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STUDY OF PROSTAGLANDIN E2 LEVEL IN PATIENTS WITH POLYPS AND COLORECTAL CANCER

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ABSTRACT

Objectives: To describe the characteristics of age, sex; histopathology; some paraclinical features and to evaluate the concentration of Prostaglandin E2 in two groups of patients with polyps and colorectal cancer (CRC).

Methods: Cross-sectional descriptive study on 308 patients: including 149 CRC patients and 109 patients with colorectal polyps diagnosed by cytology or histopathology, 50 healthy individuals; who were examined and treated at Military Hospital 175.

Results: The mean age in the CRC group was 59,64 ± 11,66; in the colorectal polyps group was 58,45±9,65; in the healthy group was 57,32±8,17; there was no difference in age between the study groups. The incidence is higher in men than in women, and this difference is statistically significant (p=0,0061). Adenocarcinoma is dominant in CRC patients (77,85%); for polyps, adenomas are dominant (83,49%). The mean PGE2 concentration in CRC patients was 7,86±2,8 pg/ml; in polyp patients was 5,29±1,3 pg/ml; in healthy people it was 2,78±0,5 pg/ml.

Conclusions: There was no difference in the concentration of PGE2 in the polyp and CRC groups (p>0,05). However, there was a significant difference in PGE2 levels in the two groups of cancer and colorectal polyps compared to healthy individuals (p< 0,05 (0,0021)).

Keyword: Prostaglandin E2; Colorectal cancer; colorectal polyps.

1. INTRODUCTION

Colorectal cancer (CRC) is one of the most common causes of cancer-related deaths worldwide [1]. Several studies have indicated that the molecular mechanisms in the formation of CRC tumors are related to the inflammatory process in the intestines [2].

In Vietnam, colorectal cancer ranks fifth in incidence, following liver, lung, breast, and stomach cancers, and is showing an increasing trend. According to the Global Cancer Observatory, in 2020, Vietnam reported 182,563 new cancer cases, of which 122,690 resulted in death [3].

Most cancer cases, including colorectal cancer, are often detected at late stages. The 5-year survival rate is only around 20% for patients diagnosed at late stages, compared to 70-90% when diagnosed and treated earlier [3]. Therefore, research aimed at better understanding the pathogenesis of colorectal cancer will significantly contribute to diagnosis, treatment monitoring, and prognosis. Recent studies on inflammatory factors have confirmed that Prostaglandin E2 (PGE2) plays a key role in the pathogenesis of colorectal cancer. Many studies also point to the relationship between gut microbiota and Prostaglandin E2 in the development of this cancer [4]. To further clarify the role of Prostaglandin E2 in colorectal cancer, we conducted this study with the objective: "To evaluate the concentration of Prostaglandin E2 in patients with colorectal polyps and colorectal cancer".

2. SUBJECT AND METHOD

2.1. Subject

This study included 308 patients, consisting of 149 CRC patients, 109 patients with colorectal polyps, and 50 healthy individuals who visited and were treated at Military Hospital 175 between January 2023 and May 2024..

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Inclusion criteria: All patients underwent a prepared colonoscopy, had adequate biopsy samples, and were diagnosed with colorectal polyps or colorectal cancer through cytology or histopathology. None of the patients had received prior treatment or surgery, and sufficient blood samples were obtained for the study. The use of biopsy samples adhered to ethical guidelines approved by the hospital's Ethics Committee, and all participants consented to be included in the study..

2.2. Methods

- *Study Design:* Cross-sectional descriptive study

- *Sampling Method:* Convenience sampling.

- *Content and Research Methods:*

+ Collection of specimen types:

++ Serum: Samples were left at room temperature for 2 hours or overnight at 4°C. Then centrifuged for 20 minutes at approximately 1000 × g. The supernatant was collected for analysis. Undiluted samples were stored at -20°C or lower.

++ Plasma: Tubes containing EDTA or heparin anticoagulant were used. Centrifuged for 15 minutes at 1,000 x g at 4°C within 30 minutes of collection. Tested immediately or aliquoted and stored at -20°C or -80°C.

+ Quantification of Prostaglandin E2 (PGE2) by ELISA technique using Human kits and equipment, quantifying PGE2 concentration in the samples according to the manufacturer's instructions.

- *Data Analysis and Processing:* Data were summarized and processed using Excel, then SPSS 21.0 software was used for graphing and analysis. The Mann-Whitney U test was used for unpaired, non-normally distributed data. The difference between two or more median values was considered statistically significant when $p<0.05$.

2.3. Research Ethics: The study was approved by the Ethics Committee of Military Hospital 175, allowing sample collection for research. The study was only conducted with the consent of the participants. The collected information was used solely for research purposes, not for any other purposes, and was kept completely confidential, without affecting the health and benefits of the study subjects.

3. RESULTS

3.1. Age and Gender Characteristics of the study group

Table 1. Age and Gender of the study group

Group		CRC	Polyp	Healthy	p value
Age	**Mean±SD**	59.64±11.66	58.45±9.65	57.32±8.17	0.3695
Gender	**Male**	102 (68.46%)	91 (83.49%)	-	0.0061
	Female	47 (31.54%)	18 (16.51%)	-	

The mean age of the CRC group was 59.64 ± 11.66; for the colorectal polyp group, it was 58.45 ± 9.65; and for the healthy group, it was 57.32 ± 8.17. Regarding gender, the incidence was higher in men than in women for both CRC and colorectal polyps, with a statistically significant difference (p = 0.0061).

3.2. Histopathological characteristics of the two study groups

Table 2. Histopathological Characteristics

Characteristics		CRC	Polyp
Tumor Location	Colon	83 (55.70%)	88 (80.73%)
	Rectum	66 (44.30%)	20 (18.35%)
Histopathological types	Adenocarcinoma	116 (77.85%)	
	Mucinous Adenocarcinoma	33 (22.15%)	
	Adenomatous Polyp		91 (83.49%)
	Hyperplastic Polyp		15 (13.76%)
	Inflammatory Polyp		2 (1.83%)
	Peutz-Jeghers Polyp		1 (0.92%)

In both the CRC and colorectal polyp groups, tumors in the colon were more common than in the rectum, with rates of 55.7% and 80.73%, respectively. Histologically, adenocarcinoma dominated in CRC patients (77.85%), while adenomatous polyps were the most prevalent in polyp patients (83.49%).

3.3. Paraclinical characteristics in the two study groups

Table 3. Paraclinical characteristics

Indexes (n = 100)	Total (n = 100)		Normal			Abnormal			p
	($\bar{X}$ ± SD)	Median	($\bar{X}$ ± SD)	Median	n	($\bar{X}$ ± SD)	Median	n	
WBC (K/uL)	8.9 ± 3.7	8.2	9.0 ± 3.7	8.2	82	8.4 ± 3.8	6.9	18	>0.05
Neutrophils (%)	65.9 ± 10.5	65.7	65.8 ± 10.0	65.6		66.4 ± 12.5	67.3		>0.05
Mono (%)	8.7 ± 3.1	8.4	8.3 ± 2.7	8.0		10.4 ± 3.8	10.0		<0.05
Lympho (%)	24.6 ± 21.9	23.4	22.9 ± 9.1	23.8		32.1 ± 46.8	19.7		<0.05
RBC (M/uL)	4.3 ± 0.6	4.3	4.4 ± 0.5	4.4		3.6 ± 0.7	3.5		<0.05
Hematocrit (%)	38.0 ± 4.4	38.6	39.2 ± 3.5	39.4		32.7 ± 4.1	32.5		<0.05
Platetes (K/uL)	288.2 ± 99.3	261.0	280.4±97.9	254.0		323.6±97.6	335.5		<0.05
AST (U/L)	29.0 ± 14.1	26.1	25.3 ± 7.2	24.2	89	58.7 ± 20.3	50.6	11	<0.05
ALT (U/L)	29.3 ± 22.9	22.7	23.7 ± 10.8	19.9		74.6 ± 38.7	58.4		<0.05
Ure (mmol/L)	5.3 ± 2.1	5.1	5.2 ± 2.1	5.1	99	9.1 ± 0.0	9.1	01	<0.05
Creatinine (umol/L)	80.5 ± 16.8	78.4	79.5 ± 14.1	78.0		173.2 ± 0.0	173.2		<0.05
Glucose (mmol/L)	6.1 ± 1.9	5.5	5.2 ± 0.5	5.2	66	8.0 ± 2.2	7.1	34	<0.05
Na+ (mmol/L)	137.8 ± 3.7	138.1	138.2 ± 3.3	138.4	87	132.5 ± 4.3	130.6	13	>0.05
K+ (mmol/L)	3.7 ± 0.4	3.7	3.8 ± 0.4	3.7		3.5 ± 0.5	3.3		>0.05
Cl- (mmol/L)	101.9 ± 3.6	102.1	102.3 ± 2.9	102.7		97.3 ± 6.2	97.8		>0.05
CEA (ng/mL)	99.3 ± 262.0	6.2	2.5 ± 1.5	2.3	39	178.0 ± 334.0	17.0	61	<0.05
CA 19-9 (ng/mL)	41.6 ± 34.8	39.7	29.6 ± 0.8	22.7	33	62.7 ± 49.5	58.2	67	<0.05

WBC: white blood cells, RBC: red blood cells

In 100 patients undergoing tests, 18% had abnormalities in peripheral blood cell counts, 11% showed abnormalities in liver enzymes (AST and ALT), 1% had kidney function abnormalities, 34% had abnormal glucose levels, 13% showed ion imbalance, and 61% had abnormal CEA markers, while 67% had abnormal CA 19-9 markers.

3.4. Results of Prostaglandin E2 quantification in peripheral blood of patients with Polyps, CRC, and healthy individuals

Table 4. Prostaglandin E2 concentration in peripheral blood of CRC patients, colorectal polyp patients, and healthy individuals

Groups	PGE2 concentration (pg/ml)		p	
	($\bar{X}$ ± SD)	Median		
CRC	7.86 ± 2.8	5.33	>0.05	<0.05
Polyp	5.29 ± 1.3	4.17		
Healthy	2.78 ± 0.5	2.23		

The average PGE2 concentration in CRC patients was 7.86 ± 2.8 pg/ml; in patients with colorectal polyps, it was 5.29 ± 1.3 pg/ml; and in the healthy group, it was 2.78 ± 0.5 pg/ml.

There was no significant difference in PGE2 concentration between the CRC and colorectal polyp groups (p>0.05), but there was a significant difference in PGE2 concentration between the cancer and colorectal polyp groups compared to the healthy group (p<0.05).

4. DISCUSSION

4.1. Age and Gender in the Two Study Groups

The mean age in the CRC group was 59.64±11.66; in the colorectal polyp group, it was 58.45±9.65. There was no significant difference in age between the two groups. The age range in this study is consistent with studies by Lê Văn Vinh (2021), Trần Thị Như Quỳnh (2019), and Lã Ngọc Quang (2019), where the average age of the sample group was around 58 years old. In this study, the highest proportion of patients was aged ≥ 60 years. The youngest patient was 27 years old, and the oldest was 83. The average age of patients in studies by Nguyễn Hoàng Bắc was 62 years, and Võ Tấn Long reported 53.4 years. Therefore, the age of CRC onset in our study is similar to other studies both in and outside Vietnam.

Meanwhile, there was a gender difference (male/female) in both CRC and colorectal polyps. In both conditions, the incidence in men was higher than in women, and this difference was statistically significant (p = 0.0061).

4.2. Histopathological and Paraclinical Characteristics in Colorectal Cancer and Polyp Groups

Histopathologically, adenocarcinoma was predominant in CRC patients, while adenomas were prevalent in polyp patients. This finding aligns with previous studies, supporting the role of colorectal polyps in the pathogenesis of CRC.

Patients in the study underwent various tests, including peripheral blood counts, biochemical tests (ion levels, liver and kidney enzyme activity, blood glucose), and tumor markers. Among the 100 patients who underwent tests, 18% had abnormal peripheral blood cell counts, 11% had abnormal liver enzyme levels (AST and ALT), 1% had abnormal kidney function (urea and creatinine), 34% had abnormal blood glucose levels, and 13% had abnormal ion levels. As for tumor markers, 6% of patients had abnormal CEA levels, and 67% had abnormal CA 19-9 levels.

4.3. Results of Prostaglandin E2 Quantification in Colorectal Polyps and CRC Patients

The PGE2 concentration in CRC patients was higher than in the colorectal polyp group, but this difference was not statistically significant (p>0.05). However, there was a significant difference in PGE2 concentration between both the CRC and polyp groups compared to the healthy group (p<0.05 (0.0021)). Chronic inflammation plays a crucial role in the pathogenesis of both polyps and CRC, with PGE2 acting as a major driver in this process.

Inada et al. demonstrated that macrophages produce PGE2 through COX-2 regulation by mucins secreted from LS180 colon cancer cell lines. They analyzed immunohistochemistry in human CRC tissues and showed that macrophages expressing COX-2 were located around regions where mucin was detectable [5].

PGE2 signaling is known to play an important role in macrophage polarization. PGE2 shifts macrophage phenotypes from M1 (tumor-suppressive) to M2 (tumor-promoting) macrophages [6, 7]. Eruslanov et al. reported that overexpression of 15-PGDH in mouse colon cancer cell lines (CT26) shifted the phenotype of CD11b cells from M2-tumor-associated macrophages (TAMs) to M1 macrophages, suggesting that PGE2 may induce monocyte differentiation towards M2-TAMs [8]. Wu et al. showed that PGE2 could be a potent inducer of VEGF in M2 TAMs under hypoxic conditions [9]. Ratcliffe et al. examined the EP receptors expressed on macrophages and found that EP2 and EP4 were primarily expressed on macrophages [10]. The difference in PGE2 concentrations between the CRC/polyp groups and the healthy group also highlights the role of chronic inflammation in patients with CRC and colorectal polyps, further demonstrating the importance of inflammation in CRC pathogenesis and pointing towards anti-inflammatory treatments for this disease.

5. CONCLUSION

A total of 308 patients were included in the study, comprising 149 CRC patients, 109 patients with colorectal polyps, and 50 healthy individuals. Results: The mean age in the CRC group was 59.64 ± 11.66; in the colorectal polyp group, it was 58.45 ± 9.65. There was no significant difference in age between the two groups. There was a gender difference (male/female) in CRC and colorectal polyps, with a higher incidence in men than in women. The concentration of PGE2 in colorectal cancer patients was 7.86 ± 2.8 pg/ml, higher than that in patients with colorectal polyps (5.29 ± 1.3 pg/ml) and in healthy individuals (2.78 ± 0.5 pg/ml).

There was no significant difference in PGE2 concentration between the polyp and colorectal cancer groups (p>0.05). However, there was a significant difference in PGE2 concentration between the CRC/polyp groups and the healthy group (p<0.05 (0.0021)).

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