Effect of Cystoscopy on Prostate-Specific Antigen, New Words about Old Subject

Rezakhaniha B[1], Arian Pour N[2], Siroosbakhat S[2]

Abstract

Background: Prostate Specific Antigen (PSA) is a protein currently used in conjunction with the digital rectal examination to detect and guide management of prostate cancer. There are several causes of increase in serum PSA including urological manipulations, medications, prostatic diseases, prostate cancer, prostate inflammation or infection, etc. some studies had reported cystoscopy to cause transient increases in PSA. The present study has been undertaken with an aim to find out the effect of rigid cystoscopy on serum PSA level.

Methods: One hundred two men referring to clinic of urology of Imam Reza Hospital from 2008 to 2010 were included in this study. Their age ranged from 31-88 years with the mean of 65.85 years. Our inclusion criteria were having an indication for cystoscopy like BPH, erection disorder, signs related to prostate or bladder carcinoma. Patients with positive urine culture, any medication affecting PSA level, history of urinary retention, any urological manipulations a few days before and ejaculation 48-72 hours before PSA assessment were excluded from the study. Blood samples were taken before and 24 hours after cystoscopy for PSA measurement. PSA was measured by Sandwich ELISA test using PSA kit (pishtaz kit - made in Iran) containing monoclonal antibody.

Results: PSA level of the study cases varied from 0.1 to 21 ng/ml. Mean PSA values before and after cystoscopy were 3.004± 3.34 and 2.92 ± 2.98 respectively indicating that after cystoscopy not only PSA value did not raise but also decreased to some extent.

Conclusion: Our findings indicate that, cystoscopy has no effect on PSA value and does not lead to its elevation. It can be concluded that serum PSA after rigid cystoscopy is an accurate and reliable finding to decide about patients condition related to prostate cancer.

Keywords: Prostatic hyperplasia; Cystoscopy; Prostate cancer; Prostate Specific Antigen

Please cite this article as: Rezakhaniha B, Arian Pour N, Siroosbakhat S. Effect of Cystoscopy on Prostate-Specific Antigen, New Words about Old Subject. Iran J Cancer Prev. 2010; Vol3, No4, p.193-98.

1. Department of Urology, Imam Reza Hospital, Military University of Medical Sciences, Tehran, Iran
2. Faculty of Medicine, Military University of Medical Sciences, Tehran, Iran

Corresponding Author:
Bijan Rezakhaniha MD, Assistant Professor of Urology
Tel: (+98)21 22 64 64 31
Email: reza.bijan@yahoo.com

Received: 5 Sep. 2010
Accepted: 2 Oct. 2010
Iran J Cancer Prev 2010; 4:193-98

Introduction

PSA is a protein produced by normal prostate cells. This enzyme participates in the dissolution of the seminal fluid coagulum and plays an important role in fertility. The highest amounts of PSA are found in the seminal fluid; some PSA escapes the prostate and can be found in the serum. PSA has been used to track the response to therapy in men with prostate cancer [1].

From practical point of view, prostate instrumentation or "trauma" due to cystoscopy, prostate biopsy, transurethral resection (TURP), colonoscopy, vigorous digital rectal examination (DRE) or ejaculation may cause transient increases in serum PSA. The PSA level tends to rise in men with benign prostatic hyperplasia (BPH) and is a good marker for prostate volume. PSA levels are usually elevated in men with acute bacterial prostatitis. The most valuable measurement of PSA is its change over time rather than the actual serum level. No identifiable PSA level guarantees normalcy; in addition, no specific level indicates that a biopsy should be performed. Instead, PSA velocity or doubling time has been shown to be a more accurate and reliable predictor for recommending a prostate biopsy and treating patients with this disease [1, 2].

Diagnostic TURP could prove useful in patients with clinical suspicion of prostate cancer (PC), susceptible

Table 1. Inter-assay PSA kit was performed using 4 sera with different concentration

Sample	Number of repetition	Mean ng/ml	Standard Division (SD)ng/ml	CV%
1	10	0.6	0.05	8.2
2	10	2.9	0.2	7
3	10	19.2	1.2	6.3
4	10	37	2.4	6.5

Table 2. Intra-assay PSA kit was performed using 4 sera with different concentration

Sample	Number of repetition	Mean ng/ml	Standard Division (SD)ng/ml	CV%
1	24	0.6	0.03	5.5
2	24	2.2	0.08	3.8
3	24	9.9	0.35	3.5
4	24	30	1.3	4.3

Table 3. Comparison of PSA levels changes between before and after cystoscopy based on age ranges

Age ranges	PSA levels before cystoscopy				PSA levels after cystoscopy			
	PSA levels	Frequency (%)	PSA levels	Frequency (%)	PSA levels	Frequency (%)	PSA levels	Frequency
40>	0-2.5	100	2.5<	0	0-2.5	100	2.5<	0
40-49	0-2.5	100	2.5<	0	0-2.5	100	2.5<	0
50-59	0-3.5	89.5	3.5<	10.5	0-3.5	89.5	3.5<	10.5
60-69	0-4.5	76	4.5<	24	0-4.5	76	4.5<	24
70-79	0-6.5	95.5	6.5<	4.5	0-6.5	95.5	6.5<	4.5
80<	0-6.5	75	6.5<	25	0-6.5	62.5	6.5<	37.5

The median PSA levels before and after cystoscopy was 3.004 (SD: 3.34) and 2.92 (SD: 2.98), respectively.

to curative treatment [3]. Some used preoperative PSA level as a marker of prostate volume and assessed its potential predictive value on the level of clinical efficacy for treating symptomatic BPH [4].

Since the PSA test was introduced into clinical practice in 1986, the early diagnosis and management of prostate cancer has been revolutionized. PSA testing not only helps in the early diagnosis but also assists in assessing the response to therapy, determining tumor progression, and, in its most controversial role, screening for prostate cancer [5]. PSA is a specific prostate cancer marker; the benefits of PSA testing outweigh its drawbacks [6].

Studies are still underway to determine definitively if PSA screening actually makes any real difference in the detection and survival of men with this disease, but most urologists would testify that they see far fewer patients with advanced prostate cancer since the PSA era began. Previously, some studies had reported cystoscopy to cause transient increases in PSA, but further studies showed cystoscopy did not affect PSA level. The data from different studies which are carried out to determine the effect of cystoscopy on PSA have shown PSA level changes is related to cystoscopy and PSA assay methods used and if cystoscopy is performed carefully and considering the anatomic points, it will not affect PSA level [7,9].

Oesterling et al (1993) in his study on 101 patients divided them on the basis of the type of cystoscopy performed into three groups i.e. those undergoing flexible cystoscopy, rigid cystoscopy, and a control cohort. The mean change in serum PSA was 0.1 ng/mL following flexible cystoscopy and 0.05 ng/mL after rigid cystoscopy. But, these changes were not statistically significant. He

therefore suggested cystoscopy did not tend to affect PSA levels [7]. Another study (1998) demonstrated that PSA level changes is due to cystoscopy and PSA assay methods and based on the method used, the results will be different [10].

The present work has been undertaken with an aim to find out the differences in PSA levels before and after cystoscopy.

Materials and Methods

Among patients referring to clinic of urology of Imam Reza Hospital from 2008 to 2010 a total of 102 men were included in this prospective, before and after study. Their age ranged from 31-88 years with the mean of 65.85 years. Our inclusion criteria were having an indication for cystoscopy like BPH, signs related to prostate or bladder carcinoma and etc. Patients with positive urine culture, any medication affecting PSA level, history of urinary retention, any urological manipulations a few days before and ejaculation 48-72 hours before measuring PSA were excluded from the study.

Patients were thoroughly examined by the urologist (The author) and laboratory tests and Para -clinical investigations were advised. A questionnaire and consent form was signed by every patient.

Blood samples were taken before and 24 hours after cystoscopy was performed. PSA was measured by Sandwich ELISA test using PSA kit (pishtaz kit - made in Iran) containing monoclonal antibody. O.D was read at 250 nm. Prior to the test optimum antigen and antibody concentrations were determined. Minimum detectable concentration of PSA using this kit was found out to be 0.1 ng/ml sera. Intra-assay and inter-assay test for PSA kit was performed using 4 sera with different concentration (Tables 1, 2).

Prior to cystoscopy, 20 cc lidocain was injected slowly into meatus. After 5 minutes, cystoscope tube covered with sheet No. 15 (Karl's Storz) was gently inserted into meatus. All the study cases were examined and cystoscopized by the same urologist (the study co-worker). PSA was again measured 24 hours after cystoscopy. Patients who did not return for follow up on due-time were excluded from the study. The data analyzed by using SPSS 11.5 program. Sample K-S test identified that our data distribution is abnormal, so Willcoxon test was used to assess the differences between the PSA before and after cystoscopy.

Results

Patients' age ranged from 31-88 years with the mean of 65.85. Forty-nine% of the patients were 60-69 years old. As is clear from Table3, considering the age-specific value of PSA [11] Majority of patients had normal PSA. But considering standard PSA as 4 ng/ml younger patients with abnormal PSA are in fact normal while among older men with normal PSA many are considered abnormal.

A look at the PSA values show that by increase in PSA value, symptoms also change from irritative towards obstructive type. As is clear from Table 4 at PSA value of 4.5-5.5 and above no patient was without symptom. At PSA value of 5.5-6.5 80% of patients had irritative symptoms while incidence of irritative and obstructive symptoms occurring at PSA range of 4.5-5.5 was highest (85.7%) and at PSA level more than 6.5 reached 60%.

PSA value more than 4.5 ng/ml is accompanied with specific symptoms. PSA value more than 10 ng/ml is suspicious of cancer. Though some cases with PSA value less than 4ng/ml is also included in the study to compare with PSA value after cystoscopy; these patients also had indications for cystoscopy such as poor steam, chronic irritative and obstructive symptoms, etc.

Out of 102 patients, only 6 (5.03%) men had PSA levels higher than10 ng/ml. These individuals had both types of symptoms (irritative as well as obstructive).

In this study, PSA values ranged from 0.1- 21 ng/ml. Mean PSA value for all the patients before and after cystoscopy were 3.004 ± 3.34 and 2.92 ± 2.98 respectively (table 5) indicating that after cystoscopy PSA value decreased to some extent, though the difference is not significant ($P=0.375$). Using willcoxon test for distribution of abnormal data, Z value was calculated as $Z= 0.887$ (Z was accurated according to positive ranks) indicating reduction of PSA value after cystoscopy though not significantly (Table 6). Therefore, it can be concluded that cystoscopy has no effect on PSA value and does not raise its titre.

Discussion

The PSA level tends to rise in men with benign prostatic hyperplasia. The most valuable measurement of PSA is its change over time rather than the actual serum level. Rigid cystoscopy is the standard method of evaluation of the bladder and urethra. PSA measurement is currently used in conjunction with the digital rectal examination to detect and guide management of prostate cancer.

Preoperative assessment of prostate cancer included symptom evaluation with the International

Table 4. Correlation between Symptoms and PSA levels changes

Symptoms PSA	Without Symptoms. (%)	Irritative (%)	Obstructive (%)	Irritative+ Obstructive (%)
0-2.5	10.2	32.9	7.5	49.4
2.5-3.5	11.1	33.4	11.1	44.5
3.5-4.5	25	50	25	0
4.5-5.5	0	14.3	0	85.7
5.5-6.5	0	80	0	20
6.5<	0	30	10	60

Table 5. PSA value before and after cystoscopy

	Number	Min	Max	Mean	Standard Deviation
PSA before cystoscopy	102	0.1	21	3.0037	3.34511
PSA after cystoscopy	102	0.1	16.1	2.9238	2.97855

Table 6. The results of PSA levels changes before and after cystoscopy using Willcoxon Test

	Number	Mean Rank	Sum of Ranks
Negative Ranks	47[a]	50.35	2366.5
Positive Ranks	45[b]	42.48	1911.5
Ties	10[c]	0	0

Findings showed that PSA levels after cystoscopy did not increase. By Willcoxon test was used for abnormal distribution, Z amount was -0.887 (Z was accounted according to positive Ranks) and this indicated less decreasing in PSA levels. There was not statistically significant (P value: 0.375) changes in PSA levels after cystoscopy .On the other hand, cystoscopy had no effect on serum PSA levels.
a: PSA levels before cystoscopy > PSA levels after cystoscopy
b: PSA levels before cystoscopy < PSA levels after cystoscopy
c: PSA levels before cystoscopy = PSA levels after cystoscopy

Prostate Symptom Score (I-PSS) and the prostate volume estimation by Trans rectal ultrasound [12].

Since the PSA test was introduced into clinical practice in 1986, the early diagnosis and management of prostate cancer has been revolutionized. PSA testing not only helps in the early diagnosis but also assists in assessing the response to therapy, determining tumor progression, and, in its most controversial role, screening for prostate cancer [5]. PSA is a specific prostate cancer marker; the benefits of PSA testing outweigh its drawbacks [6].

In the present study we also used PSA as a marker for diagnosis of prostate cancer among our patients.

The data related to the effect of cystoscopy on PSA have shown that PSA level changes due to cystoscopy and that different PSA assay methods may have different impacts on it [11].

We noticed cystoscopy had no effect on serum PSA levels. PSA levels following cystoscopy did not change significantly which is in accordance with other studies [7, 10]. There was not statistically significant (P = 0.375) difference between PSA levels before and after cystoscopy .These findings indicate that serum PSA level after cystoscopy is accurate and a reliable finding to decide about patients condition regarding prostate carcinoma.

As in this study BPH was an indication for cystoscopy, patients with higher PSA values suffered progressive form of BPH. We noticed that in cases where symptoms shifted from irritative to obstructive type, PSA increased accordingly.

Fonseca RC et al (2008) also reported mean t-PSA declined 71% after TURP and 60 days after surgery the reduction reached its peak, stabilizing afterwards [12]. According to him PSA in his study varied from 6.19 ±7.06 ng/mL before surgery to 1.75 ±1.66 ng/mL on day 60 ($p < 0.001$) [14]. In this work we obtained mean PSA level before cystoscopy as 3.004± 3.34 and after cystoscopy as 2.92 ± 2.98.

If cystoscopy is performed carefully regarding the anatomic points, it will not affect PSA levels [13]. Schwartz B F et al (2009) detected no significant

change in serum PSA levels after prolonged transrectal prostatic manipulation [13].

PSA decreases drastically in patients who undergo TURP. These low levels stabilize within 60 days after surgery. The f/t PSA ratio did not change, and the finding of chronic prostatitis did not affect the levels of these variables [12].

Other findings show that t-PSA values increased after cystoscopy from the baseline although the increase of non equimolar was much higher than equimolar. The f-PSA/t-PSA ratio (non equimolar) remains at the baseline whereas the f-PSA/t-PSA ratio (equimolar) had an important increase from the baseline. The effect of cystoscopy based on the PSA assay is different [14].

Te etal's. results suggest that there is a significant difference in efficacy in patients with a t PSA of ≤6.0 ng/mL or > or = 6.1 ng/mL before post void residual urine volume (PVR). They concluded that the overall results achieved with PVR were very positive and durable to 3 years, irrespective of t PSA level and prostate volume [4].

Employing PSA as an indicator for improvement takes less time compared to other procedures like urofometry while clinical improvement after transurethral resection of the prostate, reflected by I-PSS score, was demonstrated as early as 30 days and remained stable until the end of the follow-up [12].

Long R et al (2006) also detected complex PSA and total PSA was affected differently by prostatic manipulation with the exception of cystoscopy. This study included 113 men who underwent rigid cystoscopy [11]. According to him prostatic manipulation had minimal effect on complex PSA levels [15-17].

De Castro B J et al (2009) showed that flexible cystoscopy had no effect on serum PSA values [18].

Shim et al (2010) stated that the prostate-specific antigen level decreases after transurethral resection of the prostate. They reported PSA levels may increase after KTP laser vaporization for a certain period of time, but eventually decrease and become stabilized after 6 months. According to them it may be appropriate to wait up to 3 months if the PSA level rises after the procedure, and further investigation should be considered if the PSA level still remains high after 6 months [19].

Acknowledgement

The authors thank all members of department of urology, laboratory personnel of Imam Reza hospital and all those who helped us to complete this project.

Conflict of Interest

The authors declare that they have no conflict of interests.

Authors' Contribution

BR carried out the design and coordinated the study, participated in most of the experiments and prepared the manuscript. SS provide assistance in the design of the study, coordinated and participated in manuscript preparation. NA contributed to writing up process. All authors have read and approved the content of the manuscript.

References

1. Cooperberg MR, Lubeck DP, Meng MV, Mahta SS, Carroll PR. The changing face of low-risk prostate cancer: trends in clinical presentation and primary management. J Clin Oncol. 2004; 22: 2141-9.

2. Gelmann EP, Chia D, Pinsky PF, Andriole GL, Crawford ED, Reding D,et al. Relationship of demographic and clinical factors to free and total prostate-specific antigen. Urology. 2001; 58:561-6.

3. Rodríguez Alonso A, González Blanco A, Barbagelata López A, Pita Fernández S, Suárez Pascual G, Bonelli Martín C, et al. Importance of PSA velocity and PSA density in the prediction of prostate cancer in TURP or open prostatectomy specimen of patients with previous negative prostate biopsy. Actas Urol Esp. 2008 Sep; 32(8):779-86 .

4. Te AE, Malloy TR, Stein BS, Ulchaker JC, Nseyo UO, Hai MA. Impact of prostate-specific antigen level and prostate volume as predictors of efficacy in photoselective vaporization prostatectomy: analysis and results of an ongoing prospective multicentre study at 3 years. BJU Int. 2006 Jun; 97(6):1229-33.

5. Dalton DL. Elevated serum prostate-specific antigen due to acute bacterial prostatitis. Urology. 1989; 33(6):465.

6. Mikolajczyk SD, Mark LS, Partin AW, Rittenhouse HG. Free PSA in serum in becoming more complex. J Urology, 2002; 59:797-801.

7. Oesterling JE, Rice DC, Glenski WJ, Bergstralh EJ. Effect of cystoscopy, prostate biopsy, and transurethral resection of prostate on serum prostate-specific antigen concentration. Urology. 1993; 42: 276-82.

8. Deliveliotis C, Alivizatos G, Stavropoulos NJ, Makrychoritis K, Koutsokalis G, Kiriakakis Z, et al. Influence of digital examination, cystoscopy, transrectal ultrasonography and needle biopsy on the concentration of prostate-specific antigen. Urol Int. 1994; 53(4): 186-90.

9. Crawford ED, Schutz MJ, Clejan S, Drago J, Resnick MI, Chodak GW, et al.The effect of digital rectal examination on prostate-specific antigen levels. JAMA. 1992; 267: 2227-8.

10. Rodriguez-Rubio FI, Robles JE, Gonzalez A, Arocena J, Sanz G, Diez-Caballero F,et al. Effect of digital rectal examination and flexible cystoscopy on free and total

prostate-specific antigen, and the percentage of free prostate-specific antigen differences between two PSA assays. Euro Urol. 1998; 33(3): 255-60.

11. Long R, Giri S, Diver S, Duddy L, Mckeown D, Moran K. Effect of prostate manipulation on the serum levels of total prostatic specific antigen.Int J Urology .2006; 13(7):947-50 .

12. Fonseca RC, Gomes CM, Meireles EB, Freire GC, Srougi M. Prostate specific antigen levels following transurethral resection of the prostate. Int Braz J Urol. 2008 Jan-Feb; 34(1):41-8.

13. Schwartz B F, Faught J. The effect colonoscopy on serum prostatic specific antigen levels.BJU Int, 2009; 84(3):302-4.

14. Khan MA, Partin AW, Rittenhouse HG, Mikolajezyk SD, Sokoll LJ, Chan DW, et al. Evaluation of PSA for early detection of prostatic cancer in men .J Urology.2003;170:723-6.

15. Lynn NN, Collins GN. Prostatic manipulation effect on complex PSA levels.BJU int.2000; 86(1):65-7.

16. Catalona WJ, Bartsch G. Serum complex PSA improve cancer detection. J urol.2003; 170:2181-5.

17. Thompson IM, Ankerst DP, Chi C, Lucia MS, Goodman PJ, Cowley JJ, et al. Operating characteristics of PSA in men with an initial PSA level of 3.0ng/ml or lower. JAMA .2005; 294:66-70.

18. DeCastro B J, Baker KC. Urology. Effect of flexible cystoscopy on serum prostate-specific antigen values. Urology.2009 Feb; 73(2):237-40.

19. Shim M, Kwon T, Kim SC, Ha SH, Ahn TY. Changes in Serum Prostate-Specific Antigen Levels after Potassium-Titanyl-Phosphate (KTP) Laser Vaporization of the Prostate. Korean J Urol. 2010 Feb; 51(2):111-4.