The importance of plasma sialic acid as a tumor marker in gastric cancers

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This study was performed in General Surgery and Biochemistry Departments of Medical School of Erciyes University 30 patients with gastric cancer, 30 patients with duodenal ulcer and 30 patients with hernia were included in the study. Preoperative plasma total sialic acid (TSA) and lipid-bound sialic acid (LSA) levels were recorded higher in the cases of cancer than in the cases of peptic ulcer and hernia ($p<0.05$). In addition, the plasma TSA and LSA levels were higher in peptic ulcer patients than in control patients ($p<0.05$). The plasma TSA and LSA levels of cancer patients decreased significantly ($p<0.05$) whereas the plasma TSA and LSA levels of ulcer and control group were not affected after the operation ($p>0.05$). The plasma TSA and LSA levels of cancer patients increased in parallel to tumor stages and this increase was statistically significant ($p<0.05$). [Turk J Med Res 1993; 12(1):29-33]

Key **Words:** Sialic acid, Gastric cancer, Duodenal ulcer

Cancer is the second cause of early death and economical loss after the diseases of cardiovascular system (1). Epidemiologic, histopathologic, etiologic, diagnostic and therapeutic studies are being performed for cancer (1).

The gastrointestinal system (GIS) cancers are the second mostly seen cancer group in Turkey (2). The gastric cancer is one of the mostly seen GIS cancers (2,3).

The primary treatment method of GIS cancers is surgery. It can be combined with the other treatment modalities or used alone (1,3,4). Early diagnosis is important for an effective treatment. GIS malignancies are usually diagnosed at late stages, because of localization of GIS organs, and the similarity of the symptoms with those of other diseases (5,6).

Definite diagnosis of cancer is put only by histopathologic examination (3,7). In recent years the studies on biologic agents called Tumor Markers (TM) have increased dramatically. The sialic acid (SA), a tumor marker, was firstly defined by Blix in 1936 (8). It is a large group of ketones and composed of nine carbon atoms (9,10). SA is not found in free form, 85-90% of it is bound to protein (PSA) and 10-15% is bound to lipids (LSA) (11,12,13).

SA levels are normal in healthy people, but it incerases in a variety of diseases, especially those with cell damage (12,14,15,16).

The relation of SA with cancer has been noted and studied since 1960 (17,18,19).

We planned this study to evaluate the place of serum SA as a TM in the gastric cancer cases and to solve the problems in differential diagnosis.

MATERIALS AND METHODS

Thirty patients (12 women, 18 men) operated because of the gastric cancer in General Surgery Department of Erciyes University Medical School between February 1, 1991 and October 1, 1991 were included in this study. Thirty patients operated for duodenal ulcer and 30 patients for inguinal hernia were taken as the control group.

The patients were left hungry for 8 hours before surgery. 10 cc blood was taken in the morning and another 10 cc blood was taken 7th postoperative day. The blood samples were centrifuged and the serum parts were kept at -20°C in the deep freezer until the examination day.

The serum TSA and LSA levels were determined by the modified Katopodis technique (20).

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Tabid. The preoperative and postoperative plasma TSA and LSA levels (mg/dL) of gastric cancer patients

Groups	n	TSA (X±SE)	LSA (X±SE)
Preop.	30	139.24±4.66	42.26±2.31
Postop.	30	122.34±3.74	33.64±1.80

Table 2. The preoperative and postoperative plasma TSA and LSA levels (mg/dL) of ulcer patients

Groups	n	TSA (X±SE)	LSA (X±SE)
Preop	30	102.94±2.07	23.41±1.58
Postop	30	99.09±1.95	21.84±1.54

In the statistical analysis student t test and variance analysis were used for the comparisons within the groups and the comparisons between the groups respectively.

RESULTS

The plasma TSA and LSA levels of gastric cancer patients are shown in Table 1. TSA and LSA levels were significantly decreased postoperatively ($p<0.01$). The postoperative LSA level was 27% of TSA level whereas the preoperative LSA level was 35% of TSA level.

The plasma TSA and LSA levels of duodenal ulcer patients are given in Table 2. There was no significant difference between the preoperative and postoperative TSA and LSA levels in these patients ($p>0.05$). LSA level was 22% of TSA level in Ihe ulcer patients.

The plasma TSA and LSA levels of the control group are given in Table 3. Likewise, in this group there was no significant difference between the preoperative and postoperative TSA and LSA levels ($p>0.05$). LSA level of the control group was 11% of TSA level.

The preoperative and postoperative plasma TSA and LSA levels of 20 gastric cancer patients with resection are given in Table 4. The TSA and LSA levels were significantly decreased after resection ($p<0.05$).

The preoperative and postoperative plasma TSA and LSA levels of patients according to stages in the cancer group are shown in Table 5. The plasma TSA and LSA levels of cancer patients significantly increased in parallel to tumor stages ($p<0.05$).

DISCUSSION

The probability of an increase in the serum glycoproteins of the cancer patients has been assumed since 1957 (21). It was noted that the tumor cells had enzymes synthesizing different glycoproteins composed of a lot of SA (21-24).

Carter and Martin examined the SA levels in the serum samples of the normal people and the patients with different diseases in 1961. They defined an increase in rheumatoid artritls and amyloidosis (14).

Macbeth and Behesi found that the plasma carbohydrates bound to plasma proteins increased in malign diseases in 1962. They recorded that the corbohydrates such as glucose, galactose, SA and fucose increased in disease states, but SA and fucose especially increased in every disease showing degeneration in the tissues like malignant involvement. They found SA higher than normal in all of the malignancies except the early stage breast cancer (20).

Later in several studies it was found that the TSA and LSA started to increase patients with cancer at early stages (17,18,22,25-28). In some studies an increase in SA level was recorded in benign diseases such as infections, inflammatory conditions and those leading to cell damage, but this increase was not as high as in the cancer patients. Therefore this increase does not show the presence of a tumor (28-31).

SA was studied very mostly in GIS cancers although it is a general TM. Significant increase in SA levels were recorded in GIS cancers (32-36), but it was also found to increase in the benign pathologies of the GIS (37).

In our study the preoperative and postoperative plasma TSA levels of gastric cancer patients were

Table 3. The preoperative and postoperative plasma TSA and LSA levels (mg/dL) of the control group

Groups	n	TSA (X±SE)	LSA (X±SE)
Preop	30	82.06±2.38	9.01 ±0.38
Postop	30	80.79±2.19	9.07±0.37

Table 4. The plasma TSA and LSA levels (mg/dL) of the gastric cancer patients with resection

Groups	n	TSA (X+SE)	LSA (X±SE)
Preop	20	133.6±5.77	41.26±3.27
Postop	20	115.75±4.30	32.96+1.70

Table 5. The preoperative and' postoperative plasma TSA and LSA levels (mg/dL) of patients according to stages in the cancer group

		Preop Plasma	
STAGE	n	TSA (X±SE)	LSA (X±SE)
Ⅱ	9	117.28±3.9	37.88±2.35
Ⅲ	13	145.72±4.30	41.29±3.99
IV	8	153.41 ±10.44	48.77±4.69

measured higher than those of the control group. The preoperative and postoperative LSA levels of these patients were recorded significantly higher than those of the control group too. LSA is 11% of TSA in the normal individuals. The preoperative LSA is 35% of TSA and the postoperative LSA is 27% of TSA in the cancer patients. These findings are correlated with the studies recording more increase in plasma LSA than TSA in cancer patients and that this increase is significant (14,38,39). A significant decrease in plasma LSA was noted postoperatively. It is assumed that LSA is more closely related to malignancy because of its higher decrease after the removal of the tumor tissue when compared to TSA (39). Dunzendorfer et al reported that the rise in LSA level was higher than that of TSA in the study performed on the patients with bladder and prostate cancers (38). Our findings are also correlated the studies recording higher LSA levels in gastric cancer (40).

The preoperative plasma TSA and LSA levels of the patients with duodenal ulcer were significantly higher than those of the control group, but significantly lower than those of the cancer patients. The increase of TSA in ulcer is thought to be the result of the damage in the mucosa of the duodenum and the stomach. Mouterde et al reported that TSA increased in the children with alkalyne reflux gastritis and that SA was good indicator to determine the damage in the gastric mucosa due to alkalyne gastritis in the cases with bile reflux (37).

The preoperative and postoperative plasma TSA and LSA levels of the three groups were compared. The difference was significant. It was concluded that TSA and LSA increased more in the cancer patients than in the normal individuals and the duodenal ulcer patients and that they are important as a TM.

The preoperative plasma TSA and LSA levels were compared according to the stages in gastric cancer patients. Their levels were getting higher with the stage. Therefore it was tought that SA may be helpful in the staging of gastric cancer. Khanderia et al. discovered a relationship between the stages and plasma SA levels in 16 different histologic types of malignancies (29). Likewise Horgan-Ryan et al. found higher levels of plasma SA in late stages (III,IV) of breast cancer than in the early stages **(I,II)** (41). We think that the SA increase in the late stages is due to the growth of tumor mass, the metastases and the cell death because of the insufficient blood supply in the tumor. Plucinsky et al and Coombes et al reported significant increase in SA levels with the appearance of the metastases in different cancers (32) and in breast cancer (22) respectively.

In our study the plasma TSA and LSA levels decreased postoperatively in the cancer patients. This decrease was significant.

Khanderia et al found that the SA level decreased in patients whose tumor masses removed surgically or minimized by chemotherapy whereas it was high in the tumors not effected by chemotherapy (29). They reported that SA was an effective TM in the follow-up of treatment and recurrences after a follow-up of nine months (29,42).

It is reported that LSA is the most important criteria to determine if the SA increase in plasma is due to malign or benign causes. LSA increases in malignant diseases whereas PSA increases in benign diseases (39). We found that the plasma LSA levels of the cancer patients (35-27%) were higher than those of the ulcer and control groups in our study. In addition LSA decreased more than PSA after treatment in the cancer patients. These findings are correlated with the idea of LSA being in closer relation with the cancer. In conclusion we think that the studies on SA will give more information about the response to the treatment, the behavior of the cancer and its recurrence in addition to its help in the diagnosis.

Mide kanserinde tümör belirleyici olarak plazma sialik asidinin önemi

Bu çalışma Erciyes Üniversitesi Tıp Fakültesi Genel Cerrahi ve Biyokimya Anabilim Dallarında gerçekleştirildi. Çalışmaya 30 mide kanserli, 30 duodenal ülserli ve 30 hernili hasta alındı. Mide kanserli hastaların preoperatif plazma Total Sialik Asid (TSA) ve Lipide Bağlı Sialik Asid (LSA) değerleri ülserli hastalar ve kontrol grubundan yüksek bulundu (p<0.05). Ayrıca ülserli hastaların plazma TSA ve LSA değerleri kontrol grubundan anlamlı olarak yüksek bulundu (p<0.05). Kanserli hastaların preoperatif plazma TSA ve LSA değerleri tedavi sonrası anlamlı olarak düşüş gösterdi (p<0.05). Ülserli hastaların plazma TSA ve LSA değerleri ile kontrol grubunun plazma TSA ve LSA değerleri operasyon sonrası değişiklik göstermedi (p>0.05). Kanserli hastaların plazma TSA ve LSA değerlerinin tümör evresine paralel olarak artış gösterdiği ve bu artışın anlamlı olduğu belirlendi (p<0.05). [TurkJMedRes 1994, 12(1):29-33]

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