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Could it better to use Serum Taurine Level as a Biomarker for Colorectal Carcinoma Early Detection instead of the Specific Tumor Marker?

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ABSTRACT

Background: Taurine has been shown to provide anti-inflammatory effects and to protect cells from cytotoxic effects of inflammation. Current studies have suggested that changes in systemic taurine levels can be used to expect the formation and malignant transformation of individual tumors. Colorectal carcinoma is the third leading cause of cancer-related deaths in the USA and estimated 1.4 million cases and 693,900 deaths occurring in 2012 worldwide. In the United States in 2017, there are likely to be 135,430 patients newly diagnosed with CRC and 50,260 deaths from it. In Egypt, it remains a heavy problem as about 40% of cases occur in individuals under 40 years of age. In 2018, new cases 3477 and deaths 2051, it is the 8th cancer leading death in Egypt.

Aim: Investigate the probability of using serum Taurine level as a pre- early biomarker for colorectal carcinoma, especially in the precancerous condition in Egyptian patients. Moreover, comparing serum Taurine level and specific biomarkers before and after surgical treatment.

Patients and methods: From a lot of Egyptian patients who attended the National Cancer Institute, Cairo University, presented with abdominal troubles and gastrointestinal problems; after full examination and diagnosis; one-hundred and six patients-after their approval- were classified into three groups: The first group consisted of ninety-one patients who were diagnosed with colorectal carcinoma with various stages, the second group involved eight patients who were diagnosed as benign tumors, and the third group including only seven patients that were diagnosed with specific chronic Inflammation diseases. Ten healthy volunteers enrolled as a frank control. For the first group and second group, serum Tau were measured preoperatively (a day before the operation) and postoperatively (after 45 days from the operation).

Results: While CEA and CA 19.9 showed highly significant differences in all groups compared with the control group but still clinically- for the inflammatory group and benign tumor group-they were within normal ranges. Serum Tau level showed highly significant changes between CRC group, benign group, inflammatory group and control group, as in CRC group Tau level dropped by approximately 77.5% (13.6±1.9µmol/l) below normal in control group (60.6±6.7µmol/l) moreover, lowered by ≈61% (23.4 ± 2.6 µmol/l) in benign group compared to control group. Moreover, for the specific chronic inflammatory group; its level decreased by 50% (34.8 ± 2.7 µmol/l) compared to control.

Conclusion: Serum Tau results in our study showed that; it is more valuable and more accurate early biomarker for early detection of any malignant change which may led to CRC by other means it is the most sensitive and more specific tumor marker for CRC.

Keywords: Colorectal carcinoma, Egyptian patients, Serum Taurine, CEA, CA 19.9

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In Egypt, a population-based study in Gharbia, Egypt has shown high rates of CRC in patients aged 40 years and younger; these rates were slightly higher than rates of the same age group in the United States [1]. In our study, 26.5% of patients aged younger than 40 years and 22.6% aged between 40-50 years by other mean about 50% of patients are young. The data shows that the major group of CRC patients diagnosed as grade II (No=68), grade III and metastasis (No=12), while grade I (No= 6), the specific chronic inflammatory diseases group (No=7) and benign group (No=8); this is referring to lack of medical self- care, no awareness of periodically checkup or follow up for those positive family histories, in our patients there is about 14% positive cancer family history. In 2018, new cases 3477 and deaths 2051, it is the 8th cancer leading death in Egypt [2].

Till lately, colonoscopy has been considered the "gold standard" for detection CRC and high-risk adenomas [3, 4], but its invasiveness, associated discomfort and potential risks of complications needed for the screening itself represent marked disadvantages [5]. So, tumor biomarkers have been clinically utilized such as CEA, CA19.9 and fecal occult blood testing (FOBT). However, their sensitivity and specificity are unsatisfying [6,7]. CA19.9 has been used as a marker for CRC, but it is less sensitive than CEA [8]. It is not recommended in routine follow-up after surgery [9]. Also, the FOBT has lows sensitivity, especially for early-stage colorectal cancer. Thus, examinations involving a combination of conventional screening methods have been used for the diagnosis of colorectal cancer; however, such examinations only detect about 40% of colorectal cancers [10]. However, about 20% of CRC tumors have been reported not to produce elevated serum levels of CEA despite the metastatic disease. The role of CEA in early diagnosis of CRC is controversial due to its insufficient sensitivity and organ specificity [11, 12].

Increased concentrations of CEA are rarely observed in the early stages of the disease [12]. In our study, for CEA there is a highly significant change ($P<0.01$) between all groups and control groups but no significant different ($P>0.05$) between the inflammatory group and benign group preoperatively while postoperatively no significant changes($P>0.05$). CA19.9 (carbohydrate antigen 19-9) data showed highly significant different increased ($P<0.01$) between the specific chronic inflammatory group 4.2 (2.0-21.5) and benign group 19.9 (15.9-29.0) with frank control group but still clinically within borderline (up to 22.3 u/ml), while there is a high-significant change ($p<0.01$) between the malignant group with all patient groups and control group. But for our predictable marker; taurine, there is a high impressive observations: the decreased high- significant changes ($p<0.01$) in Tau results between all groups themselves and with control group while dropped by a proximal 77.5% (13.6±1.9 µmol/l) below normal in control group (60.6 ± 6.7 µmol/l) moreover, lowered by ≈61% (23.4 ± 2.6 µmol/l) in benign group compared by control group. Moreover, for the specific chronic inflammation diseases group; its level decreased by 50% (34.8 ± 2.7 µmol/l) compared to control. Measuring serum Tau level besides CRC biomarkers show that it is most attractive, more precious and most accurate early biomarker for early detecting of any malignant change which may led to CRC by other means it is the most sensitive and more specific tumor marker for CRC. To show its keen ability to differentiate between each stage besides its sensitivity to any malignant change, it can distinguish between precancerous and cancer stage, also with high accuracy differ between stage 1 and 2; and in our study, from clinical and histopathological examinations, all patients ranged from 27-21 µmol/l, are considered precancerous cases, in parallel with another new study the same observation was recorded in different stages of HCC [13], also in other studies [14, 15]. As in our data; we suspect the pathological condition of any patient is stage I when tau level between 20-16 µmol/land stage II when tau level ranged from 12-16 µmol/l, but tau level exhibited value lower than 12µmol/l stage III of CRC is highly suspected, so tau level also can be possibly used in the classification of cancer grades, also supported with the other recent studies.

In lately study, Tau cutoff value is 20 µmol/l between cancerous and precancerous stages means any patient with Tau below that value means cancer wherever the body [16]. Other studies have proposed that changes in systemic taurine levels can be used to predict the formation and malignant transformation of certain tumors. According to previous studies [13, 16], this can lead us to possibility of using Tau in reclassification for patients, first normal range for healthy person 50-up to 70 µmol/l, below that to 45 µmol/l it can be called save margin, to above 40 µmol/l risk area, 40-30 µmol/l highly risk area highly susceptible for cancer, above 20 µmol/l precancerous stage (benign tumor), below 20 µmol/l it means cancer.

Tau, as an effective antioxidant, may hinder the increase of reactive oxygen species (ROS) in tumors, leading to a delay in the progress of cancer [17]. Also Tau could play a role in the process of anti-tumors by down-regulating matrix metalloproteinase-2(MMP-2), up-regulating N-acetylgalactosaminyl transferase. It is said that Tau may induce apoptosis in cancer cells So, Tau significantly inhibited the cell proliferation of colon the initiation of apoptosis in human breast cancer cell lines [18]. Tau is a strong candidate for the chemotherapy of breast cancer through increasing the PUMA expression independent of p53 status. And giving supplementary dose (protective dosage) of Tau for all patients presented with gastrointestinal troubles and those who were diagnosed as chronic inflammatory disease or CD, and for those who their Tau level were less than 40 µmol/l and after surgical treatment; to decrease side effect soft chemotherapy and

radiotherapy as Tulisan Effective Antioxidant, may hinder the increase of reactive oxygen species (ROS) in tumors, leading to a delay of the development of cancer, is a highly recommended. So, from this result, we can use serum Tau level as a pre-early marker, and a biomarker for detection of any malignant change, also for staging CRC and for better follow up after surgical treatments. It is already used for enhancing the immune system and induces apoptosis and inhibit cell proliferation.

CONCLUSION

Serum Tau results in our study showed that, in addition CRC biomarkers; it is most attractive, more precious and more accurate early biomarker for early detecting of any malignant change which may led to CRC by other mean it is the most sensitive and more specific tumor marker for CRC. So, we can recommend measuring its level regularly with other prognostic tumor biomarkers and screening examination for all people with abdominal and gastrointestinal problems and for precancerous patients as a pre-early biomarker for colorectal carcinoma. As its ability to distinguish between precancerous and cancer stage, also with high accuracy differ between Stage 1 and 2, and its sensitivity to any malignant change, we recommend strongly considering taurine to be used in a national classification. And giving supplementary dose (protective dosage) of Tau for all patients presented with gastrointestinal troubles and those who were diagnosed as chronic inflammatory disease or CD, and for those who their Tau level were less than 40 µmol/land after surgical treatment; to decrease side effects of chemotherapy and radiotherapy as Tau is an effective antioxidant, may hinder the increase of reactive oxygen species (ROS) in tumors, leading to a delay of the development of cancer, is a highly recommended. So, it needs further studies to confirm that observations on large scale of population as it appears the small sample size in early stage and lack data due to limited financial resources and it needs more efforts to collect first and precancerous stages patients, to prove our investigation aim, may it help in decline CRC rises and especially in young patients.

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