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Fibrin Generation, Degradation and Thombolysis

Fibrinogen and fibrin degradation products in patients undergoing open-heart surgery

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We have determined fibrinogen and fibrin degradation products (FgDP and FbDP respectively) by an ELISA method using specific monoclonal antibodies in 100 patients undergoing cardiopulmonary bypass (CPB) for valvular heart disease and in 60 patients undergoing aorto-coronary bypass surgery. Blood samples were taken pre-operatively and on post-operative days 1 and 5. Post-operative evolution was similar in both patient groups, with a significant increase in FgDP on post-operative days 1 and 5 with respect to baseline value ($P < 0.01$). FbDP were also significantly higher on post-operative days 1 and 5 ($P < 0.001$), especially the day after surgery in patients with valvular disease as compared with coronary patients ($P < 0.01$). Our results indicate that fibrinolysis is more important than fibrinogenolysis after open-heart surgery, which may have pathophysiological implications.

Key words: Cardiac surgery, fibrinogen degradation products, fibrin degradation products, fibrinogen.

Introduction

Numerous alterations in the fibrinolytic system have been reported in patients undergoing cardiopulmonary bypass (CPB) surgery, but there is still controversy as to the relative role of fibrinolysis. Normal and increased values in fibrinolytic parameters have been reported intra-operatively, and normal and decreased values during the post-operative period.[1-4] Increased fibrinolysis could contribute to post-operative bleeding.[5,6]

The aim of this study was to evaluate some aspects of the fibrinolytic system in patients before and after cardiopulmonary bypass for valvular and coronary disease, by using specific assays for fibrinogen and fibrin degradation products.

Patients and methods

One hundred and sixty patients who underwent CPB surgery because of valvular (n = 100) or coronary (n = 60) diseases were included in the study. The baseline characteristics, the main diagnosis and the duration of bypass are listed in Table 1. Blood samples were taken in all patients pre-operatively and on post-operative days 1 and 5. Blood was collected into 0.11 mol/l trisodium citrate (9:1) and immediately centrifuged at 2 500 × g for 20 min at 4° C. The platelet-poor plasma was stored at – 70° C and thawed immediately before use.

Fibrinogen and fibrin degradation products were determined by an ELISA method as described by Nieuwenhuizen[7] using the Fibrinostika FGDP and

Table 1. Patient characteristics and duration of CPB

Total number of patients	160
Age (years)	58 ± 16
Sex (male/female)	101/59
Valvular disease	100
Mitral	48
Aortic	27
Mitral + Aortic	11
Others	14
Coronary disease	60
Duration of CBP (min)	
Valvular disease	86 ± 52
Coronary disease	79 ± 40

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Fibrinostika FBDP kits respectively (Organon Teknika, Netherlands). Briefly, the wells of polyvinyl microtitre were coated with the monoclonal antibody FDP-14 as a catching antibody specific for degradation products of both fibrin and fibrinogen. The test sample or standard is added to the well. In the next step anti-FDP (FDP-Y18) or antifibrin (FDP-DD13) labelled with horseradish peroxidase is added and the colour developed with the substrate tetramethylbenzidine.

Statistical analysis included determination of means and standard deviations. Values at different sampling times were compared using the Wilcoxon test with the cut-off for statistical significance at $P = 0.05$.

Results

One hundred and sixty patients undergoing CPB were studied. The post-operative evaluation of the parameters analysed is shown in Figure 1. There was a significant increase of both fibrinogen and fibrin degradation products on post-operative days 1 and 5 with respect to the pre-operative level in patients undergoing CPB for

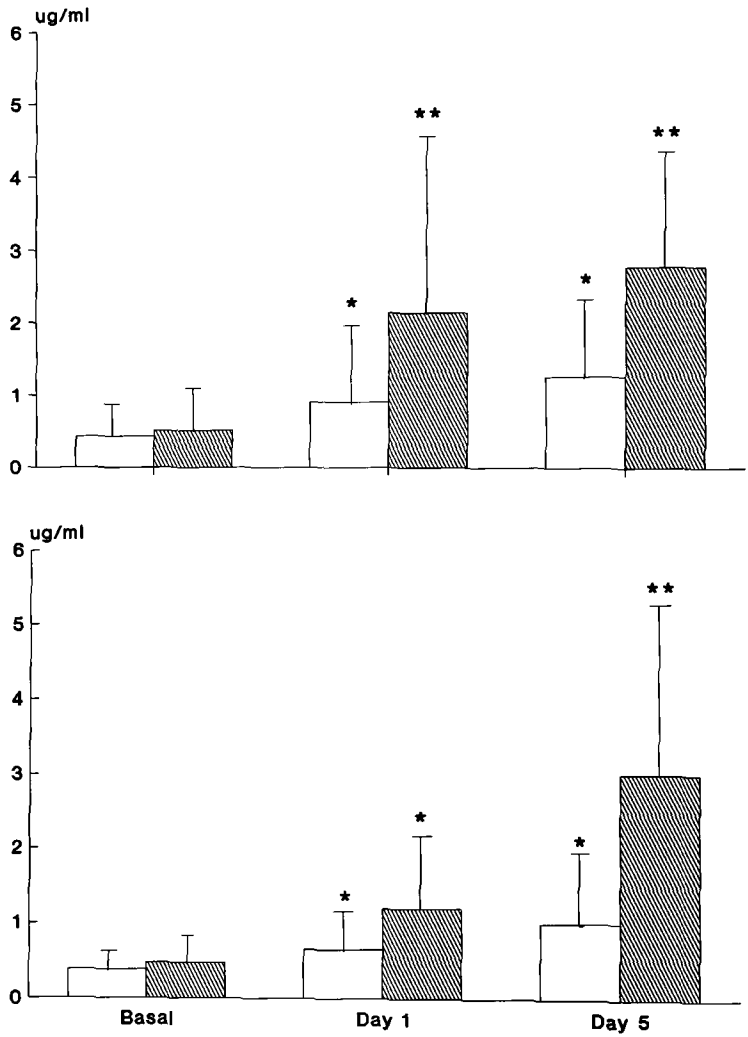

Figure 1. Plasma levels of (mean ± SD) of FgDP (open bars) and FbDP (hatched bars) in valvular surgery (top) and coronary surgery (bottom). *$P < 0.01$, **$P < 0.0001$.

valvular disease. This increase was more evident for fibrin degradation products. Similar results were observed for coronary patients, although the concentrations of fibrinogen and fibrin fragments were lower than those observed in valvular disease (Figure 1).

Whereas no differences for fibrinogen degradation products were observed to be related to the surgical procedure, fibrin degradation concentrations were significantly higher on post-operative day 1 ($P < 0.01$) in patients undergoing CPB for valvular disease as compared with changes observed in coronary surgery (Figure 2).

Discussion

We have found a significant increase in fibrinogen and fibrin degradation products during the post-operative period in patients undergoing CPB for valvular and coronary disease, suggesting an activation of the fibrinolytic system. This increased fibrinolytic activity

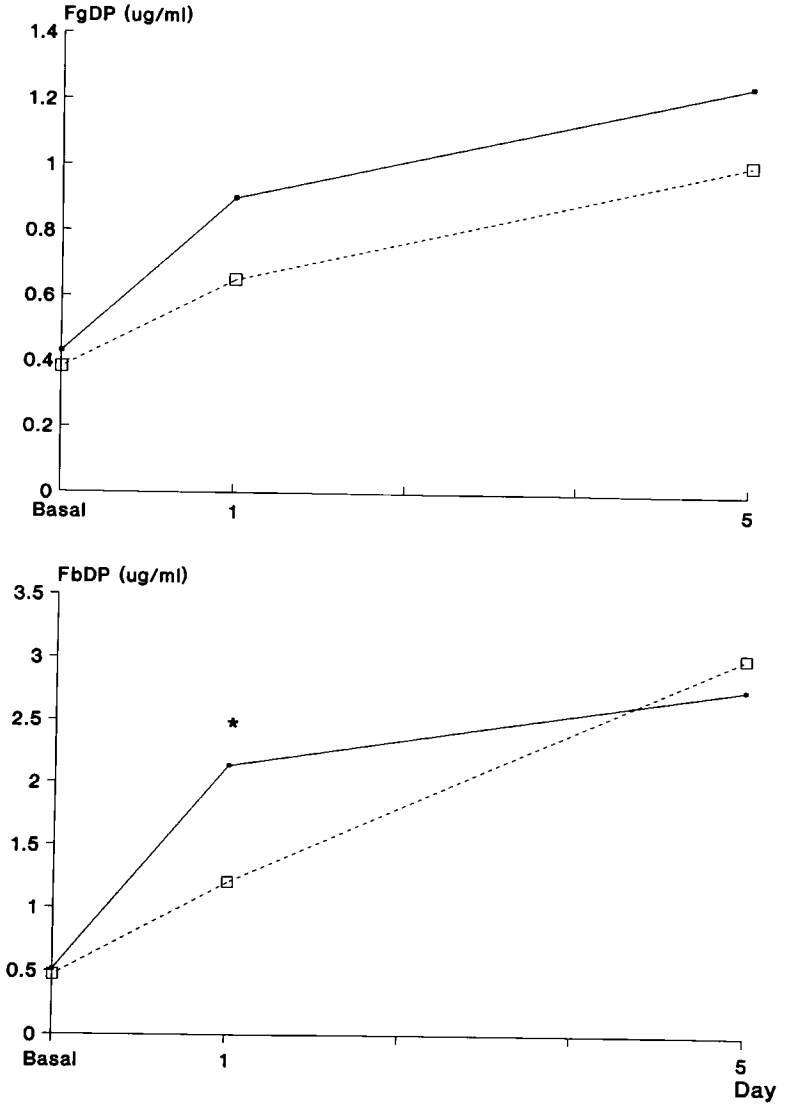

Figure 2. Post-operative evolution of FgDP and FbDP in CPB for valvular (——) and coronary (------) surgery. *$P < 0.01$.

may be the result of plasminogen activation and/or decreased plasmin inhibitors as a consequence of the cardiopulmonary bypass. In fact, previous reported results on fibrinolysis parameters during CPB surgery seem to agree with an intra-operative plasminogen activation, which to some extent could contribute to post-operative bleeding.[4, 8-11]

Higher concentrations of fibrin as compared with fibrinogen degradation products were observed in our patients, which could indicate that fibrin is newly formed in the circulation as a result of haemostatic activation during cardiopulmonary bypass and subsequently lysed by the plasmin generated following activation of the fibrinolytic system. Moreover, fibrin degradation products were significantly higher on post-opetative day 1 in patients who underwent valvular surgery as compared with changes observed in coronary surgery. The reason for this discrepancy is not clear, but might be related to the different technical procedures as well as to the relatively more prolonged duration of the bypass in valvular disease in our series.

In conclusion, the increased fibrinogen/fibrin degradation products suggest an increased fibrinolytic activity post-operatively after CPB. Our results indicate that fibrinolysis plays a more important role than fibrinogenolysis after open-heart surgery, which may have pathophysiological implications.

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