EVALUATION OF THE ROLE OF APROTININ IN THE MANAGEMENT OF CASES WITH CONSUMPTIVE COAGULOPATHY

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SUMMARY

Aprotinin was given intravenously in patients of septic abortion, placenta previa and eclampsia having consumptive coagulopathy. The drug treated group showed significant changes in coagulation parameters viz. clotting time, prothrombin time, platelet count and plasma fibrinogen (except in coagulation time in cases of eclampsia) as compared to controls. The result obtained in these cases confirmed the efficacy of Aprotinin in the treatment of consumptive coagulopathy.

Introduction

Aprotinin is an alkaline polypeptide extracted from bovine lung. It is a broad spectrum proteinase inhibitor. It has been recently introduced in the Indian market as Antagosan by Hoechest Pharmaceuticals Limited. It acts by the stabilisation of certain vital enzyme systems in the body and its therapeutic actions are based on this property e.g. in abruptio placentae it stabilises the plasamin system, in pancreatitis it inhibits trypsin and in haemorrhage and shock it stabilises kinin kallikrein system. Aprotinin has proved to be effective in reducing the blood loss after surgical procedures (Redecker *et al*, 1978). It has been used in different hypofibrinolytic disorders to reduce bleeding (Hammad and Sher, 1977; Schmutzler et al, 1966; Bhatt, 1982) and also in treatment of acute pancreatitis (Goldberg, Roy and Skyring *et al*, 1965 and Cox *et al* 1977). Often the case of septic abortion, placenta previa and eclampsia are associated with consumptive coagulopathy (disseminated intravascular coagulation-DTC). The present study has been undertaken to study the effect of the drug on the various coagulation parameters in these cases and also to evaluate its therapeutic value in these disorders.

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Material and Methods

The study was conducted in the department of Obstetrics and Gynaecology of our Institution. The total number of cases studied was 56 and this included 16 cases of septic abortion, 20 of placenta previa and 40 of eclampsia. Diagnosis of septic abortion was made on the basis of history and clinical examination whereas cases of placenta previa were diagnosed by vaginal examination under anaesthesia.

All the cases included for the study

were those who showed excessive bleeding per vaginum or showed other evidence of DIC in the form of epistaxis, bleeding from gums, bleeding from puncture site, haematuria etc.

The patients in each group were randomly divided into two equal groups, one control and other drug-treated (Trial) group before the delivery. Controls were managed on the usual line of therapy. Trial group received inj. of Aprotinin 200,00 KIU IV followed by an infusion of 200,000 KIU in 500 ml. of glucose. The infusion rate was maintained at 34 drops/minute so as to give 50,000 KIU/hour. Blood samples were collected at admission time and again after 6 hours in both the groups and were subjected to analysis of coagulation parameters. The names of the coagulation parameters and the laboratory criteria used for the diagnosis of DIC are mentioned below:

Coagulation parameter and Normal values

1. Clotting time (CT) 5-11 min.
2. Clot Retraction time (CRT) 43 ± min.
3. Prothrombin time (PT) 12 ± Second
4. Platelet count (PC) 250,000 ± 50,000/C.mm.
5. Plasma fibrinogen level (PF) 230 ± 25 mg%

Criteria for DIC diagnosis

Prolanged CT
Decreased CRT
PT more than 15 seconds
PC less than 150,000/C.mm.
PF less than 150 mg%

Results

1. A significant improvement in the consumptive coagulopathy represented by decreased CT, increased CRT. decreased PT, increased PC and an increased PF in aprotonin treated patients of septic abortion as shown in Table I.

2. In placenta praevia patients, Aprotinin treated group showed significantly decreased CT, increased CRT, decrease in PT, increase in platelet count and increase in plasma fibrinogen (Table II).

3. The changes in the coagulation parameters in eclampsia cases are shown in Table III. The difference in clotting time in the control and trial groups is not significant. However, following changes increased clot retraction time, decreased prothrombin time, increased platelet count, increased plasma fibrinogen were all significant. (Table III).

TABLE I
Coagulation Parameters in Septic Abortions

Group	CT (min)	Change from normal value			PF mg%
		CRT (min)	PT (sec)	PC/CU mm	
Central					
Mean	+1.8	—1.25	+0.5	—4500	— 4
S.D.	±0.927	±0.5809	±0.7071	±7194	± 7.211
Aprotinin					
Mean	—2.625	4.25	—2.125	25250	18.25
S.D.	±0.8557	±2.681	±0.6062	±14660	± 9.52
't'	9.2806	5.4808	7.163	4.8217	5.1506
p	<0.01	<0.01	<0.01	<0.01	<0.01

TABLE II
Coagulation Parameters in Placenta Previa Cases

Group	CT (min)	Change from normal value			PF mg%
		CRT (min)	PT (sec)	PC/CU mm	
Control					
Mean	+1.0	—1.2	+0.9	—8000	—9.2
S.D.	±1.049	±1.536	±0.8307	±2968	±4.01
Aprotinin					
Mean	—3.1	2.8	—1.6	10200	3.8
S.D.	+0.7	±0.9798	+0.4899	+3518	+5.963
't'	9.754	6.588	7.778	11.872	9.607
p	<0.01	<0.01	<0.01	<0.01	<0.01

TABLE III
Coagulation Parameters in Eclampsia Cases

Group	CT (min)	Change from normal value			PF mg%
		CRT (min)	PT (Sec)	PC/CU mm	
Control					
Mean	+1.55	—2.55	+ .55	—10500	—13.3
S.D.	±1.3118	±2.829	±0.234	±10140	± 9.717
Aprotinin					
Mean	—1.8	4.3	—1.1	+13200	13.4
S.D.	±0.265	±2.869	±1.044	±4.360	±6.055
't'	0.4588	7.4118	2.238	9.3608	10.167
p	0.05 NS	<0.01	<0.01	<0.01	<0.01

The development of consumptive coagulopathy in septic abortion is related to the release of endotoxins into the maternal circulation which bring about an activation of the fibrinolytic system. Aprotinin acts by stabilising the enzyme system and thereby inhibiting fibrinolysis. This was confirmed by an improvement in the coagulation status in the Aprotinin treated group as compared to a deterioration in the control.

No other data was available regarding trial of Aprotinin in cases of septic abortion. Acosta *et al* (1976) used Aprotinin in the treatment of septic shock and found that the patients showed significant improvement in haemodynamic and coagulation parameters and fared much better as compared to the patients who were not given the drug.

Cases of placenta praevia with DIC also showed an improvement in the coagulation parameters in the Aprotinin treated group as compared to a deterioration in the control group. To the best of our knowledge no other data is available with which we could compare our results in cases of placenta previa.

In cases of eclampsia, the cause of DIC development is probably due to damage to the placenta resulting in the liberation of tissue thromboplastin which in turn starts the intravascular coagulation process. Development of DIC in cases of severe pre-eclampsia and eclampsia is quite rare

but serious when it does occur. In assessing the prophylactic value of Aprotinin in such cases, it was found that there was a significant improvement in the coagulation parameters in the trial group.

There were no other studies with which we could compare our results of eclampsia cases, but those obtained by us suggested that Aprotinin could be used prophylactically for the prevention of DIC in these cases.

The result of our study are a pointer to the fact that Aprotinin could be of value in the treatment of septic abortion and placenta previa complicated by consumptive coagulapathy and in the prevention of this disorder in cases of eclampsia.

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