Efficacy of Vitamin-E Usage to Prevent Non-Traumatic Injury of Prostate Gland in Cases That Experienced Open Heart Surgery

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Citation

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Abstract

Background: The purpose of this study was to evaluate the prostate damage during the CABG surgery and to investigate the role of vitamin E in protection.

Methods: 33 male patients undergoing coronary artery bypass graft (CABG) surgery were enrolled in this study. The patients were randomized into two groups. In Group I (Control group, n=17), 50cc saline, and in Group II (Vitamin E Group, n=16), 300 mg water-soluble vitamin E was administered intravenously before coronary artery surgery. Blood samples of all patients were obtained at pre-determined times: 24 hours before surgery, 24 hours after surgery, 48 hours after surgery, 72 hours after surgery and 7 days after surgery. Blood samples were analyzed for total prostate specific antigen (TPSA), free prostate specific antigen (FPSA), and for prostatic acid phosphates (PAP) concentrations.

Results: Operative and demographic characteristics did not differ between the two groups. No significant difference for basal TPSA concentrations was determined between the groups but t2 (2.06±0.04, 1.05±0.02), t3 (3.74±0.54, 1.28±0.33), t4 (4.72±0.06, 1.81±0.04) and t5 (3.63±0.05, 1.23±0.03) concentrations were observed to be significantly higher in the first Group (Control Group). Prostatic acid phosphates (PAP) concentrations did not differ significantly between the groups.

Conclusion: Serious prostate gland damage was demonstrated in the male patients after coronary bypass surgery and as a result of this high prostate specific antigen levels were determined. It can be stated that the administration of vitamin E intravenously before CABG operations protects the prostate from damages caused by cardiac surgery.

INTRODUCTION

Although open cardiac coronary artery bypass grafting surgery has become a routine procedure worldwide, it causes organ dysfunction due to systemic inflammatory response, systemic oxidative stress and endothelial damage. In addition to the cardiac, renal, hepatic or pulmonary dysfunction related to coronary artery bypass graft (CABG) surgery, recently, the studies about the ischemia in the prostate gland occurring during cardiopulmonary bypass (CPB) has become important [1,2,3]. Prostate damage may lead to changes in prostate specific antigen (PSA) concentrations. The concentration of PSA, which is a specific antigen for prostate, increases not only during prostate cancer but also during benign prostate hyperplasia (BPH) and prostatitis. It's the most important biological marker for prostate and it's produced by the epithelium cells of the gland and it spreads to the extracellular space [1,2,3]. Total prostate specific antigen (TPSA), free prostate specific antigen (FPSA) and prostatic acid phosphates (PAP) concentrations are the best markers for prostate damage [1,4].

It was demonstrated that TPSA and FPSA concentrations increased after CABG due to the ischemia. Less is known about the damage and how to prevent it. Consequently further studies are necessary to evaluate this.

As it is known, vitamin E is an antioxidant that has been used in the ischemia-reperfusion models. It is the major antioxidant to prevent the formation of the oxygen-derived free radicals and at the same time it neutralizes the free radicals when formed. It has been demonstrated in several studies that because of its chemistry it neutralizes free radicals of oxygen and reduces the reperfusion injury with

its antioxidant activity [5,6,7,8].

The purpose of this study was to evaluate the prostate damage during the CABG surgery and to investigate the role of vitamin E in protection.

MATERIAL AND METHODS

This study was approved by the Ethics committee of the Trakya University Hospital. A total of 33 American Society of Anesthesiologists (ASA) ii-iii status male patients undergoing CABG were included in the study. Exclusion criteria were history of a neurological disease, poor ventricular function, and ejection fraction less than 40%, emergencies, history of a recent BPH, history of a similar CABG operation and cardiac valve operations.

The groups were randomized into two groups. 50 ml saline solution was administered intravenously before CABG in the first group (Control group, n=17). Water-soluble vitamin E (300 mg) in 50 cc saline solution was administered intravenously in the second group (Vitamin E Group, n=16). Blood samples of all patients were obtained at predetermined times (t_1: 24 hours before surgery, t_2: 24 hours after surgery, t_3: 48 hours after surgery, t_4: 72 hours before surgery, t_5: 7 days after surgery). The blood samples were analyzed for TPSA (N: 0-4 ngr/ml), FPSA (N: 0.05-0.25 ngr/ml) and PAP (N: 0-9 U/L). Using radial arterial catheter and the same monitors (Siemens SC 7000, Germany) mean arterial pressure was measured at 9 different points (During induction, at the beginning of CABG, in the middle of CABG, at the end of CABG, postoperative 2^{nd} , 6^{th} , 12^{th} , 24^{th} , 48^{th} hr).

All patients were premedicated with 10 mg morphine and 10 mg diazepam intramuscularly (i.m.) an hour before the surgery. After premedication, left radial arterial cannulation and right forearm venous cannulations were performed. In the operating room standard monitorization was carried out by using electrocardiogram (ECG), invasive arterial pressure and pulse oximeter.

The patients were all preoxygened and anesthesia was induced with diazepam 0.2 mg/kg^{-1} iv, pancuronium 0.1 mgkg^{-1} iv, fentanyl 10 µgkg^{-1} iv and anesthesia was maintained with 2% inspired sevoflurane in oxygen/air mixture and when necessary, 5 µgkg^{-1} fentanyl and 2 mg pancuronium was given i.v. after intubation. Swan Ganz catheter was placed via right vein jugularis into the pulmonary artery. Preoperative hemodynamic measurements [mean arterial pressure, heart rate, central venous pressure (CVP), pulmonary artery pressure (PAP)] were performed by using standard Siemens SC 7000, Germany monitor. Anticoagulation was provided by heparin (300 IUkg^{-1}, Liquemine Roche, Basel, Switzerland); activated clotting time (ACT) was kept about 480 seconds and to maintain this level additional doses were administered when necessary.

Then for all patients roller pump (Sarns 9000, USA) disposable membrane oxygenators (D 708 simplex adult fiber oxygenator Dideco, Mirendolai Italy) and moderate hypothermia (28-30°C core temperature) were used for CPB. Perfusion rate was kept at and above 2.4 L/m^2/min during CPB. All operations were performed under CPB which was established via the cannulation of ascending aorta and rightatrium (two stage cannula). At the time of the total bypass (TBP) after cross clamping antegrade, potassium containing blood cardioplegic (Plegisol, Abbott Lab, Chicago, Il, USA) solution was delivered into the aortic root to form cardiac arrest and to save the myocardium and it was repeated at intervals about 20 minutes. In both groups, to maintain anesthesia 5 µgkg^{-1} fentanyl and 2 mg pancuronium were administered into the pump. At the end of the operation nasopharyngeal temperature was elevated up to 37°C. With the achievement of the adequate temperature, aortic cross clamp was removed. All of the proximal anastomoses were carried out under partial aortic clamping under side clamp. After the decannulation procedure, the roller pump was withdrawn. Neutralization of heparin was done by protamine HCl (Protamine 1000 Roche, Basel, Switzerland) with a dose ratio of 1:1.

STATISTICAL ANALYSIS

Data were presented as mean±standart deviation. All analyses were performed using AXA507C775506FAN3 serial number statistica Software for Windows and differences were considered statistically significant at a probability level of less than 0.05. Grupların normal dağılıma uygunluğu için Kolmogorov Smirnov One Sample Testi uygulandı. Grupların dağılımının normal olduğu görüldükten sonra gruplararası karşılaştırmalar için ındependent sample t test uygulandı. Grup içi karşılaştırmada Paired t test kullanıldı. $p<0.05$ anlamlı kabul edildi.

RESULTS

The demographic and operative findings didn't differ between the groups (Table 1).

Figure 1

Table 1: The demographic and operative properties of cases (mean ± SD)*

	Group 1 (Control group)	Group 2 (E vit group)
Age (y)	59.6 ± 8.9	55.4 ± 8.5
Body surface area (BSA) (m^2)	1.85 ± 0.17	1.78 ± 0.12
CPBT (min)	104.2 ± 26.8	98.9 ± 22.8
CCT (min)	55.1 ± 19.6	50.7 ± 14.9

CPBT : Cardiopulmonary bypass time
CCT : Cross clamp time
* Kolmogorov-Smirnov test ve Independent Samples test anlamlı değil

During the operation and during the postoperative period the mean arterial pressure values of the cases didn't differ significantly between the groups (Table 2).

Figure 2

Table 2: Mean arterial pressure values (mean ± SD)*

MAP (mmHg)	Group 1 (Control group)	Group 2 (Vitamin E group)
Induction	67.3 ± 9.2	69.7 ± 11.3
At the beginning of CABG	86.2 ± 13.4	83.1 ± 13.0
In the middle of CABG	69.1 ± 16.3	64.1 ± 11.9
At the end of CABG	80.3 ± 11.5	74.3 ± 10.4
Postoperative 2nd hour	69.5 ± 8.1	70.6 ± 11.3
Postoperative 6th hour	68.9 ± 9.6	71.8 ± 9.8
Postoperative 12th hour	67.1 ± 11.3	71.4 ± 8.8
Postoperative 24th hour	71.5 ± 11.3	77.1 ± 12.7
Postoperative 48th hour	65.1 ± 11.3	66.9 ± 13.2

MAP : Mean arterial pressure
CABG : Coronary artery bypass graft
* Kolmogorov-Smirnov Test ve Independent Samples Test anlamlı değil

There was not a significant difference between TPSA and free PSA basal values between the two groups, but important increases were observed in control group in the latter measures. On the contrary these increases were observed to be very little in the vitamin E group (Table 3). PAP values didn't differ significantly between the groups.

Figure 3

Table 3: Total PSA, Free PSA and Prostatic Asid Phosphatase values (mean ± SD)

Time	TPSA (ng/ml)		FPSA (ng/ml)		PAP (U/L)	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
t_1	0.99±0.06[h]	0.72±0.04[m]	0.33±0.03[k]	0.28±0.02[t]	3.12±0.9	3.33±0.8[v]
t_2	2.06±0.04[i]	1.05±0.02[a,n]	0.53±0.02	0.37±0.01[u]	2.99±0.8	4.10±1.1[6,v]
t_3	3.74±0.54	1.28±0.03[b,z]	0.54±0.02	0.30±0.01	3.08±1.0	3.47±1.0
t_4	4.72±0.06	1.81±0.04[c,z]	0.65±0.03	0.24±0.01[e]	3.64±1.1	3.38±0.9[z]
t_5	3.63±0.05	1.29±0.03[d]	0.45±0.02	0.20±0.01[f]	3.53±1.0	3.76±0.8

TPSA: Total prostate specific antigen, FPSA: Free prostate specific antigen,
PAP: Prostatic acid phosphates

t_1: 24 hours before surgery t_2: 24 hours after surgery t_3: 48 hours after surgery t_4: 72 hours after surgery t_5: 7 days later after surgery

Independent Samples Test; a; p= 0.004, b; p= 0.012, c; p= 0.008, d; p= 0.007, e p=0.011, f p=0.003, g p=0.012,

Paired Samples Test;

Group 1; h; t_1 vs t_2 p= 0.001, t_1 vs t_3 p=0.003, t_1 vs t_4 p=0.000, t_1 vs t_5 p=0.002 i; t_2 vs t_4 p= 0.005, t_2 vs t_5 p=0.034 k; t_1 vs t_2 p= 0.010, t_1 vs t_3 p=0.012

Group 2; m; t_1 vs t_2 p= 0.002, t_1 vs t_3 p=0.001, t_1 vs t_4 p=0.001, t_1 vs t_5 p=0.001 n; t_2 vs t_3 p= 0.027, t_2 vs t_4 p=0.007 r; t_3 vs t_4 p=0.012 s; t_4 vs t_5 p= 0.009 t; t_1 vs t_2 p= 0.002 u; t_2 vs t_4 p=0.037, t_2 vs t_5 p=0.001 v; t_1 vs t_2 p= 0.006, t_1 vs t_5 p=0.008 y; t_2 vs t_3 p=0.021, t_2 vs t_4 p=0.029 z; t_4 vs t_5 p= 0.020

DISCUSSION

In this study it was demonstrated that, TPSA and FPSA levels increased significantly during the postoperative period of CABG operations and this increase could be prevented by vitamin E, which is a strong antioxidant. .

It was shown that prostate has suffered from non traumatic tissue damage as a result of the perfusion disorder seen in pelvic visceral organs of the cases that have undergone CABG operations. Coker et al [4]. stated that there could be an increase in prostatism symptoms after cardiac surgery and this could be determined by the increase of PSA in serum. Researchers determined that this increase in PSA levels is related to the ischemic damage of prostate, which is not traumatic, and they stated that it can stay high during postoperative 48 hours. Hagood et al [7] stated that during

the cardiac surgical operation done with CABG, PSA intensity can be seen in serum with a reason whose etiology is unknown and without any dependence on urethral catheterization. According to Guvel et al [9], the increase in the values of TPSA reaches to the maximum level postoperative on the 5th day. The increase in these antigens specific to prostate is accepted as a sign of damage in gland.

Similar to literature, important increases were determined in TPSA and FPSA values in the cases of control group and it was observed that these increases became more clear postoperative on the 4th day. There were no certain facts about process of returning back to normal values of TPSA and FPSA in other studies, besides in this study it was determined that even at the first week basal values could not be reached.

It is a fact that, the hypotension during CABG causes cerebral, renal, hepatic and pulmonary dysfunction [10,11]. In the present study hypotension didn't occur preoperatively, postoperatively or during the operation. Therefore it demonstrated that prostate perfusion pressure did not play a vital role in the increase difference in the TPSA and FPSA levels. On the other hand in this study, it was observed that the administration of vitamin E which has a strong antioxidant capacity, resulted in reduced release of TPSA and FPSA compared to the control group, and this showed that prostate was more slightly damaged. Vitamin E has been used in cardiac, intestinal, striated muscle ischemic-reperfusion models and very successful results have been achieved. The antioxidant capacity of vitamin E neutralizes free oxygen radicals, and increases the membrane stabilization on the membrane lipids so it protects from the reperfusion damage. Although these properties are known, there is no study with the prostate ischemia-reperfusion model.

Netto et al [2] stated that the levels of PSA is higher in the cases after CABG surgery. For this reason to assess the efficacy of vitamin E for the protection of prostate gland the effect of vitamin E on prostate before CABG surgeries was evaluated. As a result, it was observed that the increase in both TPSA and FPSA levels was lower in vitamin E group compared to the other group. This showed that vitamin E had an important role in preventing prostate injury.

Ascid phosphatase is an enzyme primarily found in prostate gland and semen, which highly increases during the prostate gland dysfunctions [1]. In this study in both groups the levels of PAP didn't increase significantly so, this made the researcher think that CABG operations and vitamin E aren't related to this enzyme.

In conclusion, it was demonstrated that there was serious prostate injury in male patients after CABG operations and as a result of this there were high PSA concentrations. It is thought that the administration of vitamin E before CABG protected the prostate gland from the damage caused by the CABG surgery.

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References

1. Zhang WM, Finne P, Leinonen J, Salo J, Stenman UH. Determinat?on of prostate-specific antigen complexed to alpha2-macroglobulin in serum increases the specificity of free to total PSA for prostate cancer. Urology 2000;56:267-272.
2. Netto JMR, Lima ML, Guedes MA, Patino LL, Oliveira JB. Elevation of prostate specific antigen in cardiac surgery with extracorporeal cardiopulmonary circulation. J Urol 1998;159:875-7.
3. Morote J, Encabo G, Lopez M, de Torres IM. Prediction of prostate volume based on total and free serum prostate-spesific antigen: is it reliable? Eur Urol 2000;38:91-5.
4. Coker C, Sherwood RA, Crayford T, et al. Ischemic damage to the prostate during cardiac surgery: a clinical model. Prostate 1997;32:85-8.
5. Nagel E, Meyer zu Vilsendorf A, Bartels M, Pichlmayr R. Antioxidative vitamins in prevention of ischemia/reperfusion injury. Int J Vitam Nutr Res 1997;67:298-306.
6. Coghlan JG, Flitter WD, Clutton SM, Ilsley CD, Rees A, Slater TF. Lipid peroxidation and changes in vitamin e levels during coronary arter bypass grafting. J Thorac Cardiovasc Surg 1993;106:268-74.
7. Ek B, Hallberg C, Sjogren KG, Hjalmarson A. Reoxygenation-induced celldamage of isolated neonatal rat ventricular myocytes can be reduced by chain-breaking antioxidants. Free Radic Biol Med 1994;16:117-21.
8. Canbaz S, Duran E, Ege T, Sunar H, Cikirikcioglu M, Acipayam M. The effects of intracoronary administration of vitamin E on myocardial ischemia-reperfusion injury during coronary artery surgery. Thorac Cardiovasc Surg 2003;51:57-61.
9. Hagood PG, Parra RO, Rauscher JA. Nontraumatic elevation of prostate spesific antigen following cardiac surgery and ekstracorporeal cardiopulmonary bypass. J Urol 1994;152:2043-5.
10. Guvel S, Turgoz R, Egilmez T, et al. Does ischemia-induced prostate damage during cardiac surgery involving cardiopulmonary bypass cause bladder outlet obstruction? Urol Int 2005;74:337-40.
11. Nayler WG, Elz JS. Reperfusion injury: laboratory artifact or clinical dilemma? Circulation 1986;74:215-21.
12. Kloner RA, Przyklenk K, Whittaker P. Deleterious effect of oxygen radicals in ischemia/reperfusion. Resolved and

unresolved issues. Circulation 1989;80:1115-27.
13. Yau TM, Weisel RD, Mickle DAG, et al. Vitamin E for coronary bypass operations. A prospective, double-blind, randomized trial. J Thorac Cardiovasc Surg 1994;108:302-10

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