Prognostic factor of serum carcinoembryonic antigen in colorectal cancer patients: a follow up study

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Abstract:

Colorectal cancer is a serious cancer with high mortality. Most of the recurrence usually occurred within two years after surgery. This study was conducted in Nineveh Medical Center and Al-Jammhorri Hospital to evaluate colorectal cancer patients in a follow up study for two years. Serum carcinoembryonic antigen, colonoscopy, ultrasound of the abdomen, and chest X rays were used for evaluation. One hundred and ninety-four patients with colorectal cancer were included in the study. The patients were diagnosed colorectal adenocarcinomas by histopathology and staged according to Duke's classification. The patients were undergone surgical removal of the cancer. Chemotherapy was started to the patient after two weeks of the surgery. Blood samples were taken one week before and one week after surgery. Other blood samples were taken after chemotherapy and then every six months for two years. The blood samples were analyzed for serum carcinoembryonic antigen. The patients were also checked by colonoscopy, ultrasound for abdomen, and chest X ray every six months. Serum carcinoembryonic antigen in colorectal patients was higher than 5 ng/mL and decreased significantly after surgery but still higher than 5 ng/mL. After chemotherapy serum decreased significantly compared with that after surgery. During the two-year period serum carcinoembryonic antigen was not significantly different from that in patients after chemotherapy. Twenty-one patients died after two years of the study Serum carcinoembryonic antigen in the dead patients was much significantly higher than 5 ng/mL before surgery and decreased significantly after operation and after chemotherapy but still higher than 5 ng/mL. In conclusion, colorectal cancer is a significant disease in Iraq. The mortality rate is high due to lack of education of the community to that disease. Carcinoembryonic antigen marker is still acceptable test but should be used with other clinical assessments.

Key words: Colorectal cancer, carcinoembryonic antigen, metastasis

عامل الانذار لمصل دم مستضط السرطان الجنيني لمرضى سرطان القولون: دراسة تتبعية

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الخلاصة:

يعتبر سرطان القولون مرض خطير مع ارتفاع الوفيات. ان معظم عودة حالات السرطان يحدث خلال سنتين بعد الجراحة. ان هذه الدراسة قد اجريت في مركز طب نينوى وفي المستشفى الجمهوري لتقييم مرضى سرطان القولون بدراسة تتبعية ولمدة سنتين. وقد استعمل للتقييم مصل دم مستضد السرطان الجنيني، ناظور القولون، والتشخيص للجوف بالامواج فوق الصوتية وألتصوير الشعائي للصدر. شملت الدراسة على مائة واربعة وتسعون مريضا مصابا بسرطان القولون. وقد

اجريت للمرضى جراحة استئصال للسرطان، وبدأ العلاج بادوية السرطان بعد اسبوعين من الجراحة. أخذت عينات الدم قبل وبعد أسبوع من الجراحة، واخذت عينات اخرى من الدم بعد علاج ادوية السرطان، ثم كل ستة اشهر ولمدة سنتين. حللت عينات الدم لمصل دم مستضد السرطان الجنيني. وكذلك فحص المرضى بناظور القولون، والتشخيص للبطن بالامواج فوق الصوتية. وخلال سنتين من المتابعة لم يختلف مصل دم مسنضد السرطان الجيني معنويا منه في المرضى بعد العلاج الكيميائي. وقد مات 21 شخصا بعد سنتين من العلاج. وكان مصل دم مستضد السرطان الجيني اعلى كثيرا من 5 نغم/مل قبل الجراحة وانخفض معنويا بعد الجراحة وبعد العلاج الكيمياوي لكنه بقى اعلى من 5 نغم/مل. ان الاستنتاج ان سرطان القولون ذو اهمية في العراق، وان نسبة الوفيات عالية نتيجة قلة الوعي في المجتمع حول هذا المرض. ويبقى فحص مصل دم مستضد السرطان الجيني مقبول وبشرط استعماله مع الفحوضات السريرية.

الكلمات المفتاحية: سرطان القولون، مستضد السرطان الجنيني، انتشار الورم.

Introduction:

Colorectal cancer (CRC) is a serious cancer with high mortality, it is less common than breast and lung cancers [1]. Genetic and environmental factors play a role for the disease such as diet, smoking, physical inactivity, alcohol, and certain medications [2]. The world health organization speculates an increase in newly diagnosed CRC by 77% and 80% increase in death by 2030 [3].

In US only 40% of CRC cases were diagnosed as localized stages [4]. In addition, 5-year survival rates of CRC patients were 65%; the range of the 5-year survival rates of those patients was from 90% to 70% and 13% for localized, regional and distant stages, respectively [4]. Most of the recurrence usually occurred within two years after surgery, while 90% of recurrence occurred within 5 years after surgery [5]. The disease was under control after 5 years of surgery [5].

Carcinoembryonic antigen (CEA) has been used as a tumor marker in the follow-up of colorectal cancer for more than 40 years [6]. Serum CEA can be used as a marker for monitoring the response of metastasis [7]. The sensitivity of this marker increased with the progress of the tumor stage [8]. Elevated CEA levels were considered a poor prognostic factor for CRC and correlated with cancer progression [7]. The most useful application of CEA was in the detection of liver metastases from colorectal cancers and serial determinations of CEA were recommended for cancer spread to the liver [9].

This study was conducted in order to evaluate CRC patients in a follow up study for two years. Serum CEA, colonoscopy, ultrasound of the abdomen, and chest X rays were used for evaluation

Patients and methods

This study was conducted in Nineveh Medical Center and Al-Jammhorri Hospital, Mosul, during the period 2009-2012. One hundred and ninety-four patients with colorectal cancer with mean age ± SD: 51.2 ± 14.8 years and age range: 6.5-79 years (68% male, 32% female). All patients were diagnosed colorectal adenocarcinomas by histopathology and staged according to Duke's classification. The patients were undergone surgical removal of the cancer. Chemotherapy was started to the patient after two weeks of the surgery. Chemotherapy included combination of 5-flourouracil 450 mg/m2 and leucovorin 20 mg/m2 daily for 5 days, given by infusion and the cycle was repeated every 28 days for six cycles. Blood samples were taken one week before and one week after surgery. Other blood samples were taken after chemotherapy and then every six months for two years. The blood samples were analyzed for serum CEA. The patients were also checked by colonoscopy, ultrasound for abdomen, and chest X ray every six months.

Data are presented by mean ± SD and were analyzed by using bonferroni test. Statistic was performed by using SPSS package version 16.

Results

The study included measurement of serum CEA for colorectal cancer patients for two years follow up. Table 1 shows that serum CEA in colorectal patients was higher than normal values and decreased significantly after surgery but still higher than 5 ng/mL. After chemotherapy serum decreased significantly compared with that after surgery. During the two-year period serum CEA was not significantly different from that in patients after chemotherapy. However, serum CEA started to increase during that period but the values were still less than 5 ng/mL.

Table (1): Serum CEA in adenocarcinoma patients (n = 194)

Patients	CEA ng/mL
Before surgery	11.02±6.18[a]
After surgery	5.59±4.12[b]
After chemotherapy	2.69±2.54[c]
After 6 months	2.83±2.6[c]
After 12 months	2.98±2.64[c]
After 18 months	3.10±2.82[c]
After 2 years	3.38±3.21[c]

Different letters mean significant at *p* value 0.001

Twenty-one patients died after two years of the study. Another two patients died after two and half years of the surgery. Their mean ages (dead) were 31.7 ± 6.7 years (age range between 18 to 44 years). About 95% of the dead patients were in Duke's stage D, while the rest dead patients (5%) were in Duke's stage C.

All patients with Duke's D had liver metastases. Liver metastases in 30 of 40 patients were noticed with Duke's stage C, while only 7 of 56 patients were found with Duke's stage B. No metastases in patients with Duke's stage A were noticed. All patients with stages A to C were survival after two years of the study.

Table 2 shows serum CEA in the dead patients was much higher than the normal value before surgery and decreased significantly after operation and after chemotherapy. However, serum CEA was still higher than normal.

Table (2): Serum CEA in dead patients (n=21)

Patients	CEA ng/mL
Before surgery	22.4±5.7a
After surgery	12.8±4.5b
After chemotherapy	6.8±3.1c
After 6 months	7.1±2.8c
After 12 months	7.3±2.4c
After 18 months	8.3±2.2c
After 2 years	9.3±2.4c

Different letters mean significant at *p* value 0.001

Table 3 shows frequency and percentage of colorectal cancer patients according to Dukes staging. Stage A showed the highest percentage then decreased to the lowest percentage in stage D

Table (3): Frequency and percentage of the colorectal patients according to Dukes staging

Dukes	Frequency	Percentage%
Stage A	77	39.7
Stage B	56	28.9
Stage C	40	20.6
Stage D	21	10.8
Total	194	100

Discussion

Serum CEA was measured in the studied CRC patients with colonoscopy, ultrasound for abdomen, and chest X ray. Serum CEA can be useful in CRC prognosis and postoperative surveillance of patients with CRC [10, 11]. Serum CEA is a predictor of recurrence and survival for preoperative CRC patients [12]. In the follow up study of colorectal cancer patients, serum CEA correlated well with the curative progress and survival of the patients [13].

In the present study, preoperative serum CEA decreased significantly after surgery with another significant decrease after chemotherapy. The ratio of preoperative to postoperative of CEA in colorectal cancer patients was considered as a prognostic indicator [14]. Serum CEA was also considered as independent predictor for overall survival, and disease-free survival [15]. High serum CEA postoperatively was associated with increased risk of colorectal cancer [16]. However, serum CEA is not specific for CRC disease and can be increased by other disease such as liver disease and pancreatitis, and other malignancies [17].

The mean age of the present CRC patients was 51 years. The mean age group of colorectal cancer was 65 and 70 years, respectively [18, 19]. The low education of the society may play a role for the late attendance of the patients for examination.

Serum CEA in the dead patient was high compared with that of the whole patients and still high after surgery and chemotherapy. High preoperative serum CEA and a failure to return to normal level indicated a poor prognosis and metastasis of CRC [13]. The postoperative elevation of serum CEA indicated recurrence of the disease [20].

In the present study, about 12% patients died after two years of the surgery and they were on stage D of Dukes, while other patients with stages A to C were a life. The survivals for 5 years ranged from greater than 90% in patients with stage I disease to more than 10% in patients with stage IV disease [18]. However, liver metastases were found in the studied patients with stage B and C which means bad prognosis. Stage A showed no metastases but presented only 40% of the studied patients.

The mean age of the current dead patients was 31 years. Adolescent and young adult patients with colorectal cancer had severe cancer and needed aggressive treatment without the improvement of survivals [21]. Probably, the delayed diagnosis of young adult colorectal patients was an important factor for metastasis [21].

Most of the dead patients were in Duke's D. The delayed examination of the patients due to lack of education or resistance to go to the clinic or hospital might be the reason of progresses of the disease.

In the present study, Male colorectal patients were higher than female patients. This is consistent with other studies [18, 22]. In addition, females had better survival than males, which could be due to genetic, hormonal, immunological, and environmental factors [23, 24].

In conclusion, colorectal cancer is a significant disease in Iraq. The mortality rate is high due to lack of education of the

community to that disease. CEA marker is still a good test but should be used with other clinical assessments.

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