

Original Article

Assessment of Activity of Serum Beta-galactosidase in Colon Cancer Patients: A Pathological Study

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ABSTRACT:

Background: Colorectal carcinomas are one of the most frequent neoplasms in Western society. Lysosomal- β -galactosidase is a lysosomal enzyme that hydrolyzes the terminal β -galactose from ganglioside substrates and other glycoconjugates. Hence; we planned the present study to assess the activity of serum beta-galactosidase in colon cancer patients. **Materials & methods:** We planned the present study to assess of the activity of serum beta-galactosidase in colon cancer patients. A total of 10 colon patients and 10 healthy controls were included in the present study. We assessed the activity of β -galactosidase in the serum (pkat/ml) in duplicate by the colorimetric determination of p-nitrophenol released from p-nitrophenyl- β -D galactopyranoside by β -galactosidase. All the results were analyzed by SPSS software. Chi- square test was used for assessment of level of significance. **Results:** Mean activity of serum β -galactosidase in the patients of the study group and control group were 77.5 and 69.5 pkat/ml respectively. However; we didn't observe any significant difference while comparing the mean serum β -galactosidase levels in between subjects of study group and the control group. **Conclusion:** β -galactosidase activity remains unaltered in colon cancer patients. **Key words:** β -galactosidase, Colon cancer, Pathology.

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INTRODUCTION

Colorectal carcinomas are one of the most frequent neoplasms in Western society; the macroscopic appearance of these lesions may be that of a polypoid vegetating mass or of a flat infiltrating lesion. Most of these tumours are adenocarcinomas (96%), that, in some cases, show a mucinous component. More rare malignancies of the large bowel include signet-ring cell carcinoma, squamous carcinoma, undifferentiated neoplasms and medullary type adenocarcinoma (solid carcinoma with minimal glandular differentiation or slight cellular pleomorphism).¹⁻³ Colorectal carcinoma can be graded into well, moderately and poorly differentiated lesions; there is little evidence, however, that grading may be of help in evaluating prognosis of affected patients. In conclusion, colorectal tumours cover a wide range of premalignant and malignant lesions, many of which can easily be removed at endoscopy.^{4,5} GLB1 (lysosomal- β -galactosidase) is a lysosomal enzyme that hydrolyzes the terminal β -galactose from ganglioside substrates and other glycoconjugates. The GLB1 gene was found to be the source of senescence associated- β -gal

activity (SA- β -gal), and expression correlates with SA- β -gal activity both in vitro and in vivo.^{6,7} Staining for SA- β -gal is the predominant method to identify senescent cells, but requires fresh or frozen tissue to assess enzymatic activity. Other markers associated with, but not specific for senescence include a low proliferative activity, decreased p27, as well as alterations in nuclear matrix genes including increased heterochromatin protein 1 gamma (HP1 γ).⁸ Hence; we planned the present study to assess the activity of serum beta-galactosidase in colon cancer patients.

MATERIALS & METHODS

We planned the present study in the department of general pathology of the medical institute and it included assessment of the activity of serum beta-galactosidase in colon cancer patients. Ethical approval was obtained from institutional ethical committee and written consent was obtained after explaining in detail the entire research protocol. A total of 10 colon patients and 10 healthy controls were included in the present study. Among 10 colon cancer patients, 7 were females and the remaining 3 were males. Among 10 healthy controls, 6 were females

and the remaining 4 were males. The subjects of colon cancer group were categorized as study group while the healthy subjects were categorized under control group. Only those patients were categorized under study group in which histopathological confirmation of the diagnosis of adenocarcinoma of colon was made. We assessed the activity of β -galactosidase in the serum (pkat/ml) in duplicate by the colorimetric determination of p-nitrophenol released from p-nitrophenyl- β -Dgalactopyranoside by β -galactosidase⁹. Incubation of the mixture of enzyme and substrate was done for 60 min at 37°C. All the results were analyzed by SPSS software. Chi-square test was used for assessment of level of significance. P-value of less than 0.05 was taken as significant.

RESULTS

In the present study, we analyzed a total of 20 subjects; out of which, 10 were included in the study group while the remaining 10 were included in the control group. Mean age of the subjects of study group and control group were 48.5 years and 46.2 years respectively. Majority of the subjects in the present study were females. Mean activity of serum β -galactosidase in the patients of the study group and control group were 77.5 and 69.5 pkat/ml respectively. However; we didn't observe any significant difference while comparing the mean serum β -galactosidase levels in between subjects of study group and the control group (P-value > 0.05).

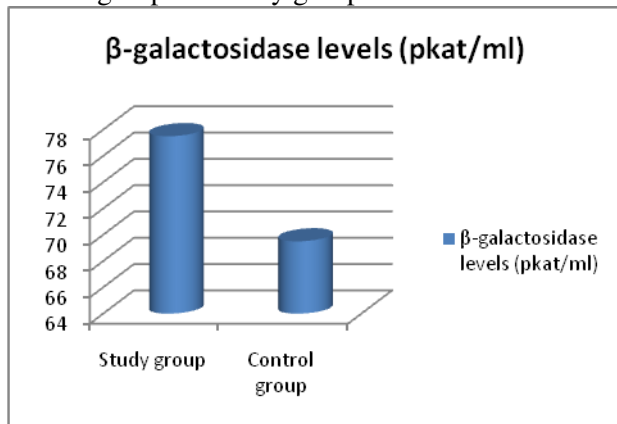
Table 1: Demographic details of the patients of the present study

| Parameter | Study group | Control group |
|------------------|-------------|---------------|
| No. of subjects | 10 | 10 |
| Males | 3 | 4 |
| Females | 7 | 6 |
| Mean age (years) | 48.5 | 46.2 |

Table 2: Activity of serum β -galactosidase in patients of control group and study group

| Group | β -galactosidase levels (pkat/ml) | P-value |
|---------------|---|---------|
| Study group | 77.5 | 0.84 |
| Control group | 69.5 | |

Graph 1: Serum β -galactosidase in patients of control group and study group



DISCUSSION

In the present study, mean activity of serum β -galactosidase in the patients of the study group and control group were 77.5 and 69.5 pkat/ml respectively. However; we didn't observe any significant difference while comparing the mean serum β -galactosidase levels in between subjects of study group and the control group (P-value > 0.05). Waszkiewicz N et al investigated the effect of chronic alcohol drinking and smoking on the activity (pKat/ml) and output (pKat/min) of salivary lysosomal exoglycosidases: α -fucosidase (FUC), α -mannosidase (MAN), β -galactosidase (GAL), and β -glucuronidase (GLU), and their applicability as markers of alcohol dependence. The activity of FUC, MAN, GAL and GLU was measured colorimetrically in the saliva of healthy social drinkers, alcohol-dependent non-smokers and alcohol-dependent smokers. They observed an increased salivary activity of FUC, GAL, GLU and MAN, as well as an increased output of GAL and GLU, in comparison with controls. The highest increase in the activity/output was found in salivary GLU and MAN (GLU, even 7- to 18-fold), and the least in GAL. We found an excellent sensitivity and specificity and a high accuracy (measured by the area under the ROC curve) for salivary FUC, GLU and MAN activities. The salivary GLU activity positively correlated with the number of days of last alcohol intoxication. Salivary activity of FUC, GAL and MAN, but not GLU, positively correlated with the periodontal parameters such as gingival index and papilla bleeding index. Although we found an excellent sensitivity and specificity as well as a high accuracy for the salivary activity of FUC, GLU and MAN, the GLU activity seems to be mostly applicable as a marker of chronic alcohol drinking (alcohol dependence).¹⁰

Waszkiewicz N et al compared the specific activity of lysosomal exoglycosidases: N-acetyl- β -D-hexosaminidase (HEX), its isoenzymes A (HEX A) and B (HEX B), β -D-galactosidase (GAL), α -fucosidase (FUC), and α -mannosidase (MAN) with the activity of cathepsin D (CD) in serum, urine, and carcinoma tissue of patients with colon adenocarcinoma. The specific activity of HEX, HEX A, HEX B, GAL, FUC, MAN, and CD was assayed in serum, urine, and carcinoma tissue of 12 patients with colon adenocarcinoma. Lysosomal exoglycosidases and CD have similar specific activity in colon adenocarcinoma tissue and urine, which is higher than their activity in serum (with the exception of the highest specific activity of CD in urine). A positive correlation was observed between the specific activity of CD and that of HEX, HEXES A, FUC, and MAN in the carcinoma tissue and urine as well as between CD and GAL in the urine of patients with colon adenocarcinoma. Negative correlations were observed between protein levels and the specific activity of HEX, HEX A, FUC, MAN, and CD in the carcinoma tissue and urine, and between protein levels and GAL in urine. Increased degradation and remodeling of glycoconjugates in the colon adenocarcinoma tissue is reflected by increased specific activity of exoglycosidases and CD. The results

suggest a strong effect of exoglycosidase action on tissue degradation and a potential role of exoglycosidases in the initiation of proteolysis.¹¹ Waszkiewicz N et al evaluated the activity of the serum senescence marker Beta-galactosidase (GAL) in colon cancer patients with a history of alcohol and nicotine dependence, as a potential factor of worse cancer prognosis. The material was serum of 18 colon cancer patients and 10 healthy volunteers. Ten colon cancer patients met alcohol and nicotine dependence criteria. The activity of beta-galactosidase (pkat/ml) was determined by the colorimetric method. Comparisons between groups were made using the Kruskal-Wallis analysis and differences evaluated using the Mann-Whitney U test. Spearman's rank correlation coefficient was used to measure the statistical dependence between two variables. The activity of serum GAL was significantly higher in colon cancer patients with a history of alcohol and nicotine dependence, in comparison to colon cancer patients without a history of drinking/smoking ($p=0.015$; 46% increase), and the controls ($p=0.0002$; 81% increase). The activity of serum GAL in colon cancer patients without a history of alcohol/nicotine dependence was higher than the activity in the controls ($p = 0.043$; 24% increase). Higher activity of beta-galactosidase may potentially reflect the accelerated growth of the cancer, invasion, metastases, and maturation, when alcohol and nicotine dependence coincide with colon cancer.¹²

CONCLUSION

From the above results, the authors conclude that β -galactosidase activity remains unaltered in colon cancer patients. However; future studies are recommended.

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