ORIGINAL ARTICLE

Effect of Different Manipulations on Serum Prostate-Specific Antigen (PSA) Level in Patients with Symptomatic Benign Prostatic Hyperplasia and Suspicion of Carcinoma Prostate

ASHFAQ AHMAD[1], MUHAMMAD IQBAL[2], SOHAIL HASSAN[3], *SHAH JEHAN-UR-REHMAN[4], AMMAR BASHIR[5]*
[1]Associate Prof. of Urology
[2]AP Urology, Social Security Teaching Hospital Lahore
[3]Associate Prof. Social Security Teaching Hospital Lahore
[4]AP Urology Lahore General Hospital, Lahore
[5] Resident Urology AFIU Rawalpindi
Correspondence: Dr. Ahfaq Ahmad, Email: raja0508@yahoo.com

ABSTRACT

Background: Prostate specific antigen is an organ specific marker. A temporary rise in prostate specific antigen serum level has been reported in various situations like, digital rectal examination, urethral catheterization, transurethral resection of prostate and transrectal ultrasound guided prostatic needle biopsy.
Methodology: This comparative study is conducted at Department of Urology and Renal Transplantation Div, HQ. Teaching Hospital Mirpur Azad Kashmir from 1st June 2017 to 31st May 2018. Patients with symptomatic benign prostate hyperplasia and suspicion of carcinoma prostate on digital rectal examination with age above 50 years were included. All patients were divided into four groups. Group A comprised, patients who underwent digital rectal examination. Group B comprised, patients who underwent transurethral resection of prostate. Group C comprised, patients who underwent transurethral Foley catheterization due to retention of urine. Group D comprised, patients who underwent transrectal ultrasound guided prostatic needle biopsy for suspicion of ca prostate on digital rectal examination. Serum PSA was detected by enzyme linked immunosorbent serum assay (ELISA) method.
Results: In group A pre manipulation mean serum PSA level was 1.22ng/ml, after 30 minutes it was 2.52ng/ml, where as after 72 hrs mean serum PSA level was 1.56ng/ml and after one week it dropped to 1.1ng/ml.In group B pre manipulation mean serum PSA level was 3.41ng/ml, after 30 minutes of manipulation it was 29.89ng/ml, after 72 hours and one week of manipulation it was 8.22ng/ml and 4.25ng/ml respectively and after 2 weeks it dropped to 3.78ng/ml. In group C pre manipulation mean serum PSA level was 2.81ng/ml, after 30 minutes it was 4.54ng/ml, where as after 72 hrs and 1 week of manipulation it was 3.76ng/ml and 2.40ng/ml respectively. In group D pre manipulation mean serum PSA level was 2.61ng/ml, after 30 minutes it was 4.53ng/ml, where as after 72 hrs and 1 week of manipulation it was 3.42ng/ml and 2.56ng/ml respectively.
Conclusion: There is significant rise in serum prostate specific antigen after different manipulations except DRE.
Key words: Prostatic specific antigen, benign prostatic hyperplasia, Carcinoma prostate.

INTRODUCTION

Prostate-specific antigen (PSA) is a tumor marker helpful in the diagnosis and follow-up of prostate cancer. PSA level may rise due to other causes than prostate cancer such as benign prostatic hyperplasia (BPH), acute and chronic prostatitis.[1] Benign prostatic hyperplasia is by far the most common pathological process affecting the prostate gland. Its incidence is approximately 20% in men at 40 years of age that increases to 70% by the age of 60 and to 90% by the age of 70 years[2].

Early diagnosis of prostate carcinoma has led to more potentially curable cases.[3] Prostate carcinoma is a significant cause of morbidity and mortality. It is the most common malignancy amongst men.[4] Prostate cancer is second leading cause of death in America, second to lung cancer. It has become one of the leading male cancers in Asian countries as well.[5] Prostate cancer is also common in Pakistan. It is the third most common cancer occupying about 7% of all malignancies.[6] Prostate specific antigen is a proteolytic enzyme currently used as a serum tumor marker for cancer of prostate. It is produced and secreted by the epithelial cells lining the acini and ducts of the prostate. It forms the part of seminal ejaculate.[7] Its biological function is the hydrolysis of the high molecular weight seminal proteins seminogelin and fibronectin. This action leads to liquefaction and liberating the spermatozoa from the jelly like coagulum[8].

Prostate specific antigen is a single chain glycoprotein of 237 amino acids and four Carbohydrate side chains.[11] It has molecular weight of 34 kilo Dalton.[12] A serological test was developed to measure the human serum level of prostate specific antigen.[13] It is expressed in both benign and malignant disease processes involving epithelial cells of the prostate gland. Under normal physiological conditions, it is secreted into the Lumina of the prostatic ducts and present in the seminal plasma in high concentration[14].

The objective of the study was to determine the influence of transurethral catheterization, digital rectal examination and transurethral resection of prostate on serum prostate specific antigen,.to determine the influence of transrectal ultrasound guided prostatic needle biopsy on serum prostate specific antigen level in patients with suspicion of carcinoma prostate on digital rectal examination. to determine the time interval when serum prostate specific antigen level returns the base line after respective manipulation and to determine correlation between the size of prostate, amount of tissue resected and serum prostate specific antigen level.

RESULTS

Group A was comprised of 15 patients with age range 52-70 years; mean 58.86 years. The size of prostate in this group varied from 20-50grams, mean 35.33 grams. Pre-manipulation (DRE) mean serum PSA was 1.22+0.57ng/ml. After 30 minutes of manipulation mean serum PSA level increased to 2.52+0.64ng/ml, after 72 hrs it was 1.56+0.60ng/ml and after one week of DRE mean serum PSA level dropped to 1.11+0.42ng/ml. Pre and post-manipulation mean serum PSA difference after 30 minutes was 1.30ng/ml and after 72 hours it

was 0.34ng/ml (Table 1). Pre and post-manipulation (DRE) serum PSA difference showed that there was statistically insignificant rise in serum PSA after 30 minutes of manipulation (P <0.05). Post manipulation mean serum PSA rise was also calculated according to size of the prostate in this group. In patients where prostate size ranged from 20-30gms, mean rise of serum PSA was 2.44+0.64ng/ml, in patients with 31-40gms of prostate mean serum PSA rise was 2.45+0.30ng/ml and in patients with 41-50gms of prostate size mean serum PSA rise was 2.73+0.95ng/ml after 30 minutes of manipulation (Table 2).

Group B was comprised of 15 patients with age range of 56-83years means 69.26 years. The size of prostate varied from 25-65gms mean 42gms.Ten patients presented with retention of urine where as five patients presented with severe LUTS. All these patients underwent TURP. Prior to TURP mean serum PSA level was 3.41+0.65ng/ml. After 30 minutes of TURP mean Serum PSA increased to 30.69+6.28ng/ml, after 72 hours and one week after TUR-P mean serum PSA was 8.22+0.97ng/ml &4.25+0.45ng/ml respectively. After 2 weeks of TUR-P mean serum PSA level dropped to 3.78+0.42ng/ml (Figure 12). Five patients had resected tissue in the range of 10-20gms; eight had in the range of 21-30gms while two had in range of 31-40gms. Pre and post-manipulation(TUR-P) mean serum PSA difference after 30 minutes was 27.28ng/ml and after 72 hours it was 4.81ng/ml, after one week serum PSA difference was 0.84ng/ml and after 2 week of post-manipulation mean serum PSA difference was 0.37ng/ml (Table 3). The results showed that there was a statistical significant rise in mean serum PSA levels after 30 minutes,72 hours and one week of TURP (P <0.05). Post manipulation mean serum PSA rise was also calculated according to size of the prostate in this group. In patients where prostate size ranged from 25-35gms, mean rise of serum PSA was 23.88+1.36ng/ml, in patients with 36-45gms of prostate mean serum PSA rise was 30.95+2.92ng/ml, in patients with 46-55gms of prostate size mean serum PSA rise was 38.30+1.27ng/ml and in patients with 56-65gms of prostate size mean rise in serum PSA was 39.30+1.98ng/ml after 30 minutes of manipulation (Table 4). The patients, who had resected tissue in the range of 10-20grams, mean serum PSA rise was 23.88+1.36ng/ml after 30 minutes of TUR-P. Those patients who had resected tissue in the range of 21-30 grams, mean serum PSA rise was 32.79+4.23ng/ml where as those patients who had resected tissue in the range of 31-40gms had mean serum PSA rise of 39.30+1.98ng/ml after 30 minutes of resection (Table 5).

Group C was comprised of 15 patients with age range 55-78 years mean 63 years. The size of prostate varied from 30-70gms mean 46.6 grams. These patients underwent transurethral catheterization due to retention of urine. Pre catheterization blood sample for serum PSA was taken in all these patients. After Foley catheterization samples of blood were taken at 30 minutes, 72 hours and after 1 week. Pre-catheterization mean serum PSA level was 2.85+0.56ng/ml, 30 minutes post-catheterization mean of PSA increased to 4.50+0.80ng/ml after 72 hours of catheterization mean serum PSA was 3.70+0.63ng/ml and after 1 week of catheterization mean serum PSA dropped to 3.20+0.57ng/ml. Pre and post-manipulation mean serum PSA difference after 30 minutes was 1.65ng/ml and after 72 hours it was 0.85ng/ml, after one week of catheterization serum PSA level dropped to baseline 0.35ng/ml (Table 6). The results showed that a significant rise in mean PSA after 30 minutes and 72 hrs of Foley catheterization (P <0.05). Post manipulation mean serum PSA rise was also calculated according to size of the prostate in this group. In patients where prostate size ranged from 30-40gms, mean rise of serum PSA was 4.37+0.23ng/ml, in patients with 41-50gms of prostate mean serum PSA rise was 3.50+0.0ng/ml, in patients with 51-60gms of prostate size mean serum PSA rise was 4.38+1.04ng/ml and in patients with 61-70gms of prostate size mean rise in serum PSA was 4.83+0.73ng/ml after 30 minutes of manipulation (Table 7).

Group D was comprised of 15 patients with age range 57-79 years mean 65 years with suspicion of CA prostate on DRE. The size of prostate varied from 25-55gms mean 37 grams. These patients underwent TRUS guided prostatic needle biopsy. Pre-manipulation (biopsy) mean serum PSA was 2.48+1.46ng/ml. Post-manipulation (biopsy) mean serum PSA level after 30 minutes was 4.64+2.38ng/ml, after 72 hours of manipulation mean serum PSA was 4.37+2.09ng/ml. After 1 week of manipulation mean serum PSA level was 2.65+1.48ng/ml. Pre and post-manipulation (biopsy) mean serum PSA difference after 30 minutes was 2.16ng/ml, after 72 hours it was 1.89ng/ml, and after one week serum PSA difference dropped to baseline 0.17ng/ml. The results showed a significant rise in mean PSA after 30 minutes of TRUS guided biopsy (P <0.05). Post manipulation mean serum PSA rise was also calculated according to size of the prostate in this group. In patients where prostate size ranged from 25-35gms, mean rise of serum PSA was 6.32+3.65ng/ml, in patients with 36-45gms of prostate mean serum PSA rise was 3.78+0.91ng/ml and in patients with 46-55gms of prostate size mean serum PSA rise was 2.85+0.35ng/ml after 30 minutes of manipulation (Table 8).

Table 1 (Group A): Serum PSA Elevation after DRE

Category	**Mean± SD**	**Category**	**Mean± SD**	**Diff.**
Pre-Manipulation	1.22±0.57	30 Minutes after Manipulation	2.52±0.64	1.30
Pre-Manipulation	1.22±0.57	72 Hours after Manipulation	1.56±0.60	0.34
Pre-Manipulation	1.22±0.57	One Week	1.11±0.42	-0.11

*P<0.05

Table 2 (Group A): Mean rise of PSA 30 minutes after DRE according to size of prostate

Size of prostate	**No.**	**Mean rise after 30 minutes with SD**
20–30gm	7	2.44+0.64ng/ml
31–40gm	4	2.45+0.30ng/ml
41–50gm	4	2.73+0.95ng/ml
*p<0.05		

Table 3 (Group B): Mean rise of PSA 30 minutes after TUR-P according to size of prostate

Size of prostate	**No.**	**Mean rise after 30 minutes with SD**
25–35gm	5	23.88+1.36ng/ml
36–45gm	6	30.95+2.92ng/ml
46–55gm	2	38.30+1.27ng/ml
56–65gms	2	39.30+1.98ng/ml

Table 4 (Group B): Comparison of means using Tukey test

Size of prostate	Mean± SD	Category	Mean± SD	Mean difference
10-20	23.88±1.36	21-30	32.79±4.23	8.90
10-20	23.88±1.36	31-40	39.30±1.98	15.42
21-30	32.79±4.23	31-40	39.30±1.98	6.51

*P<0.05

Table 5 (Group C): Comparison of means using Tukey test

Category	Mean±SD	Category	Mean± SD	Mean difference
Pre-Manipulation	2.85±0.56	30 Minutes after Manipulation	4.50±0.80	1.65
Pre-Manipulation	2.85±0.56	72 Hours after Manipulation	3.70±0.63	0.85
Pre-Manipulation	2.85±0.56	One Week	3.20±0.57	0.35

*P<0.05

Table 6 (Group C): Mean rise of PSA 30 minutes after Foley Catheterization according to size of prostate

Size of prostate	No.	Mean rise after 30 minutes with SD
30 – 40gms	3	4.37+0.23ng/ml
41 – 50gms	1	3.50+0.00ng/ml
51 – 60gms	5	4.38+1.04ng/ml
61 – 70gms	6	4.83+0.73ng/ml

Table 7 Group D: Comparison of means using Tukey test

Category	Mean± SD	Category	Mean ±SD	Difference
Pre-Manipulation	2.48±1.46	30 Minutes after Manipulation	4.64±2.38	2.16
Pre-Manipulation	2.48±1.46	72 Hours after Manipulation	4.37±2.09	1.89
Pre-Manipulation	2.48±1.46	One Week	2.65±1.48	0.17

*P<0.05

Table 8 Group D: Mean rise of PSA 30 minutes after TRUS Guided Prostatic Needle Biopsy According to size of prostate

Size of prostate	No.	Mean rise after 30 minutes with SD
25–35gms	5	6.32+3.65ng/ml
36–45gms	8	3.78+0.91ng/ml
46–55gms	2	2.85+0.35ng/ml

DISCUSSION

In our study pre manipulation (DRE) mean serum PSA was 1.22+0.57ng/ml and post manipulation DRE mean serum PSA was 2.52+0.64ng/ml. Our result showed no statistically significant rise in serum PSA after DRE in patients having clinically symptomatic benign prostatic enlargement (P >0.05).

In 1992, Breul et al[15] conducted a study to evaluate the effect of DRE on serum PSA. No noteworthy contrast was seen in PSA values before and after DRE when blood tests were taken 1-3 min after palpation of the prostate, which corelates well with our study.

Klomp et al[16] conducted a study to see the effect of TRUS and DRE on serum PSA level. PSA was firm in patients immediately and after 1 week after TRUS and DRE. In some group of patients PSA was firm at various times after DRE and TRUS. The PSA showed a significant rise of 20% immediately after DRE and TRUS. After 7 days PSA had returned to their initial levels. When applying the diagnostic triad PSA, DRE and TRUS blood samples for PSA should first taken before DRE, TRUS guided Prostatic needle biopsy. Our study showed no significant rise in serum PSA after DRE whereas after TRUS guided prostatic needle biopsy statistically significant rise in serum PSA (P <0.05). So the blood sample must be taken before TRUS to avoid false positive results. Another explanation is that the combination of DRE and TRUS implies a more serious manipulation of the prostate than DRE alone.

Lynn et al[17] did a study to evaluate the impact of prostatic control on complexed prostate-explicit antigen (cPSA), as different types of prostatic control are known to increase the serum free and complete PSA level. A study of 92 men (58 after prostatic biopsy, 16 after advanced rectal examination and 18 after flexible cystoscopy) were evaluated. Blood tests were taken from every patient previously and 30 min after manipulation. A total cPSA levels were estimated utilizing proper tests. There was no significant increment in cPSA levels after flexible cystoscopy and computerized rectal examination, yet prostate biopsy caused a measurably critical albeit insignificant ascent in cPSA level. These findings co-relate well with our study.

In our study pre manipulation (TURP) mean serum PSA level was 3.41+0.65ng/ml whereas after 30 minutes it was 30.69+6.28ng/ml which showed that significant rise in serum PSA 30 minutes after TURP (P <0.05). In TRUS guided prostatic needle biopsy pre manipulation mean serum PSA level was 2.61+1.49ng/ml whereas after 30 minutes of manipulation it was 4.50+2.47ng/ml which showed significant rise in serum PSA 30 minutes after TRUS guided prostatic needle biopsy (p <0.05).

Oesterling et al[18] conducted a study in 1993 to survey the impact of cystoscopy, prostate biopsy and transurethral resection of the prostate (TURP) on the serum prostate-explicit antigen (PSA) focus, 101 patients were assessed. For cystoscopic examination, 69 men were randomized in a forthcoming way to one of three gatherings: flexible cystoscopy, inflexible cystoscopy and a control cohort. The middle change in serum PSA was 0.1ng/ml following flexible cystoscopy 0.05ng/ml after unbending cystoscopy and 0.05ng/ml for the control bunch in which two serum PSA assurance were acquired without an interceding cystoscopy. The contrasts between the three groups were not significant. The impact of prostate biopsy and TURP was analyzed in 32 men. Prostate biopsy caused a quick rise in the serum PSA level with a middle increment of 7.9ng/ml (p <0.0001). Also TURP delivered a rise in the serum PSA fixation with a median

difference in 5.9ng/ml (p <0.001). The middle time required for the serum PSA incentive to come back to a steady dimension after prostate biopsy was fifteen days (run: 5-21 days) for men with prostate malignant growth and seventeen days (extend: 3-30+ days) for men without cancer and eighteen days (12-30+ days) for men who undergone TURP. In our study mean serum PSA level dropped to baseline (2.65+1.48ng/ml) after 1 week of TRUS guided prostatic needle biopsy in TURP patients it dropped to baseline (3.78+0.42ng/ml) after 02 weeks of manipulation which co-relates well with the study of Oesterling et al.

In 2003, Kubilay et al[19,]conducted a study to decide the impact of Foley catheterization on serum PSA. Thirty five male patients with mean age of 63.7 years, had AUR were catheterize. These patients were haphazardly part into two groups, 18 patients underwent Foley catheterization of 16-18 fr (catheterization group) while the remaining 17 undergone suprapubic percutaneous cystostomy without any urethral manipulation (cystostomy group). Samples of blood were obtained from all patients before 2 and 12 hours and 7 days after the treatment. There was significant difference for catheterization group (p <0.05) but not for cystostomy group. Our study also showed statistically significant rise in serum PSA after Foley catheterization (p<0.05).

In 2010 Lin et al[20,] conducted a study on 160 male patients in China. Of these patients 23 had DRE, 21 had Foley catheterization, 28 had rigid cystoscopy, 35 had prostate biopsy, 35 had TURP and 18 had suprapubic prostatectomy. Blood sample were taken before, 24 hours and 4 weeks after manipulation for serum PSA. The DRE had no significant effect on serum PSA. Foley catheterization and cystoscopy had significant effect but there was marked increase in t PSA and f PSA after 24 hours of biopsy. TURP and suprapubic prostatectomy had significant effect on serum PSA levels and it came back to baseline after 4 weeks of manipulation. In our study there was no statistically significant effect on serum PSA level after DRE (P >0.05) whereas there was statistically significant rise in serum PSA level after TURP (P<0.05), TRUS guided prostatic needle biopsy (P<0.05) and Foley Catheterization (P<0.05).

CONCLUSION

It is concluded that prostatic manipulation causes an ascent in serum PSA, in our patients DRE did not cause measurably critical ascent in serum PSA where as Foley catheterization, TURP and TRUS guided prostatic needle biopsy cause significant rise in serum PSA. Maximum ascent in serum PSA was seen after TURP. After initial rise in serum PSA, it dropped to baseline within one week of manipulation in Foley catheterization and TRUS guided prostatic needle biopsy where as it took about 2 weeks to return to baseline in TURP patients. That serum PSA rise was also prostate size dependent. In patients with large prostate and relatively increased amount of tissue resection, serum PSA rise was more and took longer time to return to baseline. In view of these facts, it is therefore recommended that serum PSA level should be determined prior to any prostatic manipulation and one should wait for at least 2 weeks after prostatic manipulation to get an accurate result and to avoid any false positive rise in serum PSA.

REFERENCES

1. Walsh C, Patrick WC. Campbell's urology. Anatomy of lower urinary tract and male genitalia. 8th ed. Philadelphia: WB Saunders, 2002: 41-70.
2. Clifford GM, Logie J, Farmer RDT. How do symptoms indicative of BPH progress in real life practice? The UK experience. Eur Urol 2000; 38: 48-53.
3. Grande M. Tissue prostatic specific antigen. A way to predict and understand the development of prostate cancer. Doctor's Thesis from Korolinska Insitute, 2001.
4. Pu YS, Chiang HS, Lin CC, Huang CY, Huang KH, Chen J. Changing trends of prostate cancer in Asia. Aging Male 2004; 7: 120-32.
5. Elgamal AA, Holmes EH, Su LS, Tino WT, Sinmons SJ, Peterson M, Greene TG, Boyntan AL, Murphy GP. Prostate specific membrane antrogen current benefits and future value. Semin Surg Oncol 2000; 18: 10-16.
6. Lilja H. A kallikrein like serine protease in prostatic fluid cleaves the predominant seminal protein. J Clin Invest 1985; 76; 1899-1903.
7. Lilja HJ. Biologic function of prostatic specific antigen: enzyme action and reactions with extra cellular protease inhibitors. Eur Urol 1995; 27: 2-8.
8. Hara M, Koyanagi Y, Inoue T, Fukuyama T. Some physicochemical characteristics of gamma-seminoprotein, an antigenic component specific for human seminal plasma. Nippon Hoigaku zasshi 1971; 25: 322-4.
9. Li T, Beling C. Isolation and characterization of two specific antigens of woman seminal plasma. Fertile Steril 1973; 24: 134-44.
10. Lundwall A, Lilja H. Molecular cloning of the human prostate specific antigenc DNA. FEBS 1987; 214: 317-22.
11. Wang M, Vlenzue L, Murphy G, et al. Purification of a human prostate specific antigen. Invest Urol 1979; 17: 159-63.
12. Papsidero L, Wang M, Valenzuela L, et al. A prostate antigen in sera of prostatic cancer patients. Cancer1980;40:2428-32.
13. Schellhammer P, Wright G Jr. Bimolecular and clinical characteristics of PSA and other candidate prostate tumor markers. Urol Clin North Am 1993;20:597-600.
14. Christenson A, Laurel CB, Lilja H. Enzymatic activity of prostate specific antigen and its reaction with serine proteinase inhibiters. Eur J Biochem 1990; 194: 755-63.
15. Breul J, Binder K, Block T, Hartung R. Effect of digital rectal examination on serum concentration of prostate-specific antigen: Eur Urol 1992; 21: 195-9.
16. Klomp ML, Hendrikx AJ, Keyzer JJ. The effect of transrectal ultrasonography (TRUS) including digital rectal examination (DRE) of the prostate on the level of prostate specific antigen (PSA). Br J Urol 1994; 73: 71-4.
17. Lynn NN, Collins GN, O'Reilly PH. Prostatic manipulation has a minimal effect on complexed prostate-specific antigen levels. BJU Int 2000; 86: 65-7.
18. Oesterling JE, Jacobsen SJ, Chute CG. Serum prostate specific antigen in a community-based population of healthy men: Establishment of age-specific reference ranges. JAMA 1993;270:860-5.
19. Kubilay E, Mesut G, Sinan K, Feridun S. The effect of Uretheral Catheterization on serum Prostate Specific Antigen levels in male patients with Acute Urinary Retention. Medical J 2003; 44:676-78.
20. Lin YH, Jiang YG, Li MC, Luo Y, Wang JS. Effects of prostate manipulation on serum total and free prostate specific antigen, and free-to-total prostate specific antigen ratio. Saudi Med J 2010;31:999-1004.