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위암에서 비단백용해성 효소의 임상적 의의

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The Clinical Implication of Non-Proteolytic EnzYme Activities in Stomach Cancer

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Abstract

Backgrounds : Beta-glucuronidase and lactic dehydrogenase are non-proteolytic enzymes related to the inflammation. In recent years there are a few reports that these 2 enzymes may be markers of gastric cancer. **Material and Methods** : The study was to observe whether the measurement of enzyme activity had any critical role in assessment of diagnostic value, beta-glucuronidase and lactic dehydrogenase activities in neoplastic tissue of stomach were compared with those in the gastric muosa of non-neoplastic antral and body area, which were obtained from products of gastrectomy of 27 cases. The enzyme immunoassay was used for the estimate of the activity of enxymes. **Results** : The activity of enzymes was compared with each differentiation and metastasis of the tumor. beta-glucuronidase activity in tumor was higher that that of normal mucosa and activity of antral mucosa with intestinal metaplasia was higher than that of body. Lactic dehydrogenase activity in tumor was similar to that in the antral mucosa with intestinal metaplasia, and it was higher than that in the body mucosa of stomach. There were no significant statistical difference of actvities of both enzymes between metastatic and non-metastatic groups($p>0.01$). No significant correlation between activities of both enzymes was not seen in the tumor mass($r=0.347$, $p>0.05$). **Conclusions** : These results support that enzyme activities of beta-glucuronidase and LDH in gastric tissues and tumor mass could reflect the histopathologic status of stomach and the assessment of the activity of enzymes may be of value in the identification of high-risk groups.

Key words : Gastric Cancer, LDH, Beta-glucuronidase

Introduction

There have been studies about gastric enzymes as a screening test for gastric cancer [1-,3)]. Among these enzymes, beta-glucuronidase and LDH (Lactic Dehydrogenase) was found to be a significant increased in the gastric juices or washing samples.[1-,3)] The activity of beta-glucuronidase was investigated cytochemically in neutrophils from the peripheral blood and differences in the activity of enzymes studied were demonstrated between patients at different clinical stages of cancer advancement, as well as between cancer patients and control healthy subjects by Sulowicz.[4-5)] Most significant changes, as reported literatures, were observed in patients with initial (1st stage) cancer.[6)] But Moshchynski et al [5)] reported that the levels of LDH and beta-glucuronidase were not increased in neutrophils of peripheral blood. The enzyme activities of peripheral blood and body secretion or fluids in tumor patients are supposed to depend on the release from carcinomatous

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tissues, surrounding non-neoplastic tissues, increased permeability and necrosis of carcinomatous tissue. This might explain the reason why these enzymatic activities did not parallel the extent and macroscopic appearance of the tumor and there have been reported common false positivity, more than 10% in the gastric juices and peripheral blood.[5] The purpose of this study was in an attempt to determine the significance of increased beta-glucuronidase and LDH in intestinal metaplastic gastric mucosal tissues and tumor tissues and to evaluate changes of activities of these enzymes.

Material and Method

Homogenates of gastric body mucosa, antral mucosa having intestinal metaplasia, and carcinoma tissues obtained from gastrectomy stored at a low temperature (-70° C) were used. All samples from the same sites were also examined microscopically. And the enzyme activities were assayed by EIA referring Sigma Quality control test procedures [8].

The statistical analysis was preformed using SPSS (version11). The comparison between 2 groups were used by X^2 test and log-rank and pearson test. The statistical significance was accepted as p valus < 0.05.

Results

Beta-glucuronidase activity in tumor(24.079 unit) was higher that that of normal budy mucosas(6.484 unit), and actvity of antral mucosa with intestinal metaplasia(14.070 unit) was higher than that of body(Table 1.). Lactic dehydrogenase activity in tumor(643.272 unit) was similar to that in the antral mucosa with intestinal metaplasia(550.025 unit), and was higher than that in the body mucosa(431.615 unit) of stomach (Table 2.). Activities of both enzymes in well-differentiated carcinoma were slightly higher than in poorly-differentiated one, but did not find significant difference (p>0.01) (Table 3.). There were no significant statistical difference of actvities of both enzymes between metastatic and non-metastatic groups(p>0.01) (Table 3.). No significant correlation between activities of both enzymes was not seen in the tumor mass(r=0.347, p>0.05) (Table 3.).

Table 1. Beta-glucuronidase Activity of Gastric Mucosa in 27 patients with stomach carcinoma

No.	Site		
	Body (unit)	Antrum (unit)	Carcinoma (unit)
1	1.072	14.124	55.301
2	11.287	16.931	28.218
3	2.822	7.346	11.289
4	0.564	8.467	12.983
5	5.644	15.805	34.997
6	8.467	8.467	38.383
7	1.129	5.645	5.645
8	10.725	28.788	27.659
9	5.080	19.756	23.143
10	8.467	12.983	12.983
11	11.289	20.321	24.272
12	9.031	16.934	17.498
13	9.596	16.396	16.934
14	11.854	24.272	25.401
15	1.693	16.934	27.699
16	1.129	1.129	4.516
17	11.387	11.584	54.188
18	1.693	27.659	16.934
19	11.287	27.083	27.083
20	16.902	23.707	23.707
21	1.702	5.644	47.985
22	2.822	1.129	8.467
23	5.080	5.644	6.774
24	16.934	9.596	17.498
25	0.565	0.565	16.931
26	1.693	11.289	14.112
27	4.516	21.450	22.578
Mean	6.484	14.070	23.079

Body: means non-metaplastic tissues. Antrum:: means intestinal metaplasia.

X2-X1=7.586, t=4.055(p<0.01), X3-X1=16.595, t=5.983 (p,0.01),

X3-X2= 9.009,t=2.934(p<0.01)

Table 2. LDH activity of gastric mucosa in 27 patients with gastric carcinoma

No	site		
	Body (unit)	Antrum (unit)	Carcinoma (unit)
1	412.371	644.330	876.289
2	534.021	659.794	752.577
3	762.887	824.742	855.670
4	644.329	721.649	804.124
5	360.825	465.979	525.773
6	721.649	814.433	917.516
7	721.650	659.794	711.340
8	257.732	350.515	422.680
9	309.278	350.515	422.680
10	103.093	371.134	412.371
11	185.567	350.515	463.918
12	164.948	309.278	360.825
13	489.691	577.320	690.722
14	164.948	443.299	463.198
15	421.372	422.680	536.082
16	247.423	536.082	721.649
17	391.753	412.371	917.526
18	371.134	231.959	273.196
19	711.340	776.289	776.289
20	329.897	505.125	505.155
21	463.918	711.340	905.217
22	628.866	536.082	716.495
23	195.876	659.794	510.309
24	521.649	597.938	773.196
25	762.887	824.742	855.670
26	257.732	391.753	432.990
27	525.773	701.031	762.887
Mean	431.615	550.025	643.272

Body: means non-metaplastic tissues. Antrum:: means intestinal metaplasia

X2-X1=119.010, t=2.294($p<0.05$) X3-X1=211.657, t=3.881($p<0.01$)

X3-X2=93.247, t=1.842($p>0.05$)

Discussion

beta-glucuronidase was activated cytochemically in neutrophils from the peripheral blood and has been known that it has the relationship with inflammation and cancer development in stomach[9] There has been reported the differences in the activity of enzymes were demonstrated between patients at different clinical stages of cancer advancement, as well as between cancer patients and control healthy subjects by Sulowicz [4]

Tablele 3. Correlation between beta-glucuronidase and LDH activity of cancer tissue and clinico-pathological parameters in 27 patients with gastric carcinoma

No.	Enzymes Activities		clinicopathological parameters	
	Beta-glucuronidase1	LDH[2]	metastasis	differentiatiom**
1	55.301	876.289	M	W
2	28.218	752.577	M	P
3	11.289	855.670	M	P
4	12.983	804.124	M	W
5	34.997	525.773	M	P
6	38.383	917.516	N	W
7	5.645	711.340	M	W
8	27.659	422.680	M	W
9	23.143	422.680	M	W
10	12.983	412.371	N	P
11	24.272	463.918	N	P
12	17.498	360.825	M	P
13	16.934	690.722	M	W
14	25.401	463.198	N	P
15	27.659	536.082	M	P
16	4.516	721.649	M	P
17	54.188	917.526	M	P
18	16.934	273.196	M	P
19	27.083	776.289	N	W
20	23.707	505.155	M	P
21	47.185	905.217	N	W
22	8.467	716.495	M	W
23	6.774	510.309	M	P
24	17.498	773.196	M	W
25	16.931	855.670	M	P
26	14.112	432.990	N	P
27	22.578	762.887	N	P

r^{12}=0.347($P>0.05$), Beta-glucuronidase: *,$P>0.05$, **$P>0.05$
LDH: *,$P>0.05$ **,$P>0.05$

Tayer [10] reported that the activity of beta-glucuronidase and LDH increased in gastric juices of patients with gastric cancer. However, Williams reported that false positivity was around the 10%. Rogers[11] reported 11.5 % of false positive reaction of 2 enzymes in gastric juices. Most significant changes of gastric

enzymes, as reported literatures, were observed in patients with initial (1st stage) cancer. But Moshchynski [5] et al reported that the levels of LDH and beta-glucuronidase were not increased in neutrophils of peripheral blood. Theorotically, the enzyme level of blood and gastric juices depend on the release from carcinomatous tissue, surrounding non-neoplastic tissues, increased permeability and necrosis of carcinomatous tissues.[11] However, those enzymatic activities did not parallel the extent and macroscopic appearance of the tumor. This might explain the reason why these enzymatic activities did not parallel the extent and macroscopic appearance of the tumor and there have been reported common false positivity, more than 10% in the gastric juices and peripheral blood .[5]

Therefore, although there has been some studies about the enzyme activity in gastric juices, the study in non-neoplastic and neoplastic tissues of stomach is needed.

This study showed that beta-glucuronidase activity in tumor(24.079) was higher that that of normal budy mucosas(6.484), and actvity of antral mucosa with intestinal metaplasia(14.070) was higher than that of body. Lactic dehydrogenase activity in tumor(643.272) was similar to that in the antral mucosa with intestinal metaplasia(550.025), and was higher than that in the body mucosa(431.615) of stomach (Table 2.). These results were accordant with that of previous studies. Finch[12] reported cancer showed that positive rate was 91.% in the gastric juice of cancer patient 30% in patients with intestinal metaplasia, and 95.8% in patients with chronic atrophic gastritis. But they studied the frequency of 2 enzymes not the level of enzyme. We interpretated the positive means the higher activity than normal activity. The higher level of 2 enzymes in intestinal metaplasia can be explained due to lung standing inflammation inducing intestinal metaplasia.

Activities of both enzymes in well-differentiated carcinoma were slightly higher than in poorly-differentiated one, but did not find significant difference ($p>0.01$). There were no significant statistical difference of actvities of both enzymes between metastatic and non-metastatic groups($p>0.01$). If the assessment of 2 enzymes in blood not tissues would be done, the enzyme activity might be different significantly between non-metastatic and metastatic groups.

These results support that enzyme activities of 2 enzymes in tissues from patients with gastric disease could reflect the histopathologic status of stomach including intestinal metaplasia and cancer and the assessment of the activity of enzymes may be of value in the identification of high-risk groups for gastric carcinoma.

Conclusion

These results support that enzyme activities of beta-glucuronidase and LDH in gastric tissues and tumor mass could reflect the histopathologic status of stomach and the assessment of the activity of enzymes may be of value in the identification of high-risk groups.

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국문 초록

배경 및 목적 : 위액에서 beta-glucuronidase (bGlu)와 LDH에 대한 연구가 위암 선별 검사목적에서 이루어져 왔으나, 이를 위해서는 위암과 점막조직에서의 효소활성치에 대한 연구가 선행되어야한다. **재료 및 방법** : 27예의 위암으로 수술받은 환자의 화생이 없는 체부점막조직, 화생이 일어난 전정부 점막조직, 위암조직을 신선한 상태에서 절취하여, 효소측정법으로 활성도를 측정한다. **결과** : bGlu는 위암(24.079)에서 체부조직(6.484)와 화생전정부(14.070)보다 의의있게 높았다($p<0.05$). LDH는 위암(643.272)과 화생전정부 점막(550.025)에서 위체부(431.615)보다 의의 있게 높았다.($p<0.05$). 분화가 좋은 암에서 두 효소가 다소 높은 수치를 보였으나, 의미는 없었고, 림프절 전이 유무와도 효소 수치가 관련이 없었다. 두효소간의 상관성도 인정되지 않았다. **결론** : 위 질환자의 위조직에서 bGlu와 LDH의 측정은 위의 위암이나 위염으로 인한 화생등의 병리조직학적인 상태를 반영할 수 있으며, 화생등의 전암성 병변을 예측할 수 있으므로 두 효소의 활성도 측정은 위암의 고위험군 색출에 이용할 수 있겠다.