Original Article

The Prevalence Of Elevated Carcinoembroynic Antigen At Gorgan South- East Caspian Sea Of Northern Iran

Pathology Section

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ABSTRACT

The aim of this study was to find out the prevalence of CEA elevation among subjects, regardless of the contradictory arguments about the senstivity and specificity of this tumor marker. Carcinoemroyonic antigen (CEA) is a tumor marker widely practiced to screen, diagnose, monitor and follow-up patients with gastrointestinal, and particularly colorectal tumor. This tumor marker is not a specific antigen for colorectal carcinoma and its concentration may be elevated in other forms of carcinomas, such as breast, ovary liver and pancreas, but still its elevated serum concentration is a valuable index widely used in clinical practice for gastrointestinal carcinogen. The data for this retrospective study obtained from data base of Danesh medical diagnostic laboratory in Gorgan located in northern Iran.The conclusion of the findings of this investigation indicated that 17.39% suspected patients had tumor marker for a particular carcinoma, the CEA elevated level should be considered either for tumor or its recurrence. The findings of this study indicated that even among all controversial arguments about CEA as a specific and alarming tool to both the patients and clinician, which is the least contribution CEA level can offer in cancer patient management.

Key Words: Cancer, Gastrointestinal, Colorectal, Carcinoma

INTRODUCTION

CEA mainly is practiced to screen for the follow-up treatment of cancer, particularly the colorectal cancer, also this tumor marker is probably elevated in many other Carcinoma such as stomach, breast and ovary. CEA which originally is produced by the gastrointestinal tract in early fetal life is not considered as a screening test for carcinoma, but it is a significant tumor marker to establish the dimension of digestive tract and breast Carcinoma. The serum tumor marker concentration routinely is measured to monitor the status of patient recovery following the prescribed therapy.

Carcinoembryonic antigen is a glycoprotein having a molecular weight of approximately 200,000 Dalton [1],[2] CEA originally was found in year 1965 [1].CEA originally can be produced by embryonic and fetal life and the CEA production should be stopped after birth, but practically CEA produced even after birth and the upper limit of 5 ng/ml CEA concentration is accepted as normal and the upper limit of 7ng/ml is accepted for cigarette smokers. Serum Carcino-embryonic Antigen (CEA) Concentration is a Tumor marker which is widely prescribed for the diagnosis of colorectal carcinoma. This tumor marker is believed to have the potential to diagnose either the incidence or the recurrent of the disease following recovery of the cession, at a very early phase, prior to any clinical manifestations of the disease onset. The CEA is also widely observed for the diagnosis of gastric cancer either pre-operatively or post-operatively.[3]

CEA is a colorectal tumor marker and in some incidence it can predict the onset of the disease ahead of the clinical Symptoms of the disease itself, and this observation is considered unique amongst some other laboratory tests.

Although CEA measurement generally is used to Follow-up and screen with subsequent treatment of patients with Cancer, Particularly subjects with cancer of colon, but there are many reports with contradictory findings (4-8)CEA cannot be only specifically considered for the diagnosis and Follow-up of the colorectal cancer, There are many reports on the usefulness of CEA as a tumor marker for various types of cancer, including, breast ovary, among female patients, and CEA Tumor marker was widely used before other more specific test such as CA15.3 was intoduced. It means that now days, CEA is not routinely used to diagnose or monitor the female cancer Such as breast and ovary and other other available laboratory test such as CA15.3 are more specific [9-11],[12],[13]

Although as it was stated already CEA can also be used as a Tumor marker For other cancers such as rectum, stomach, breast, ovary and in Some Points For, Lung, liver, and pancreas but it seems among the presence of many Contradictory results, the measurement of CEA is a useful method for colorectal carcinoma during the diagnosis, follow-up and treatment of colorectal cancer. [6-17] Among all these contradictory literature about the Specificity of this Tumor marker, the aim of this retrospective study was only to investigate the status serum CEA Level among the Patients, referred by clinicians to Danesh medical diagnostic laboratory in Gorgan, located in northern Iran.

MATERIAL AND METHOD

The data for this study was obtained from Danesh medical diagnostic laboratory located in Gorgan northern Iran, south east of Caspian sea during one year period (March2009-2010). In this study the data of 207 subjects) 120 female, 87males, which referred to the above laboratory during one year (2009-10), were obtained on collecting the data of CEA serum level from the above center, each patient name was replaced with a code-name to observe the anonymity of patients. The patients mainly were age over 35 years of age.

The quantitative measurement of carcinoma embryonic antigen (CEA (for the above patients had been carried out by VIDAS CEA,

an automated test, which was applied using the ELFA technique (Enzyme linked Fluorescent assay). This technique consists of a 2-step enzymes immunoassay sandwiched method with final fluorescent detection ELFA. Once the assay is completed, results are analyzed and automatically measured.

Fluorescence is measured twice in the Reagent Strips reading curette for each sample tested. The results are automatically calculated by the instrument using calibration curves which are stored by the instrument the serum CEA concentration, were presented in ng/ml .(1,18)

RESULTS

In this study of 207 patients (120 females, 87males) referred to our center by the clinicians,16 patients from 120 female subjects showed to have CEA level of more than 7ng/ml, and only 3 female patients showed to have CEA level of between 5-7ng/ml. According to the upper limit of reference intervals of CEA, normal concentration range for CEA is 5ng/ml and only on condition of cigarette smoking, the upper limit of normal range for CEA level can be increased to 7ng/ml, as it is argued that smoking also induce CEA production, but Cigarette smoking among females is hardly seen in our region.

Only 3 females in our study showed to have CEA level of 5-7 ng/ml. and according to what was mentioned above, these 3 females are also considered to have been taken as the females with elevated CEA concentration, and as a whole 19 females out of 120 females showed to have elevated CEA levels of being at risk. According to our findings 13.33% of women showed to have elevated CEA level of more than 7ng/ml. and only2.5% showed to have the CEA value of between 5-7ng/ml, but as it was mentioned practically 15.8% should be considered for further examination in oncology.

In this study 17 patients out of 87 men referred to our laboratory for CEA determination, showed to have elevated CEA level, of more than 7ng/ml. statistically 19.5% of our male subjects should be considered for further assessment of cancer examination

In general, in this study 36 patients out of 207 subjects, (17.39%) had elevated CEA level of more than 7ng/ml. although the CEA level of more than 5ng/ml should be considered as elevated CEA, and subjects having CEA level >5ng/ml should be examined for further medical examinations, but all 17 male patient in our study with elevated CEA showed to have serum CEA of more than 7ng/ml. In summary according to the manufacture CEA kit 19.5% of men and 15.8% of females are among subjects of being at risk, and should be further examined for tumor assessment.

As a whole in this study 17.39% of sample population, referred to our laboratory, by the clinicians on the suspicion of Tumors, should be further followed up to reach to a comprehensive conclusion on the patient's health status.

We did not know the patient's medical history, which should be considered as a limitation of this present study, but it is absolutely clear that according to the standard protocols which are practiced the serum CEA level are requested by the clinicians on the either tumor diagnosis or tumor recurrence and the tumor response to the either of drug therapy or surgery. Therefore considering the findings of this study, it can be argued that the prevalence of CEA elevation of males and females which can be considered a risk to the patient, is about 17.39%.

It seems that in this region according to Table-1 more men than women are at risk (19.54, vs., 17.39%). On the basis of this study it can be argued that the prevalence of CEA elevation which should be considered as risk factors in this region located in northern Iran, south-east of Caspian sea is about 17.39% .

Gender	Total No	No:With <5ng/ml	No: With 5-7ng/ml	No:with >7ng/ml	No.Of Patient At Risk
Men	87	60	-	17(19.54%)	17(19.54%)
Women	120	111	3(2.5%)	16(13.39%)	19(15.89%)
Total Men, Women	207	171	3(1.44%)	33(15.94%)	36(17.39%)

[Table/Fig 1]: The prevalence of elevated CEA, and patients at risk.

DISCUSSION

There are many arguments about the CEA efficacy to be a effective tool in an oncologists hand to prevent the harm due to the Carcinoma including reducing the cancer patient mortality [19]. Contradictory to the latter statement the significance of CEA as a important tumor marker to check the disease recurrence, and response to the therapeutic regiment can not be ignored. The other significant explanation about this tumor marker among other available medical laboratory examination is the suitable speed to inform the medical team on the cancer patient's Condition of life [16],[17]

Although the important key role which CEA is playing in the clinical management is absolutely obvious, but still there are many reports, against the effectiveness of CEA as tumor marker, to Follow-up the state of carcinoma. The other problem facing the serum CEA concentration in playing a role as tumor marker in oncology is the interference of other substance causing the serum elevation of CEA, examples of such material are tobacco and cigarette. There are various reports indicating that smoking can elevate level of CEA [19], and producing false positive results, and therefore can be a misguide factor to the clinician in proper management of the cancer patients [19-22],[23],[24]

On the basis of these reports, the medical diagnostic laboratories kit introducing the reference interval ranges for the serum CEA level according to the smokers and non-smokers subjects.

The normal reference intervals for serum CEA considered to be < 5ng /ml and < 7ng/ml for non-smoker and smoker respectively. Among all these controversial arguments about the non-specificity of CEA level , still its serum concentration can be a valuable tool that can be used in clinical medicine and CEA Serum level can be helpful in monitoring the outcome of therapy regiment and for the assessment of cancer recurrence, particularly gastrointestinal carcinoma , although as it was mentioned above CEA can be used for evaluation of other cancers as well, and the value of CEA cannot be ignored, for screening, diagnosing, and monitoring carcinoma response to medical regiment , although CEA can not be considered adequately Sensitive and specific, and other complementary medical set up clinically should be utilized.

Serum CEA level is commonly used as a tumor marker and in particular for the gastrointestinal carcinoma in Gorgan northern Iran, and CEA is one of the common routine tumor marker requested by the clinician to be measured by the medical diagnostic laboratories and widely practiced in medicine in this region. According to our investigation in Danesh medical diagnostic laboratory research center in Gorgan, CEA is considered to be a valuable index, and on the basis of this index and other available clinical investigation tools the Cancer patients can be managed. The aim of this study was to assess the incidence of elevated CEA tumor marker in this region and on the basis of this finding, the rate and prevalence of Cancer

and in particular the gastrointestinal Carcinoma was determined. This study was designed to assess the elevation of CEA above its normal range and in this study the values of (>5ng/ml) were considered as elevated tumor marker and can be considered for further examination.

In this study we did not concentrate on the patient history, which can be considered as the limitation of the study, but the only concept we were looking for was the prevalence of CEA elevation and to establish the possible rate of cancer occurrence in this region of northern Iran located in the South east of Caspian Sea. We aimed to establish probable Cancer incidence of gastrointestinal particularly in this region, utilizing a serum tumor marker such as CEA, and whether the clinicians can be helped to manage the patient at a very early stage of disease onset, keeping in mind the laboratory expenses of various tests, perhaps the patients blood test can be started with a single CEA test to be followed by other examinations, if it was advised by the clinicians.

Therefore CEA elevation may be a starting point to be aware of a danger ahead and on the basis of the elevated CEA level the patient can be assessed and evaluated at early stage of carcinoma, of gastrointestinal in first line and other carcinoma in second line of clinical examination. After analysis of serum CEA levels we found that 36 patients had elevated CEA concentration, which means 17.39 % of people referred to this center can be considered for further examination of Carcinoma. In our study we found more men than women are at risk (19.5% vs. 15.8%) if this means that gender in this case can play a role, this idea can be a topic for future study in this region. The literature review of this study mostly indicated that the CEA can not be considered sensitive and specific, but the aim of this study was not to agree or disagree with literature finding and in addition disagree with those reports for, or, against the CEA sensitivity, because this study was not to designed to approach that idea. We argue amongst all these literature with contradictory findings, that one fact was completely clear and that there was a unique acceptance of CEA as tumor marker which can be produced by variety of carcinoma, of course with some disagreement on type of tissues which can be involved. We found that among the reports of the literature study, the colon, rectum, stomach, breast and ovary are front runner carcinoma with CEA elevation , although lung, liver pancreases cancer may also produce this tumor marker, although the gastrointestinal tumors are at first lines investigation. But we argue regardless of which type of cancer induce the elevated production CEA, the measurement of this tumor marker by the laboratory at least can be a first clue for the clinician to continue further investigation of such killer disease

In this study we found that all affected men exhibited CEA level of ≥ 7ng/ml. The same finding was noticed among women of this study with exception of 2.5% of female with CEA concentration of 5-7 ng/ml which is over the acceptable higher limit of normal of 5ng/ml In this study we did not know the history of cigarette smoking among our subjects. Even if we consider for the sake of argument that all of the patients referred to this laboratory center are heavy smoker, the value of CEA > 7 ng/ml seriously should be considered as a risk factor, and the patient with CEA > 7ng/ml in this study for sure were required further attention. This argument is valid when we are definitely dealing with patients who are cigarette smokers, but we argue as for as getting a proper history of cigarette smoking , and the number and the length of cigarette consumption can not be easily explained even by the patients themselves , therefore we suggest the normal range of 5ng/ml should be considered the upper border line and the value > 5ng/ml to be requested for further laboratory and other Para- clinical examination of carcinoma but, in our study all suspected patients except 3 patients exhibited to have CEA of more than 7ng/ml. There are also some reports that CEA Serum concentration, among light hookah smoker are usually within normal reference range and therefore the interference of smoking in elevation of CEA should be ignored in such killer disease, and the patient should be further assessed for possible carcinoma, to avoid the irreversible consequences, by ordering further examination and evaluations to be able to mange the patient on time.

CONCLUSION

1. On the basis of literature review in this study serum CEA level is elevated, also, not specifically in variety of cancers, including breast, ovary, lung, but it seems CEA Serum concentration is more predominantly elevated in patients with gastrointestinal, particularly colon carcinoma.
2. Although the upper reference normal range for serum CEA level for non-smoker and smoker are < 5ng/ml and<7ng/ml respectively but some reports the normal upper limit for light smokers and non-smokers do not differ and therefore the CEA level of >5ng/ml can be considered as a CEA elevation.
3. On the basis of above definition for the upper limit normal for CEA level the prevalence of elevated CEA level with possibility of considering either cancer or its recurrence incidence in our region within northern Iran can be assessed to be as 17.39%
4. On the basis of 17.39% prevalence of serum CEA elevation among subjects suspected of being cancer patients, and unique nature of CEA in cancer detection the opportunity for further clinical examination should not be lost and complementary examinations should be followed when serum CEA concentration was elevated above the upper limit of normal of 5ng/ml
5. In our investigation it seemed more men are at risk of having elevated CEA of more than 7ng/ml, a matter which can be a topic for further study in this region.

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