogen and ganglioside-TSA levels were positively correlated ($r = 0.01$, $P < 0.01$). Plasmalogen and total cholesterol were also positively correlated ($r = 0.82$, $P < 0.01$), and plasmalogen and total phospholipid were negatively correlated ($r = -0.82$, $p < 0.01$).

Conclusions: In gastric carcinoma patients, the plasma plasmalogen content was significantly elevated and was positively correlated with elevated level of gangliosides and total cholesterol, but it was negatively correlated with level of total phospholipids.

MeSH Keywords: **Amnion • Cholestasis • Plasmalogens • Stomach Neoplasms**

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Background

Plasmalogen are phospholipids possessing a vinyl ether bond at the S_{n-1} position instead of the usual ester bond found in diacylphospholipids. They are widely distributed in membranes but their role is not well understood. However, their physico-chemical properties suggest that they play an important role as membrane constituents. For example, they are involved in signal transduction due to their high level of arachidonic acid at S_{n-2} and may also act as endogenous antioxidants. The reactivity of vinyl may be linked with control of reactive oxygen species [1,2].

Gangliosides (GIS) are important lipid constituents of cell membranes. Chemically, gangliosides are glycosphingolipids containing sialic acid (SA) and are particularly abundant in the membrane microdomain; they are considered as highly organized units with a variety of specific functions [3,4]. Gangliosides are involved in many significant cellular processes, such as cell growth, proliferation, differentiation, and oncogenic transformation [5,6].

In this study we compared plasma content variation and the correlation of plasmalogen, membrane glycolipid, total cholesterol, and total phospholipid in gastric carcinoma patients.

Material and Methods

Material

The clinical diagnosis of 29 gastric carcinoma patients was reliably made by final pathohistological analysis of postoperative tumor tissue.

Methods

Plasma plasmalogen content was determined according to the method for determining vinyl ester bond [7], including the standard curve of inorganic phosphorus, the extract of total lipid, alkali hydrolysis-produced plasmalogen, and the determination of vinyl ester bond of plasmalogen according to iodine disappearance. The gangliosides were determined according to the method of Sevennerholm, including the extraction of plasma

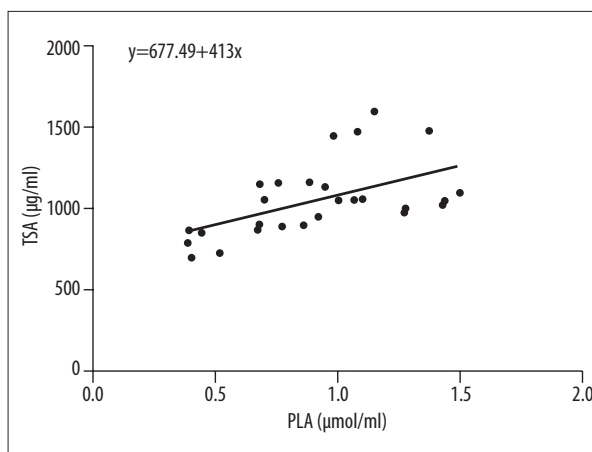


Figure 1. Correlation of PLA and TSA levels in gastric carcinoma patients ($r=0.61$, $t=4.00$, $p<0.01$).

ganglioside using chloroform, methanol, and water in a final volume ratio of 1:1:0.8 (C:M:W, v/v/v). Higher phases containing gangliosides were collected and air-dried and the obtained dry ganglioside extract was finally purified by dialysis and filtration. Purified ganglioside was used for quantitative analysis by resorcinol spectrometry method. The total cholesterol and total phospholipid were determined by routine method.

Results

The plasmalogen content compared with ganglioside TSA and LSA of gastric carcinoma patients is shown in Table 1.

Comparison of plasmalogens and TSA and LSA content of gastric carcinoma patients.

Table 1 shows that plasma plasmalogen level of gastric carcinoma was significantly higher than in the normal control group ($p<0.01$), while the ganglioside lipid-bound sialic acid (LSA) and total sialic acid (TSA) levels were higher than in the normal control group ($p<0.05$).

Figure 1 shows the straight-line regression correlation of plasmalogen (PLA) and total sialic acid (TSA) content in gastric carcinoma patients.

Table 1. The plasmalogen content compared with ganglioside TSA and LSA of gastric carcinoma patients.

Group	N	Plasmalogen (µmol/ml)	TSA (µg/ml)	LSA (µg/ml)
Gastric carcinoma	29	0.93±0.34	1122.09±118.89	364.77±69.59
Normal control	30	0.64±0.26	934.04±132.91	266.45±57.43
P		<0.01	<0.05	<0.05

Table 2. Comparison of plasma plasmalogen, TPL, and TC content in gastric carcinoma patients.

Group	N	Plasmalogen (umol/ml)	TPL (umol/ml)	TC (umol/ml)
Gastric carcinoma	29	0.93±0.34	2.72±0.59	4.96±1.64
Normal control	30	0.69±0.26	3.02±0.34	3.89±0.69
P		<0.01	<0.05	<0.02

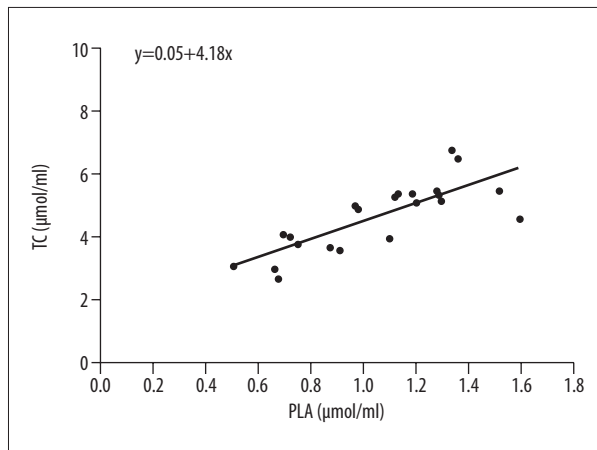


Figure 2. Correlation of PLA and TC levels in gastric carcinoma patients ($r=0.82$, $t=7.44$, $P<0.01$).

Figure 1 shows that, in gastric carcinoma patients, plasma plasmalogen content was positively correlated with elevation of TSA ($r=0.61$).

Table 2 compares the plasma plasmalogen with total phospholipid and total cholesterol content of gastric carcinoma patients.

Table 2 shows that the plasma plasmalogen content of gastric carcinoma patients was significantly higher than in the normal control group ($p<0.01$), and the plasma TPL content of gastric carcinoma patients was lower than in the normal control group ($p<0.05$). The plasma TC content of gastric carcinoma patients was significantly higher than in the normal control group ($p<0.02$).

Figure 2 shows the straight-line regression correlation of plasmalogen (PLA) and total cholesterol (TC) in gastric carcinoma patients.

Figure 2 shows that, in gastric carcinoma patients, plasma plasmalogen content was positively correlated with TC.

Figure 3 shows the straight-line regression correlation of plasmalogen (PLA) and total phospholipid (TPL) in gastric carcinoma patients.

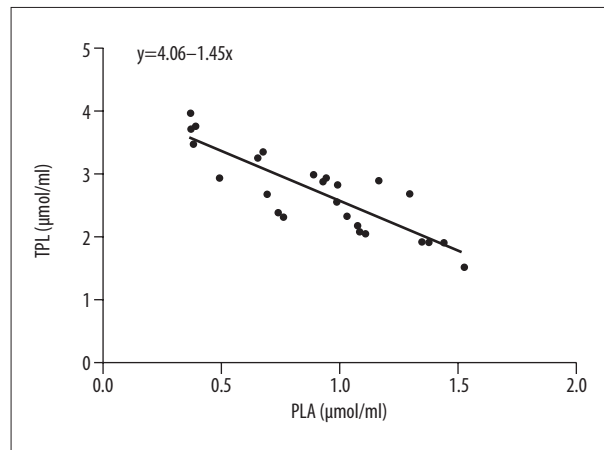


Figure 3. Correlation of PLA and TPL levels in gastric carcinoma patients ($r=-0.82$, $t=7.44$, $p<0.01$).

Figure 3 shows that the plasma plasmalogen content in gastric carcinoma patients was negatively associated with TPL ($r=-0.82$).

Discussion

Cells contain a membrane system composed of membrane protein and membrane lipid. Membrane lipid includes phospholipid, glycolipid, cholesterol, and cholesterol ester. Phospholipid (specific glycerophosphatide) is the main lipid in biological membranes, accounting for about 70% of total membrane lipids [8].

Plasmalogen exists in mammals and contains vinyl ether bond glycerol phospholipids such as plasmenyl ethanolamine, plasmenyl choline, and plasmenyl serine. Plasmenyl ethanolamine is the major storage depot of arachidonic acid [9]. Arachidonic acid is metabolized to eicosanoids and the lysoplasmenylcholine can activate myocardial cAMP-dependent protein kinase. This suggests that lysoplasmenylcholine serves as a second messenger in signal transduction [10]. Concerning the relationship of plasmalogen and tumors, Merchant et al. reported that the plasmalogen levels of 16 malignant and 11 non-malignant human colon specimens were analyzed using a chloroform-methanol analytical reagent in conjunction with 31p magnetic resonance spectroscopy (MRS). Results show a statistically significant elevation in the relative concentration of lysophosphatidylcholine and phosphatidylcholine plasmalogen.

Sphingomyelin was lower in malignant tissues [11,12]. In our research, the plasma plasmalogen level of gastric carcinoma was significantly higher than in the normal control group ($p < 0.01$). Although many studies consistently reported higher concentration of plasma plasmalogen in cancer patients, the mechanism is not yet understood. The mechanism may be that the key plasmalogen enzyme, phosphodihydroxyacetone acyltransferase, strengthens activity [13]. Phosphatidyl cytonucleotide transferase activity can strengthen synthesis of plasmalogen [8]. However, expression of plasmalogen phospholipase C and phospholipids D was reduced [14].

The term “gangliosides” includes GIS-containing sialic acid, which consists of lipid-bound sialic acid (LSA) and total sialic acid (TSA). We found that the plasma LSA and TSA levels of gastric carcinoma patients was significantly higher than in the normal control group ($p < 0.05$). The mechanism by which ganglioside levels are increased in gastric carcinoma patients may be the sudden change of the chromatin cancer gene due to physical, chemical, or biological factors [15]. The increase in glycolipid glycosyltransferases activity strengthens membrane glycolipid biosynthesis [16]. It has been reported that

tumor cells may shed their gangliosides into the circulation, resulting in higher ganglioside concentration in gastric carcinoma patients [17].

Gastric carcinoma patients have high total cholesterol and low phospholipids, as well as abundant low-density lipoprotein, plasmalogen, and cholesterol. High cholesterol levels may increase plasmalogen levels. A nearly 2-fold increase in the cholesterol synthetic key enzyme HMGCoA-reductase activity in liver tumor cells was reported [18]. In 14 meningioma patients, plasmalogen content rose because of plasmenyl ethanolamine increase, and the decreased total phospholipids levels caused lower levels of phosphatidylcholine, lysophosphatidylcholine, and phosphatidylinositol [19].

Conclusions

In gastric carcinoma patients, the plasma plasmalogen content was significantly elevated; it was positively correlated with elevation of gangliosides and total cholesterol, and was negatively correlated with total phospholipids levels.

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