RESEARCH ARTICLE

Serum Levels of CA15-3, AFP, CA19-9 and CEA Tumor Markers in Cancer Care and Treatment of Patients with Impaired Renal Function on Hemodialysis

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Abstract

Since renal failure causes decrease in tumor marker excretion, use of these markers in cancer care and treatment in patients with renal insufficiency or hemodialysis is controversial. The aim of this study was to investigate differences of serum levels of tumor markers CA15-3, AFP, CA19-9 and CEA in patients with impaired renal function. A total of 100 patients referred to the Tabriz Immam Reza and Amiralmomenin hospital from June 2010 to November 2011 were selected for study. Subjects were divided to 3 groups of healthy, dialysis and renal failure but non hemodialysis cases, the last category being re-grouped based on creatinine clearance. No significant relationship between different groups in serum levels of CEA (P=0.99) and CA19-9 (P=0.29) tumor markers was found. A significant correlation was observed between serum levels of AFP (P<0.001) and CA15-3 (P<0.001) and also a tendency between creatinine clearance and CEA (r=0.05, P=0.625). Creatinine clearance significantly correlated with AFP (P<0.001, r=0.53) and CA15-3 (p=0.00, r=-0.412), but not CA19-9 (P=0.089, r=-0.171). According to results of this study it appears that use of tumor markers in patients with impaired renal function should be performed with special precautions.

Keywords: Cancer cases -chronic kidney disease - tumor markers - hemodialysis - impaired renal function

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Introduction

Although tumor markers have been used for many years but little information exists about their metabolism, especially in Renal patients (Richard and Pincus, 2007; Tzitzikos et al., 2010). Since the liver and kidney failure causing decrease of tumor markers excretion kinetics and shown that the concentration of some tumor markers in chronic kidney disease even without existence of malignancies generating these markers is higher than healthy individuals serum concentration. Therefore the use of these diagnostic markers it has been debated and clashes in hemodialysis patients (Filella et al., 1990; Richard and Pincus, 2007; Tzitzikos et al., 2010).

The first tumor markers was recognized in 1847 and so far, about 100 various tumor markers have been identified (Richard and Pincus, 2007; Tzitzikos et al., 2010). The serum tumor markers are proteins or glycoprotein which depending on their type are secreted by tumoral and normal cells (Tzitzikos et al., 2010). Application of these secreted substances can be used as a) Population Screening tests b) Diagnosis and identification of individuals with the disease in the early stages of the disease c) evaluation and Prognosis of the disease and d) follow up and assessment of disease recurrence (Polenakovic et al., 1997; Danişman et al., 2000; Richard and Pincus, 2007). Tumor marker concentrations in healthy individuals is low or zero, and its increasing suggest the incidence of related Tumor (Danişman et al., 2000; Richard and Pincus 2007; Xiaofang et al., 2007; Tzitzikos et al., 2010). Because the liver and kidney failure causing decrease the kinetic of tumor markers excretion and shown that the concentration of some tumor markers in patients with chronic kidney disease without malignancy is higher than its concentration in normal individuals in this respect, the use of these markers in hemodialysis patients is highly debated (Visser et al., 1995; Xiaofang et al., 2007; Tzitzikos et al., 2010). metabolism and excretion mechanisms of many tumor markers remains unknown so far and in some articles It has been shown that chronic renal failure is associated with disturbances in the excretion of these tumor markers which causes changes in their serum level (Danişman et al., 2000; Richard and Pincus, 2007; Rampino, 2009). Although tumor markers have being used for many years but there is little information about their metabolism and catabolism particularly in those who has abnormal renal function (Cases et al., 1991; Danişman et al., 2000; Richard and Pincus, 2007; Xiaofang et al., 2007; Rampino,

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2009).

There are several metabolic abnormalities in chronic renal failure certainly, this disorder could influence on serum concentrations of various proteins such as tumor marker to Ascending and descending also the diagnostic value of tumor markers in the diagnosis, treatment and follow-up of patients with cancer and chronic renal failure in simultaneous involvement being questioned (Walz et al., 1988; Djavan et al., 1999; Danişman et al., 2000; Xiaofang et al., 2007; Tzitzikos et al., 2010).

The results of several studies in this field has not yet been reached to a final decision whereas some studies indicate the effects of chronic renal failure on tumor markers but some articles have not confirmed the existence such a relationship (Odagiri et al., 1991; Lye et al., 1994; Arik et al., 1996; Arican et al., 1999; Danişman et al., 2000; Engin et al., 2007; Rampino, 2009; Tzitzikos et al., 2010; Shu et al., 2012).

The aim of this study was the evaluation of renal function and hemodialysis on serum tumor markers according to their importance in a period of one year from June 2010 to November 2011.

Materials and Methods

This study is a descriptive – analytic study from 473 people of Participants referred to the Tabriz Immam reza and Amiralmomenin hospital laboratories from June 2010 to November 2011 According to inclusion and exclusion criteria such as kidney disease duration less than 6 months, having any malignancy, having any other Specific disease history except kidney disease, abnormal laboratory results except those related to renal disease, Erythropoietin consumption with other than doses of 400 (conventional dose administered in patients with renal insufficiency) 100 people were selected for study and the serum levels of tumor markers (CEA 'CA15-3 'AFP 'CA19-9)measurements along with measurements of creatinine in serum and urine was performed .

In this study, the patients studied were divided into 5 groups as follows: a) Control group b) Dialysis group c) Non dialysis renal failure patients d) Individuals with creatinine clearance greater than 50 ml/min (n=21) e) Individuals with creatinine clearance between 25-50 ml/min (n=16) and f) Individuals with creatinine clearance less than 25 ml/min (n=21).

Blood samples of dialysis patients were collected before periodic dialysis and Fasting blood samples were taken at other people Samples were collected gradually in Central laboratories of Imam reza and Amiralmomenin hospitals and after separating of serum they were kept at a temperature of -70 degrees and for preventing the reduction of tumor markers serum levels at the time of sample collection experiments were performed in several different time.

For the measurements of tumor markers (CEA 'AFP 'CA15-3 'CA19-9), Can Ag Laboratory kit (Fujirebio Diagnostics Inc, USA) by the ELISA method By the ELISA AUTOMATIC HUMAN (Made in Germany) was used.

Statistical analysis

Statistical analysis was performed using by SPSS™ 16.0 software. ANOVA with Spearman's and Kendall's Correlation test was used. The results have been considered significant in case of P≤0.05.

Results

The subjects are grouped into the following: a) those people who need hemodialysis; b) healthy subjects; c) people with chronic kidney disease without dialysis and creatinine clearance above 50; d) People with chronic kidney disease without dialysis and creatinine clearance between 50-25; e) People with chronic kidney disease without dialysis and creatinine clearance less than 25.
The results obtained showed no significant correlation in levels of CEA (P=0.99) and CA19-9 (P=0.29) between different groups However, a significant relationship was seen between different groups in levels of AFP (P<0.001) and CA15-3 (P<0.001). Significant correlation was not found between different groups in body mass index (BMI).

Figure 1A shows the correlation between creatinine clearance and CEA which is not statistically significant also Figure 1B also shows the correlation between creatinine clearance and AFP, which is statistically significant (P<0.001, r=0.53).
Figure 1C shows that there was a significant correlation between creatinine clearance and CA19-9 (P=0.089, r=-0.171). Figure 1D shows that There was a significant correlation between creatinine clearance and CA15-3 which was statistically significant (p=0.00, r=-0.412).

Table 1. Mean the Serum Levels of Four Tumor Markers in Different Groups

	Group 1 n=27	Group 2 n=23	Group 3 n=13	Group 4 n=16	Group 5 n=21
CEA	1.48±2.03	1.53±1.35	1.63±1.55	1.59±1.32	1.71±1.45
AFP	0.85±1.34	5.29±2.32	5.55±2.12	5.03±2.64	4.36±2.96
CA19-9	29.4±46.6	13.6±7.74	21.8±10.6	21.0±8.70	24.7±10.16
CA15-3	33.0±15.4	11.7±5.49	14.5±8.10	16.1±7.57	15.1±10.07

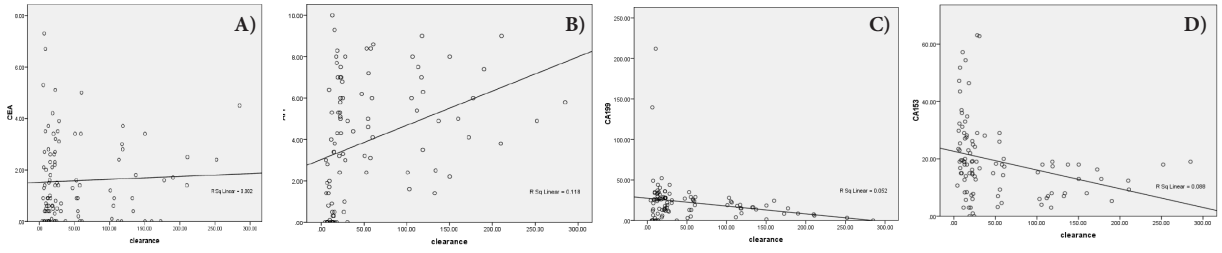

Figure 1. The Correlation between Creatinin Clearances and A) CEA, B) AFP, C) CA19-9 and D) CA15-3

Discussion

Tumor markers that could be made of protein and carbohydrate or glycoprotein and occasionally they have Hormonal or enzymatic properties nowadays they have an important role in the diagnosis and treatment of patients in different tumors, benign and malignant (Richard, 2007; Xiaofang et al., 2007; Tzitzikos et al., 2010). Since the excretion and destruction of some tumor markers is done through the kidneys that can affect their serum levels with regard to level of clearance and renal function (Richard, 2007; Jiang and Pu, 2010).

In this study, to clarify the role of the kidney and its effect on serum tumor markers levels four different measurements of tumor marker that commonly used in patients with malignancy was performed.

This marker was including CEA, AFP, CA1553 and CA19-9 and five groups of patients with and without renal failure and dialysis according to creatinine clearance rate was measured.

As seen in the results of the above tables significant differences between the groups with adequate renal function and mild or complete kidney failure in AFP, CA15-3 tumor markers with a P-value less than 0.0001 was seen but these relationship between the CEA, CA19-9 tumor markers was not found.

These results compared with other studies, including a study of Tzitzikos and Colleagues Shows similar results on markers CA15-3, CEA, CA19-9 but the results of the AFP unlike the above study did not show a significant difference in different groups that represents an increase in AFP in patients with renal insufficiency (Tzitzikos et al., 2010).

However, in another study by Xiaofang and Colleagues that have been done with further sample size (n=232) about AFP has also obtained results similar to a recent study (Xiaofang et al., 2007).

Because the number of patients in the previous studies was less than the number of patients in the current study (Engin et al., 2007; Tzitzikos et al., 2010) these differences may be solved by increasing sample size.

Thus for the diagnosis and follow-up of AFP, CA15-3 in patients with kidney failure should be take the necessary precautions and If possible another more reliable method that is not affected by renal failure be used.

But the remaining two markers CEA, CA19-9 can be used for diagnosis and follow up in patients with renal insufficiency like other patients and normal subjects.

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