

## EFFECT OF HEMODIALYSIS ON TOTAL, FREE AND PERCENT-FREE PROSTATE-SPECIFIC ANTIGEN

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### ABSTRACT

**Objective:** To evaluate the effect of hemodialysis on serum total, free and percent free prostate specific antigen (PSA).

**Patients and Methods:** This study included 34 men with chronic renal failure (mean age 58 years, range 45-80) who received hemodialysis with low flux membranes. We measured pre- and post-hemodialysis total PSA (tPSA), free PSA (fPSA) and hematocrit (Htc) at one dialysis session. Additionally, the percent fPSA to tPSA (f/t PSA) ratio was calculated before and after dialysis. Htc was measured before and after dialysis to determine the degree of hemoconcentration and the correlation between PSA levels and Htc.

**Results:** There were statistically significant increments in the mean values of tPSA (pre-dialysis 1.2, post-dialysis 1.4 ng/ml) and f/tPSA ratio (pre-dialysis 28.2%, post-dialysis 35.2%). In addition, a significant increase in Htc was noted after dialysis. The mean pre-dialysis fPSA was 0.4 and

the post-dialysis value was 0.43 ng/ml (difference not statistically significant). The degree of hemoconcentration was not statistically correlated with the elevation in the values of tPSA, fPSA and f/tPSA

**Conclusions:** Although the increment in tPSA was statistically significant, it was not clinically meaningful. The most likely explanation for the increment in tPSA and fPSA after hemodialysis is volume contraction, and hemodialysis with low flux membranes appears to have no effect on PSA clearance. Pre-dialysis determination of tPSA probably provides no false-positive results. Therefore, we advocate that serum PSA determination is done in conjunction with digital rectal examination (DRE) and/or transrectal ultrasonography (TRUS) in patients on dialysis, especially those who are candidates for renal transplantation, to rule out prostate cancer.

**Key words:** Hemodialysis, total PSA, free PSA.

### INTRODUCTION

The incidence of malignancy is increased in hemodialysis patients compared to the general population<sup>1,2</sup>. The absent or minimal existence of symptoms of prostatism makes the utility of PSA more significant in patients on hemodialysis. Furthermore, the relative increase in the age of patients currently undergoing renal transplantation with adjunctive immunosuppressive therapy could be catastrophic in the face of a pre-existing non-detected malignancy. Therefore, it is necessary to know the effect of hemodialysis

on PSA. In this study, we investigated the influence of one hemodialysis session on tPSA, fPSA, f/t PSA ratio and the relation with hemoconcentration.

### PATIENTS AND METHODS

The study included 34 patients with a mean age of  $58.2 \pm 1.7$  years (range 45 - 80). All patients suffered end-stage renal failure and underwent hemodialysis three times per week at a single outpatient hemodialysis

**Table 1:** Pre- and post-dialysis PSA and Htc values

	Pre-dialysis	Post-dialysis	Increment (%)	P
tPSA (ng/ml)	1.2 ± 0.2	1.4 ± 0.3	16.8	0.0001
fPSA (ng/ml)	0.4 ± 0.09	0.43 ± 0.6	7.50	0.73
f/t PSA ratio( %)	28.2 ± 2.9	35.2 ± 2.8	24.5	0.0001
Htc	32.2 ± 0.7	36.9 ± 0.8	14.8	0.0001

Data are given as mean ± standard deviation

tPSA: total PSA

fPSA: free PSA

Htc: hematocrit

center. Any patient with known urinary tract infection, recent digital rectal examination (DRE) or urethral or prostatic manipulation was excluded. All patients received standard bicarbonate dialysis with non-celluloid, low flux membrane and polysulfone (blood flow rate = 200 ml/min, dialysate flow rate = 500 ml/min). Blood samples were obtained from the arteriovenous fistula immediately before and after one dialysis session. All patients were evaluated by determining tPSA, fPSA, percent fPSA and Htc pre- and post-dialysis. The PSA levels were measured using an enzyme linked fluorescent assay (Biomerieux, France) and the reference normal value of tPSA was considered as <4 ng/ml.

#### Statistical Analysis:

All data are expressed as mean ± standard deviation (SD). A Student's two-tailed paired t-test was used to compare blood test values. Pearson's correlation test was used to determine the correlation between the Htc and serum PSA values (tPSA, fPSA, f/tPSA).

## RESULTS

For all patients, the mean post-dialysis tPSA ± SD (1.4 ± 0.3 ng/ml) was greater than that of the pre-dialysis level (1.2 ± 0.2 ng/ml). The mean increase was 16.8% ( $p = 0.0001$ ; Table 1). While there was no significant increase in fPSA after dialysis (mean increment = 7.5%,  $p = 0.73$ ), there was a significant increase in percent fPSA (mean increment = 24.5%,  $p = 0.0009$ ; Table 1). The mean Htc after dialysis (36.9 ± 0.8)

was greater than that before dialysis (32.2 ± 0.7) ( $p = 0.0001$ ; Table 1). However, there was no correlation between the elevation in Htc and PSA values, including tPSA, fPSA and f/t PSA (Pearson coefficient factor  $r = 0.19$ ,  $r = 0.12$ ,  $r = 0.23$ , respectively).

## DISCUSSION

It is believed that tPSA (molecular weight 100 kd) is excreted rather by hepatobiliary mechanisms than eliminated by dialysis or renal clearance<sup>3</sup>. Some animal studies indicate that PSA is metabolized and excreted by the hepatobiliary system without definite evidence of renal clearance<sup>4</sup>. It is also suggested that it is possible to remove fPSA additionally by renal clearance due to its low molecular weight (33 kd)<sup>5</sup>. However the currently used flux membranes usually do not pass molecules even with the low molecular weight of fPSA.

Studies in hemodialysis patients regarding the level of tPSA or f/t PSA ratio provided conflicting results<sup>3,5-7</sup>. While many studies<sup>1,8-10</sup> showed an elevation in the post-dialysis tPSA serum level compared with pre-dialysis tPSA values, Djavan et al.<sup>3</sup> found no significant decrease in post-dialysis tPSA serum level. In our study we observed an elevation in the tPSA values in all but one of our patients. All the values of tPSA before and after dialysis were < 4 ng/ml, except for one patient whose tPSA values were > 4 ng/ml before and after dialysis (7.5 ng/ml, 8.9 ng/ml respectively). This means that, although the increase

in mean tPSA was statistically significant (16.8%,  $P = 0.0001$ ), it was not clinically meaningful. While the average increment in tPSA (16.8%) was close to that of the Htc increment (14.8%,  $P=0.0001$ ), the mean elevation in fPSA (7.5%,  $P = 0.73$ ) and f/t PSA ratio (24.5%,  $P = 0.0001$ ) was different from that of Htc.

The most likely explanation for the elevation in PSA values is plasma volume contraction which causes hemoconcentration. However, there was no correlation between the increment in Htc and the tPSA, fPSA, or f/t PSA ratio in our study. Thus, due to the relatively high molecular weight of PSA (33 – 100 kd) hemodialysis with low flux membranes (cutoff value 12 kd) has no influence on PSA clearance. Otherwise one should expect a decrease in the PSA values after hemodialysis.

The diagnostic value of tPSA in hemodialysis patients is a debatable issue. Total PSA levels in these patients were shown to be lower than those in the general population<sup>11</sup>, although previous studies have not shown any difference between the PSA levels of male patients on hemodialysis and those of the general population<sup>1,12-14</sup>. Harper et al. noted that false-positive results were unlikely when tPSA was measured in patients with end-stage renal disease, but that no ultimate comment could be made on the likelihood of false negative results<sup>7</sup>. In our study, although we did not have a control group and it was difficult to make a definitive comment regarding this issue, the tPSA values seem to be less than the expected values in age-matched general population groups. Therefore, we advocate that serum PSA determination be done in conjunction with DRE and/or TRUS in patients on dialysis, especially those who are candidates for renal transplantation, to rule out prostate cancer.

Bruun and his colleagues<sup>15</sup> found that percent fPSA of patients on hemodialysis was significantly higher than in controls (39.1% versus 28.1%, respectively). They concluded that the recommended reference ranges for patients with normal renal function did not apply to uremic patients, and that

a high level of percent fPSA should not be considered a sign of benign disease. In our study, percent fPSA after dialysis was 35.2%. The increment in percent fPSA was more than that of hemoconcentration and there was no statistically significant correlation between them. Therefore, we believe that the recommended level of percent fPSA for the general population should not be applied to uremic patients on dialysis. Further studies should be carried out to answer the question as to whether the results found in this study would also be valid for abnormal values of PSA.

In conclusion, the most likely explanation for the increment in tPSA and fPSA after hemodialysis is volume contraction, and hemodialysis with low flux membranes appears to have no effect on PSA clearance. Pre-dialysis determination of PSA probably provides no false-positive results. Therefore, we advocate that serum PSA determination be done in conjunction with DRE and/or TRUS in patients on dialysis, especially those who are candidates for renal transplantation, to rule out prostate cancer.

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## RESUME

### EFFET DE L'HEMODIALYSE SUR L'ANTIGENE SPECIFIQUE DE LA PROSTATE TOTAL, LIBRE ET LA FRACTION LIBRE

**Objectif:** Evaluer l'effet de l'hémodialyse sur l'antigène spécifique de la prostate (PSA) total, libre et la fraction libre.

**Matériel et Méthodes:** Cette étude a inclus 34 hommes présentant une insuffisance rénale chronique (âge moyen 58 ans, extrêmes 45-80) qui ont eu une hémodialyse avec les membranes à flux bas. Nous avons mesuré en pré et post hémodialyse le taux de PSA total (tPSA), PSA libre (fPSA) et hématocrite (Htc) lors d'une cession de dialyse. Le rapport fPSA/tPSA a été calculé avant et après dialyse. De plus, l'hématocrite a été mesuré avant et après dialyse pour objectiver le degré d'hémoconcentration et voir s'il y a une corrélation entre l'augmentation dans les niveaux de PSA et les hématocrites.

**Résultats:** Il y avait des augmentations considérables dans les valeurs moyennes de tPSA (pré dialyse 1.2, post dialyse 1.4 ng/ml) et le ratio du f/tPSA (pré dialyse 28.2, post dialyse 35.2). Une augmentation considérable dans la valeur de l'hématocrite a été notée après dialyse.

Le taux de fPSA moyen pré-dialyse était 0.4 et post dialyse était 0.43 ng/ml et le changement n'était pas statistiquement considérable. Cependant, le degré d'hémoconcentration n'a pas été corrélé statistiquement avec l'élévation dans les valeurs de tPSA, fPSA et f/tPSA.

**Conclusions:** Bien que l'augmentation du tPSA fût statistiquement considérable, ce n'était pas d'une manière clinique significative. Très probablement l'explication pour l'augmentation de tPSA et fPSA après hémodialyse soit la contraction du volume. L'hémodialyse avec les membranes à flux bas n'a aucun effet sur le taux de PSA. La détermination du taux de tPSA ne fournit probablement pas faux positifs. Par conséquent, nous préconisons que le dosage du taux de PSA soit fait conjointement avec l'examen endo rectal numérique et/ou ultrasonographique chez les malades dialysés, surtout ceux qui sont candidats pour une transplantation rénale, pour éliminer un cancer de la prostate.

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