ORIGINAL ARTICLE

Postoperative Plasma Antithrombin III Concentration in Gynecological Surgery

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ABSTRACT

Aim: Thromboembolic accidents are frequently responsible for morbidity and mortality after major gynecologic surgery. This study was designed primarily to evaluate changes in antithrombin III (ATIII) levels during a period extending from a day before surgery to 3rd postoperative day.
Place and duration of study: Lady Aitchison hospital, Lahore, Pakistan, from January 1998 to December 1998.
Design: It was an observational study.
Methodology: Thirty female patients were enlisted in this study project from department of gynecological surgery of Lady Aitchison hospital Lahore. Mean age of these patients was 50.4 years. Two samples of citrate anticoagulated blood were drawn from each patient. First citrated blood sample was taken one day prior to surgery and second sample on third day after surgery. Only one blood sample was drawn from each control.
Results: Significant decrease in concentration of antithrombin III was noticed in patient group. This critical fall of about 30% in antithrombin III level may be the result of strong activation of coagulation pathways. This activation of coagulation may result from circulation stasis at surgical site, trauma to local vascular endothelial lining and severe tissue damage from complicated extensive surgery.
Conclusion: Our study results confirmed a very highly significant decrease in concentrationof AT III on 3rd postoperative day in patients undergoing gynecological surgery.
Keywords: Gynecological surgery, AT III, Preoperative and Postoperative.

INTRODUCTION

Human antithrombin III (ATIII), a glycoprotein constituted by serial linkages of 432 amino acids in the form of a single chain. It is a vitamin K independent natural anticoagulant. Its half life is 48-72 hours with a normal plasma level of 100-140 mg /dL[1].

All serine proteases which are produced as a result of coagulation pathways activation are inhibited by plasma antithrombin III. It is the thrombin which is primarily inhibited, followed by free activated coagulation factors: Xa, IXa, VIIa, plasmin and kallikrein[2]. Protease inactivation by antithrombin III is through formation of a 1:1 stoichiometric irreversible complex with activated enzyme[3]. The speed of complex formation between antithrombin III and serine protease is greatly enhanced in the presence of heparin. In plasma, AT III occurs as α- antithrombin and β-antithrombin. Quantitative and qualitative deficiencies of AT III are risk factors for thromboembolism[4].

The physiological importance of AT III is clearly demonstrated in individuals who suffer from inherited or acquired deficiency of antithrombin III and frequently suffer from recurrent thromboembolic accidents[5,6]. Incidence of inherited AT III deficiency is rare. Acquired deficiency is much more frequently seen after severe trauma, extensive surgical procedure, use of estrogen containing medications and precipitated thrombotic complications[7]. It is also suggested that female patients who are undergoing major surgical intervention must stop taking medicines containing estrogens few weeks before surgery and also for few weeks after surgery[8]. Venous system is frequently affected by thrombotic complications of AT III deficiency, whereas arterial system is rarely affected. The veins of lower extremities, mesenteric veins and cave veins are frequently involved[9].

AT III accounts for approximately 70% of antithrombotic activity of plasma[10]. High risk situations like major surgery, extensive trauma and parturition result in increased and accelerated consumption of AT III. Intraoperative and postoperative decrease in AT III may lead to 12-40 % fall in the concentration of plasma AT III concentration and could predispose patients to postoperative venous thrombosis[11,12]. Antithrombin III level of less than 80 % of normal during postoperative period is high risk for thromboembolic disorder[13].Depression of more than 30 % in the level of AT III seems critical for the development of thrombosis, at this level AT III is not effective in inactivating the procoagulant factors and in preventing thrombosis. Wound healing, pus production and hemostasis at surgical trauma site may be the etiological factor of postoperative AT III fall, as it is consumed during these events.

PATIENTS AND METHODS

Site selected for this study was gynecologic surgery department of Lady Aitchison hospital, Lahore. Duration of this study extended from 1stJanuary 1998 to 31st December 1998. Two groups were constituted for this study. Group first comprised of forty female patients who were included

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in planned majorgynecological surgery list and for second group ten healthy females were selected who were matched with patient group regarding age.Ethically verbal and written approval was taken from all 40 subjects participating in this study. Citrated blood samples were taken from each subject. Two citrated venous blood samples from patients and only one from controls were taken. First patient sample was taken a day prior to surgery and second on third day after surgery. Only one blood sample was taken from subjects of control group. Each blood sample of 1.8 mL was delivered to a vacutainer containing 0.2 mL of trisodium citrate. After proper mixing a platelet poor plasma was obtained from each sample. Radial immunodiffusion plates containing monospecific sheep polyclonal antibodies were used to calculate concentration of ATIII in platelet poor plasma.Following patients were not included in this study;

1. Individuals suffering from chronic renal disease, chronic liver disease, recent myocardial infarction and inflammatory intestinal disorder, all ultimately leading to profound decrease in ATIII levels.
2. Patients who were suffering from some bleeding disorder, history of thromboembolic event, taking drugs like estrogens, contraceptive pills and parenteral anticoagulants.

RESULTS

In this study thirty female patients were selected who were included in the list of major surgery for gynecologic indications. Out of these thirty patients, fifteen had benign pathology whereas remaining fifteen were suffering from malignant disorders (Table I).In patient group age ranged from 39 to 66 years, mean was 50.4 years. Antithrombin III concentration reduced after surgery for both benign and malignant gynecologic disorders. In our study, AT III concentration of control and preoperative subjects showed very highly significant difference when compared with postoperative values. Percentage decrease in concentration of AT III was 25.1 % in our patients of major gynecologic surgery.

Table 1: Details of gynecological surgery cases.

TYPE OF OPERATION	**NO OF CASES (n=30)**
Ovarian malignancy	06
Cervical cancer	05
Endometrial cancer	03
Ovarian cysts	06
Uterine fibroids	10
(Benign disorders 15/ Malignant disordres 15)	**n= 30**

Table 2: Comparison of plasma antithrombin III levels in major gynecologic surgery patients and controls (The values are expressed as mean ± SD (mg / L)

Control(n=10)	**Patients (n=30)**	
	Pre-operative	**Post-operative**
261.7 ± 22.41 (240 – 295)	273.7 ± 62.09 (225 – 475)	205.1 ± 41.81 (110 – 275)
B vs C2 P < 0.001 C1 vs C2 < 0.001	P < 0.001 Very highly significant P > 0.05 Not significant C1: Preoperative value C2: Postoperative value	

DISCUSSION

Events of thromboembolism are of great concern to surgeon during the early postoperative period of major gynecologic surgery. It is documented that 12-40% postoperative fall in concentration of AT III can increase the risk of venous thromboembolism[14,11,12]. In our study AT III levels before operation was 273.7±62.09 mg /L with a range from 225 to 475 mg /L. This preoperative value was statistically non-significant when compared to AT III concentration of control subjects. On third postoperative day antithrombin III plasma concentration was 205.1±41.81 mg / L with a range from 110 to 275. This postoperative value of AT III was statistically highly significant when it was compared with values of control group and preoperative subjects. Decrease in concentration of AT III in this study was 25.1 %, favoringearlier studies results in declaring gynecologic surgery as a moderate risk surgery. This postoperative decrease in AT III concentration might be due to increased consumption of antithrombin at surgical incision site for achieving hemostasis. Plasma AT III levels are also reduced during healing activity postoperatively.

This finding of our study was in conformity with many other international studies conducted by Sagar et al[15], Manahan et al[16], Gitel et al[17], Gallus et al[18], Rheaume et al[19] and Breddin and Kirchmaier[20].Donati et al[21] concluded in their study that there was no statistically significant difference between preoperative and postoperative AT III levels.

CONCLUSION

Results of this study concluded a highly significant fall in the levels of AT III during the early postoperative period. It can also be concluded from results of study that major gynecologic surgery is a moderate risk surgery for thromboembolic events during the early postoperative period. It is already documented that a fall of more than 30 % in AT III levels during postoperative period is high risk period for patient. Ultimate suggestion from this study for surgeons is that plasma antithrombin levels must be advised before and after major gynecologic surgery to know percentage decrease in AT III concentration. This valuable information will be very helpful for surgeon to decide whether patient needs anticoagulation therapy and at which time. My message for surgeons is that by knowing preoperative and postoperative AT III levels, they will not only limit thromboembolic events after surgery but also be contributing in reducing morbidity and mortality in patients who have undergone major gynecologic surgery.

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