ejpmr, 2021,8(4), 90-94

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

Research Article

ISSN 2394-3211

EJPMR

EFFECT OF HEMODIALYSIS ON CONCENTRATION OF TOTAL PROSTATE SPECIFIC ANTIGEN AMONG PATIENTS WITH CHRONIC RENAL FAILURE ATTENDING BRACK GENERAL HOSPITAL AL-SHATI, LIBYA

Ali, F. Hawad[1], Abdullah Shebah[2]*, Eljelani Salim[2], A.A. Elwafa[2], Abdulbasit Naiel[2], Maryam M. Bisher[2], Nabiha Aljoaad[2], Albashir M. A. Yhmed[2], Mohamed Farag Elbreki[2] and Hamzah Saad[3]

[1]Department of Biochemistry, Faculty of Medicine, Sebha University, Libya.
[2]Department of Medical Lab Technology, Faculty of Engineering Science and Technology, Sebha University.
[3]HigherInstitute of Sciencs Medical Techniques, Al-Shati, Libya.

***Corresponding Author: Abdullah Shebah**

Department of Medical Lab Technology, Faculty of Engineering Science and Technology, Sebha University

Article Received on 04/02/2021 **Article Revised on 24/02/2021** **Article Accepted on 14/03/2021**

ABSTRACT

Hemodialysis is the most common method used for renal replacement therapy for patients with kidney disease. Tumor markers (TMs) are widely used for the follow-up of progression and response to treatment of certain neoplastic diseases, but their specificity in hemodialysis patients is controversial. Prostate-specific antigen (PSA) has been shown to be a useful marker in the early detection of prostate cancer. **Objective:** this study were aimed to determine the total prostate–specific antigen (t–PSA) levels in hemodialysis patients in comparison to normal subjects, as well as the influence of the dialysis duration on its levels. **Materials and Methods:** This study was conducted on 44 persones, from which 22 hemodialysis patients suffering from Renal Failure and 22 persones seemingly healthy people, they were used as control samples. **Results:** t-PSA in hemodialysis patients had higher t-PSA levels compared with the healthy subjects (0.8 ±0.80 vs.0. 6 ±0.33 ng/ml, $p > 0.05$), although this difference was not statistically significant. Concentration of t-PSA was varied among patient groups according to their dialysis periods, hence t-PSA levels were decreased as dialysis period increased. However, this variation was not statistically significant ($p > 0.05$). **Conclusion:** In this present study, the increased levels of t-PSA concentration were recorded among both hemodialysis patients and Dialysis patients who have fewer years of dialysis, however, statistical analysis has shown no significance. as the P-value was ($p > 0.05$).

KEYWORDS: Prostate-specific antigen, Renal failure, Hemodialysis, TMs, Dialysis periods.

INTRODUCTION

Chronic renal disease (CRD) is a patho-physiological process with various etiologies, resulting in the unavoidable slow destruction of nephrons number and function and frequently leading to end-stage renal disease (ESRD). In turn, ESRD represents a clinical state or condition which lead to irreversible loss of endogenous renal function, of adegree sufficient to render the patient permanently dependent upon renal replacement therapy (dialysis or transplantation) in order to save life.[1] Since the first hemodialysis machine was established in the 1940s, this machine is thought to be competent of prolonging a person's life and curing uremia symptoms. In the 1970s, the spread of this machine has expanded and can save the lives of patients who have acute kidney failure or end-stage renal failure.[2] CRDis the most common cancer in males from Europe, North America and some African countries, occurring in 9.7% of all cancers in males, reaching 15.3% in developed countries and 4.3% in developing countries.[3] TMs represent useful tools in diagnosis and clinical management of patients with cancer, since they are simple to use, minimally invasive, and easily measured in blood and urine. More than 20 different substances (hormones, metabolites, enzymes, immunoglobulins, tumour associated antigens, and oncogenes) have been identified as TMs and are currently employed in clinical analysis. Some markers are positive in a single type of cancer, others are detectable in more than one type. TMs are widely used for the follow-up of progression and response to treatment of certain neoplastic diseases, but their specificity in hemodialysis patients is controversial.[4] The use of the TMs in dialysis patients is a largely debated subject in the literature because the candidates for transplantation and hemodialysis are persons with a high risk for developing malignancies and because the half-time of the serum TMs' concentrations depends upon the renal and hepatic function.[5] PSA is a glycoprotein produced primarily by the epithelial cells that line the acini and ducts of the prostate gland. PSA is concentrated in prostatic tissue, and serum PSA levels

are normally very low.[6] Disruption of the normal prostatic architecture, such as by prostatic disease, allows greater amounts of PSA to enter the general circulation. Elevated serum PSA levels have become an important marker of prostate pathologies—which include benign prostatic hyperplasia, prostatitis, and subsequent needle core biopsy or transurethral resection of the prostate (TURP).[7] Prostatic intraepithelial neoplasia (PIN) does not appear to raise serum PSA levels.[8] The measurement of serum PSA is an important clinical tool for the detection and monitoring of prostate cancer.[9] Prostate-specific antigen (PSA) has been shown to be a useful marker in the early detection of prostate cancer. But the diagnostic validity of PSA is uncertain in hemodialysis patients. Previous studies have demonstrated that PSA was not eliminated by hemodialysis, and have noted that post-dialysis levels were actually slightly higher than pre-dialysis levels.[10]

The aims of this investigation were to evaluate the influence of hemodialysis and the duration of hemodialysis on the leveles of Prostate-Specific Antigen in hemodialysis patients.

MATERIALS AND METHODS

Patients and controls

This Study was conducted on forty four (44) patients, from which twenty two (22) were suffering from end-stage renal disease, attending dialysis unit at Brack general hospital, and twenty two (22) were used as control (seemed to be free from any diseases that may affect the urinary system or other diseases related to hyperplasia in the prostate and prostate tumors). Their ages were ranged from 18-70 and 22-70, respectively.

Samples collection and preparation

Five (5) ml of venous blood were withdrawn in sterile free anticoagulant tubes. Samples were then subjected to centrifugal force at a speed of 3000 rpm for 5 minutes, for serum separation. After centrifugation, serum samples were transferred into sterile eppendorf tubes using a semi-automatic pipette and stored at -20 ° C until used.

Measurement methods

Following samples collection and preparation, the levels of serum t-PSA were measured using **ichroma™ PSA Plus** (Boditech, Korea)**, which** is a fluorescence Immunoassay (FIA), for the quantitative determination of Prostate Specific Antigen in human serum level of t-PSA was determined based on amount of fluorescence generated from antigen-antibody interaction, sample considered to have higher level of t-PSA if its concentration excesses the reaction cut-off (4ng/ml).[11]

The principle of interaction

The test use a sandwich immunodetection method; dried detector antibody in buffer binds to antigen in sample, forming antigen-antibody complexes, and migrates onto nitrocellulose matrix to be captured by the other immobilized-antibody on test strip.The more antigen in sample forms the more antigen-antibody complex and leads to stronger intensity of fluorescence signal on detector antibody, which is processed by instrument for ichroma™ tests to show PSA concentration in sample.

Statistical analysis

The results of the effect of hemodailysis and duration on t-PSA levels in hemodailysis patients compared with that of control group were expressed as means ± standards deviation and analyze the statistical by means of t-test by using computer-based statistical software Minitab program (version 17). The P values were considered to be significant at levels of less than or equal ≤ 0.05. Data were graphically represented using Microsoft Excel computer program.

RESULTS

The serum levels of t-PSA in hemodialysis patients were increased (0.80 ±0.80 ng/ml) higher than that of controls group (0.60 ±0.33 ng/ml). However, these differences were not statistically significant (p>0.05), table 1 and figure 1 displayed PSA levels (Mean ± SD) in control and hemodialysis patients.

Table 1: Showing PSA levels (Mean ± SD) in Control and Hemodialysis Patients.

M* = Mean

Variables	No	PSA (ng/ml)M*±SD**	p-value
(N.S)	22	0.8±0.80	0.25
control	22	0.6±0.33	**(N.S)**

SD** = Standard deviation

N.S =Not significant at P > 0.05

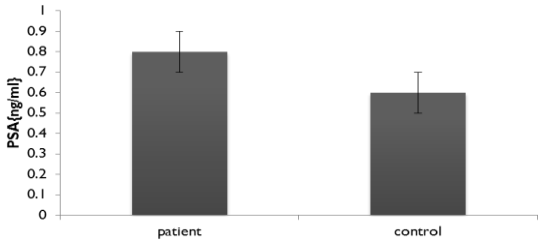

Figure 1: Serum levels of total PSA in controls and hemodialysis patients.

Table (2) displays the mean ± standard deviation of the levels of serum t-PSA among hemodialysis patients based on the number of years of dialysis, The mean ± standard deviation of t-PSA level was increased by 0.26 in patients who were subjected to short period of dialysis (0- 5 years) compared with those who have had lengthier dialysis period (6-11 years). Reliant on statistical comparison, no significant difference (p = 0.4) were recorded among both categories, as shown in table 2 and figure 2.

Table 2. Displays effect of duration period of dialysis on t-PSA levels in hemodialvsis patients.
M* = Mean

Duration of dialysis	No	PSA (ng/ml) M*±SD**	p-value
0 -5 years	10	0.92±1.03	0.4 .25
6-11years	12	0.66±0.60	(N.S)

SD**= Standard deviation
N.S =Not significant at P > 0.05

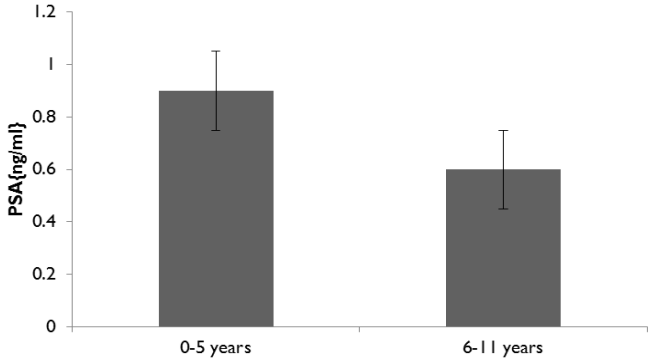

Figure 2: duration period of dialysis on t-PSA levels in hemodialvsis patients.

DISCUSSION

Raised levels of a number of tumour markers can be normally identified in patients with diminished kidney function because their renal removal is retarded or because a neoplasia is really existing, given the higher risk of developing malignancies in these patients, because of altered immune-surveillance induced by the inflammatory state or by immunosuppressive therapies. Therefore, cancer screening and surveillance are important in this population, the possibility of false positive results notably reduces the diagnostic value of those markers that are mainly removed by renal elimination.[12-15] The complication and metabolism impairment in patients with impaired renal function, including those with proteinuria, reduction of glomerular filtration rate (GFR) with chronic kidney disease, end stage renal disease (ESRD), on renal replacement therapy by hemodialysis, peritoneal dialysis, or having had kidney transplantation, because of glomerular filtration rate reduction which can lead to impaired excretion of most tumour markers, proteinuria may affect the metabolism and excretion of protein biomarkers, the chronic inflammatory state associated with kidney disease can affect plasmatic and urinary levels of some markers and the markers with small molecular size could be eliminated by dialysis. This leads to, levels of tumour markers can be higher in patients with renal dysfunction because of reduced urinary elimination or even lower because of removal by the dialysis procedure[16]. The prostate specific antigen remain the preferable and greatest widely used tumor marker for prostate in clinical practice currently. It is a glycoprotein with a molecular weight of 33KD. Prostate disease especially is normally used in the diagnosis and follow-up of prostate disease specifically prostatic cancer.[16] evaluation of serum PSA is currently recognized as first-line investigation in the diagnosis of prostate cancer.[17] In this study the t-PSA levels were increased as compared with that of control, Although there was no significant differences (p>0.05), in spite of that the result was within the normal range. The results of this study was consistent with that of.[18-24] who observed increase of the level t-PSA after dialysis, whereas, contrasts with those of[25-26] who observed lower level of t-PSA in hemodialyzed group compared with control, they rationalize their result to the small molecular weight of the PSA which can be eliminated by dialysis. Whereas, the effect of dialysis duration on t-PSA levels in hemodialysis patients in this study decreased t-PSA levels as the dialysis duration increased, this finding is consistance with that of.[27] It is assumed that tPSA is excreted rather by hepatobiliary mechanisms than eradicated by dialysis or renal clearance.[28] Certain animal studies indicate that PSA is processed and emitted by hepatobiliary system without definite evidence of renal clearance[29]. Studies in hemodialysis patients regarding the level tPSA or f/t ratio provided conflicting results.[28,30,32] Although many studies.[33,34,36] Exhibited an elevaion in the post-dialysis tPSA serum level compared with pre-dialysis tPSA levels, Djavan et al found no significant reduction in post-dialysis tPSA serum level.[28]

CONCLUSION

Hemodialysis, can impact the level of t-PSA, by constriction of blood volume with elimination of wastes leads to increase t-PSA level, whereas, increase in dialysis duration period decrease t-PSA level.

The **limitations** of this study were low number of patients where we can not study the impact of age on the t-PSA level, also it was not possible to measure.

ACKNOWLEDGEMENT

The authors like to acknowledge the haemodialysis patient for their participation in this study and also the haemodialysis unit workers for their valuable contribution.

REFERENCES

1. Hakim, Yasir AH, et al. "The effect of hemodialysis on hemoglobin concentration, platelets count and white blood cells count in end stage renal failure." International Journal of Medical Research & Health Sciences, 2016; 5.5: 22-35.
2. Mandayam S, Shahinian VB. Are Chronic dialysis patients at increased risk of cancer?. J Nephrol, 2008; 21: 166-174.
3. Grönberg, Henrik. "Prostate cancer epidemiology." The Lancet, 2003; 859-864.
4. Yu, Xiaofang, Xialian Xu, and Zhibin Ye. "Effect of renal function and hemodialysis on the serum tumor markers in patients with chronic kidney disease." Frontiers of medicine in China, 2007; 308-311.
5. Gireada, Alexandra, et al. "TUMOR MARKERS IN HEMODIALYZED PATIENTS." Romanian Medical Journal, 2016.
6. Cookson, Michael S., et al. "Variation in the definition of biochemical recurrence in patients treated for localized prostate cancer: the American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel report and recommendations for a standard in the reporting of surgical outcomes." The Journal of urology, 2007; 540-545.
7. Schroder FH, Wildhagen MF: Screening for prostate cancer, evidence and perspectives. BJU Int, 2001; 88: 811–817.
8. Alexander, Erik E., et al. "Prostatic intraepithelial neoplasia does not appear to raise serum prostate-specific antigen concentration." Urology, 1996; 693-698.
9. Tzitzikos, G., et al. "Measurement of tumor markers in chronic hemodialysis patients." Saudi Journal of Kidney Diseases and Transplantation, 2010; 50.
10. Sumura, Masahiro, et al. "Diagnostic value of serum prostate specific antigen in hemodialysis patients." International journal of urology, 2003; 247-250.
11. Jung K, Klinggr P, Brux B, et al. Preanalytical Determinants of Total and Free Prostate-Specific Antigen and Their Ratio: Blood Collection and Storage Conditions. Clin. Chem, 1998; 44: 685-688.
12. P. Maisonneuve, L. Agodoa, R. Gellert et al., "Cancer in patients on dialysis for end-stage renal disease: an international collaborative study," The Lancet, 1999; pp. 93–99.
13. P.-H. Weng, K.-Y. Hung, H.-L. Huang, J.-H. Chen, P.-K. Sung, and K.-C. Huang, "Cancer-specific mortality in chronic kidney disease: longitudinal follow-up of a large cohort," Clinical Journal of the American Society of Nephrology, 2011; pp. 1121–1128.
14. M. Buemi, A. Lacquaniti, D. Bolignano et al., "Dialysis and the elderly: an underestimated problem," Kidney and Blood Pressure Research, 2008; pp. 330–336.
15. M. Buemi, F. Floccari, C. Costa et al., "Dialysis-related genotoxicity: sister chromatid exchanges and DNA lesions in T and B lymphocytes of uremic patients. Genomic damage in patients on hemodiafiltration," Blood Purification, 2006; pp. 569–574.
16. A. Cases, X. Filella, R. Molina, A. M. Ballesta, J. Lopez-Pedret, and L. Revert, "Tumor markers in chronic renal failure and hemodialysis patients," Nephron, 1991; pp. 183–186.
17. Polascik TJ, Oesterling JE, Partin WA: Prostate-specific antigen: a decade of discovery– What we have learned and where we are going. J Urol, 1999; 162: 293–306.
18. Mehdi, Wesen & Wahed.AL-Helfee, Wiaam & Dawood, Ashgan. Study of Several Anti oxidants , Total Acid Phosphatase, Prostatic Acid Phosphatase, Total and Free Prostate-Specific Antigen in Sera of Man with Chronic kidney failure. Kerbala Journal of Pharmaceutical Sciences, 2012; 4: 155-165.
19. cancerCarter HB, Pearson DJ, Matter JE, Brant LJ, Chan DW, Andres R, Fozard JL, Walsh PC: Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease, 1992; 267: 2215-2220.
20. Reissigl A, Bartsch G. Prostate-specific antigen as a screening test. The Austrian experience. Urol Clin North Am, 1997; 24: 315-21.
21. Greene, Kirsten & Albertsen, Peter & Carter, Ballentine & Gann, Peter & Han, Misop & Kuban, Deborah & Sartor, A & Stanford, Janet & Zietman, Anthony & Carroll, Peter, 2009. Prostate Specific Antigen Best Practice Statement: 2009 Update. The Journal of urology. 182. 2232-41. 10.1016/j.juro.2009.07.093.944
22. Danişman A, Kiliç S, Kukul E, Yakupoğlu G, Güntekin E, Baykara M, Sevük M. Do renal failure and hemodialysis have any effect on the elimination of free and total prostate-specific antigen? Eur Urol, 2000; 37(5): 579-81.
23. Maoujoud O, El Machtani S, Asseraji M, et al. Serum tumor markers in hemodialysis patients. The International Journal of Artificial Organs, 2014; 37(2): 126-132.

24. Sasagawa I, Kubota Y, Hayami S, Adachi M, Nakada T, Miura H, Imai K. Serum levels of total and free prostate specific antigen in men on hemodialysis. J Urol, 1998; 160(1): 83-5. PMID: 9628610.
25. Douville, Pierre, and Marco Tiberi. "Effect of terminal renal failure on the ratio of free to total prostate-specific antigen." Tumor biology, 1998; 113-117.
26. Tzanakis, Ioannis, et al. "Prostate-specific antigen in hemodialysis patients and the influence of dialysis in its levels." Nephron, 2002; 230-233.
27. GÜMÜS, BILAL, et al. "SERUM LEVELS OF TOTAL ACID PHOSPHATASE, PROSTATIC ACID PHOSPHATASE, TOTAL AND FREE PROSTATE-SPECIFIC ANTIGEN IN PATIENTS WITHIN CHRONIC HEMODIALYSIS PROGRAM." Official Journal of the Brazilian Society of Urology, 2001; 133-135.
28. DJAVAN, Bob, et al. Impact of chronic dialysis on serum PSA, free PSA, and free/total PSA ratio: is prostate cancer detection compromised in patients receiving long-term dialysis?. Urology, 1999; 53.6: 1169-1174.
29. GLEAVE, Martin E., et al. Serum prostate specific antigen levels in mice bearing human prostate LNCaP tumors are determined by tumor volume and endocrine and growth factors. Cancer research, 1992; 52.6: 1598-1605.
30. Port FK, Ragheb NE, Schwartz AG, Hawthorne VM. Neoplasms in dialysis patients: a population-based study. Am J Kidney Dis, 1989; 14(2): 119-23. doi: 10.1016/s0272-6386(89)80187-8. PMID: 2787957.
31. Marple JT, MacDougall M. Development of malignancy in the end-stage renal disease patient. Semin Nephrol, 1993; 13(3): 306-14. PMID: 8321930.
32. Harper, L., et al. "Prostate-specific antigen levels in patients receiving long-term dialysis." British journal of urology, 1995; 482-483.
33. Sasagawa I, Kubota Y, Hayami S, Adachi M, Nakada T, Miura H, Imai K. Serum levels of total and free prostate specific antigen in men on hemodialysis. J Urol, 1998; 160(1): 83-5. PMID: 9628610.
34. Kabalin, John N., and John C. Hornberger. "Prostate-specific antigen is not excretedby human kidney or eliminated by routine hemodialysis." Urology, 1991; 308-310.
35. Sasagawa, Isoji, et al. "Serum prostatic acid phosphatase, gamma-seminoprotein and prostatic specific antigen in hemodialysis patients." Urologia internationalis, 1992; 181-183.
36. Monath, James R., et al. "Effects of hemodialysis on prostate-specific antigen." *Urology*, 1993; 398-400.