

General anesthesia does not affect the serum complexed and free prostate specific antigen levels

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Summary

Principles: Serum prostate-specific antigen (PSA) level is a widely used serum marker for diagnosis and management of prostate cancer. Although not well-defined, liver appears to be the most likely site of PSA metabolism. However, general anaesthesia usually changes hepatic blood flow, therefore it may affect the metabolism of PSA. In this study we investigated the affect of general anaesthesia on the serum total PSA, free PSA and free to total PSA levels.

Methods: 30 male patients who were hospitalised in the internal medicine clinic (non-surgery group) and 30 male patients who would undergo operation under general anaesthesia (15 for cholecystectomy and 15 for inguinal hernia repair) enrolled into the study. PSA measurement was done on the day of the hospitalisation (which was also the day of operation for surgery group), on the 24th hour following the first measurement and on the 21st day. Anaesthesia was standardized for all patients.

Results: There was no statistically significant difference in serum total PSA ($p > 0.05$), free PSA levels ($p > 0.05$) and free to total PSA ratio ($p > 0.05$) between the surgery and non-surgery groups. There were statistically significant decreases in the 24th hour total PSA levels (13.8% in surgery group, $p < 0.05$, and 13.1% in non-surgery group, $p < 0.05$) and in the free PSA levels (4.0% in surgery group, $p < 0.05$, and 8.2% in non-surgery group, $p < 0.05$). There was no statistically significant difference in the free to total PSA ratios ($p > 0.05$ and $p > 0.05$, respectively).

Conclusions: Anaesthesia does not affect PSA levels alone. However, hospitalisation decreases total and free PSA levels, although it does not have an affect on free to total PSA ratio.

Key words: prostate specific antigen; anaesthesia; measurement

Introduction

Serum prostate-specific antigen (PSA) level is a widely used serum marker for diagnosis and follow-up of prostate cancer. Because PSA is not specific of prostate cancer, an elevated serum level may not indicate prostate cancer; just like a value in the normal range may not suggest the absence of prostate cancer [1]. Serum PSA levels may be elevated in prostate cancer, and in some other clinical conditions such as BPH, urinary system infection, prostatic abscess or infarction, after prostatic needle biopsy, cystoscopy, 24 hours after transurethral resection of prostate, and a decrease may follow prostatectomy, finasteride therapy and radiation therapy [1–13]. By using the percent free

PSA in men with total PSA levels between 2.5–10 ngr/mL the specificity of PSA in predicting the presence of prostate cancer was improved. Although the site of the metabolism of the PSA is not well-defined, the liver was cited as the most likely site of PSA metabolism [14–17].

As general anaesthesia usually changes hepatic blood flow, it may decrease the metabolic function of the liver and the metabolism of PSA. In this study we aimed to find the affect of general anaesthesia on the serum levels of total (tPSA) and free PSA (fPSA), and to evaluate the reliability of PSA testing following anaesthesia.

Patients and methods

Between May 2003 and January 2004, 60 consecutive male patients were enrolled in this prospective study. Thirty of these patients were from the general surgery clinic, and were defined as the surgery patients. They had a mean age of 58 (range 45 to 77), and were to undergo an operation (15 for open inguinal hernia repair, 15 for laparoscopic colectomy), under general anaesthesia. All of these 30 patients had their serum total and free PSA measurements made between 8.00–10.00 a.m. (all were hospitalised on the operation day) 24 hours after the operation and 21 days following the operation. During the operation, a standardized general anaesthesia technique was used. Premedication with midazolam 0.15 mgr/kg i.v. was given. Thiopental 5 mgr/kg (Pental® Sodyum, IE Ulagay) was given for induction of anaesthesia combined with 100–200 µgr/kg min 2, 6-diisoprophyl fenol (Propofol®, Abbott). All patients were given 0.1 mgr/kg vecuronium (Norcuron®, Organon) i.v. to facilitate intubation, and they received a 65% NO₂ in O₂ gas mixture. The patients were intubated and ventilated mechanically to maintain an end tidal concentration between 30 to 40 mm Hg. Fentanyl citrate 2–4 µgr/kg hour (Fentanyl®, Abbot) i.v. was applied as maintenance anaesthetic. Mean operation time was 82 minutes (range 62–120). None of the patients had a urinary catheter during surgery or through out the study period.

The second group consisted of 30 patients with a mean age of 61 (range 45 to 86), which was defined as the non-surgery group. Those patients were recruited from the internal medicine clinic. Twenty-two of those 30 men were diabetic and hospitalised for regulation of blood glu-

cose levels, while 9 were hospitalised for peptic ulcer. The patients in the non-surgery group also had their first PSA measurement on the hospitalisation day, 24 hours after the first measurement and 21 day after the first one. All blood samples were obtained between 8.00 a.m. and 10.00 a.m.

Exclusion criteria were previous prostatic operation, pyuria, bacteriuria, symptomatic urinary tract infection, and recent urological manipulations such as prostate biopsy in the last six weeks, transrectal ultrasonography in the last two weeks, urethral catheterization in the last three weeks and hepatic dysfunction. Any urological manipulations or therapeutic interventions were avoided until the end of the study. The protocol was approved by the ethical committee at the University Of Mersin School Of Medicine for Human Investigation, and previous informed consent was obtained from each patient.

Serum total PSA and free PSA were measured with the electrochemiluminescence immunoassay "ECLIA" (Roche Diagnostics GmbH, Mannheim, Germany).

The mean values in the text were given as "mean ± Standard Deviation". Statistical analysis was performed by using:

- Independent Samples T Test for comparing the ages of the two groups,
- General Linear Model Repeated Measures Test for comparing the surgery and non-surgery groups' PSA values and PSA values of the patients underwent inguinal hernia repair and colectomy,
- Paired Samples T Test for comparing the PSA values of each group.

Results

There was no statistically significant difference between the ages of the patients in the groups ($p > 0.05$). The overall mean serum tPSA, fPSA and free to total PSA ratios (f/t PSA) and standard deviations are summarized in table 1. There was no PSA value greater than 2.5 ngr/mL.

When surgery and non-surgery groups were compared for tPSA values, no statistically significant difference was found between the groups (Table 1). In the 24th hour measurements, there was a 13.8% decrease in the surgery group and a 13.1% decrease in the non-surgery group, and the differ-

ence was statistically significant when compared to the first measurement ($p < 0.05$ for surgery group, $p < 0.05$ for non-surgery group). However, there was no statistical difference between first and 21st day tPSA values of both groups when compared with the first measurements ($p > 0.05$, $p > 0.05$, respectively).

There was no statistically significant difference between the two groups, with the respect to fPSA values (Table 1). However, when the first and the 24th hour fPSA values were compared, a 4.0% decrease in surgery group and an 8.2% decrease in

Table 1. Summary of the total PSA, the free PSA values and the f/t PSA ratios of the patients.

Group	Total PSA (ng/ml) ± SD			Free PSA (ng/ml) ± SD			Free/Total PSA Ratio ± SD		
	First	24th hour	21th Day	First	24th hour	21th Day	First	24th hour	21th Day
Surgery	1.61 ± 0.89	1.47 ± 0.83	1.57 ± 0.88	0.67 ± 0.43	0.63 ± 0.45	0.75 ± 0.45	0.42 ± 0.15	0.44 ± 0.15	0.46 ± 0.12
Non-surgery	1.99 ± 0.89	1.86 ± 0.90	1.96 ± 0.93	0.88 ± 0.43	0.80 ± 0.31	0.87 ± 0.40	0.44 ± 0.10	0.46 ± 0.14	0.44 ± 0.12
p value	>0.05			>0.05			>0.05		

Table 2. Summary of the total PSA, the free PSA values and the f/t PSA ratios of the patients grouped according to operation type.

	Total PSA (ng/ml) ± SD			Free PSA (ng/ml) ± SD			Free/Total PSA Ratio ± SD		
	First	24th hour	21th Day	First	24th hour	21th Day	First	24th hour	21th Day
Colectomy	1.82 ± 0.98	1.68 ± 0.85	1.85 ± 0.90	0.83 ± 0.41	0.81 ± 0.41	0.81 ± 0.37	0.48 ± 0.09	0.50 ± 0.08	0.46 ± 0.11
Inguinal Hernia Repair	1.51 ± 0.86	1.36 ± 0.86	1.43 ± 0.90	0.56 ± 0.44	0.50 ± 0.46	0.62 ± 0.45	0.37 ± 0.17	0.40 ± 0.18	0.46 ± 0.15
p value	>0.05			>0.05			>0.05		

non-surgery group was found ($p < 0.05$, $p < 0.05$, respectively). As in tPSA values, there was no statistical difference between the values of the first and the 21st day ($p > 0.05$, $p > 0.05$, respectively).

Furthermore, f/t PSA ratios showed no statistically significant difference between the surgery and non-surgery groups (Table 1). Although there were fluctuations in tPSA and fPSA measurements, there was no statistically significant difference between the first and the 24th hour values ($p > 0.05$ in surgery group, $p > 0.05$ in non-surgery group), and the first and the 21st day f/t PSA ratios ($p > 0.05$, $p > 0.05$, respectively).

A comparison was made within the surgery group according to the type of the operation. No statistically significant difference was detected between the ages (57.0 ± 10.3 years, 60.5 ± 11.1 years, $p > 0.05$, respectively) and duration of anaesthesia of the patients (122 ± 18 minutes, 113 ± 22 minutes, $p > 0.05$, respectively) who underwent hernia repair and laparoscopic colecystectomy. There was no statistically significant difference between tPSA, fPSA values and f/t PSA ratios, either. The PSA measurements and p values are summarized in Table 2.

Discussion

Little is known about the effect of anaesthesia on the metabolism of PSA. Junior et al investigated serum PSA levels of patients who underwent cardiac surgery with symptomatic benign prostatic hyperplasia, operated with and without extracorporeal cardiopulmonary circulation [18]. All of the patients were catheterised with an 18 F Foley catheter for the first 24 hours. They found that there were statistically significant elevations in the postoperative serum PSA levels of the patients who were operated with extracorporeal cardiopulmonary circulation, while there was no statistically significant difference in serum PSA levels in those who were operated without extracorporeal cardiopulmonary circulation. Although the study pointed out the effect of extracorporeal cardiopulmonary circulation on serum PSA levels, it is hard to draw a conclusion about the effect of anaesthesia on serum PSA levels from the study. However, we showed that there was no significant difference between the tPSA and fPSA values of the men who had operation under general anaesthesia and those who did not.

The surgery group consisted of two subgroups because the type of the surgery might affect the results, especially for the laparoscopic cholecystectomy that might cause a greater reduction in the hepatic blood flow. However, when we compared the results of the patients in the surgery group, we could not find any statistically significant difference in the serum tPSA, fPSA levels and the f/t PSA ratios between the patients who underwent laparoscopic cholecystectomy and those who underwent inguinal hernia repair.

Tekin et al. found an average serum PSA decrease of 12% and Stamey et al. found a decrease of 18% after hospitalisation [19, 20]. Our results were consistent with these reports. The decreases that were demonstrated in two groups were similar, hence, anaesthesia could not be the cause of those decreases. As concluded by Stamey et al., decreased physical activity might be the cause of the decrease in serum PSA levels.

Although changes in serum tPSA and fPSA levels were found, there was no statistically significant change in the f/t PSA ratio. Similarly, Çetinkaya et al. investigated the short-term effect of transurethral resection on serum tPSA and fPSA levels. They found that serum tPSA and fPSA levels were increased significantly, however, without any meaningful change in serum f/t PSA ratio, so serum f/t PSA ratio could be a reliable parameter in the follow-up of patients after prostatic manipulations and hospitalisation [1].

Anaesthesia alone does not affect serum tPSA or fPSA levels, while hospitalisation does. PSA measurement of patients who are to be hospitalised and operated on should be done either before or three weeks after the hospitalisation in order to detect and stage prostate cancer.

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