ROLE OF APROTONIN IN ABRUPTIO PLACENTAE

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SUMMARY

Aprotonin (Antagosan) has been administered to patients of abruptio placentae with a view to improve their consumptive coagulopathy and also to evaluate the utility and limitations of the drug.

Aprotonin produced significant improvement in all coagulation parameters as compared with control group patients. It stopped bleeding from various sites. None of the patients showed any side/ toxic effects when the drug was employed.

Introduction

The discovery of Aprotonin from bovine lung in 1930 by Werle was the beginning of series of clinical trials to evaluate this broad spectrum proteinase inhibitor.

The plasmin system was found to be one among the several enzyme systems on which Aprotinin was found to have a stabilising action. This action was made use of in the treatment of cases of Abruptio placentae complicated by consumption coagulopathy. Among those who used Aprotinin in cases oof Abruptio placentae were Sher (1975, 1977, 1981) and Daftary and Agarwala (1933), Aprotonin is a relatively new drug for India. Our study endeavoured to find out the exact use and limitations of this drug in cases of Abruptio placentae.

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Material and Methods

This study was conducted in Department of Obstetrics and Gynaecology, G.S.V.M. Medical College, Kanpur. 40 cases were taken up in all, out of which 20 served as controls.

The patients were between the age of 20-30 years. On admission detailed history was taken regarding the pain in abdomen onset of bleeding P/v so that a fairly accurate estimation of the time of abruption could be made. Detailed physical examination was then carried out, which included noting the pulse, BP, abdominal girth, fundal height, tenseness of the abdominal wall and amount of bleeding per vagina. No heparin, fibrinogen or antifibrinolytic agent was administered.

Consumptive coagulopathy was suspected when there were asociated features like epistaxis, bleeding from gums bleeding from puncture sites, haematuria etc. It was confirmed by the following laboratory values.

(i) Prolonged clotting time 11 min (Normal range 5-11 min).

(ii) Prorthombin time 15 sec. (Normal range 12 sec. ± 1sec.).

(iii) Platelet count < 1,50,000/C.mm (Normal range 2,50,000 ± 50,000).

(iv) Plasma fibrinogen < 150 mg% (Normal range 230 + 35 mg%).

The cases were divided randomly into two groups control and trial and were treated as follows:

(A) Control group: These cases were managed along the usual lines including recording of blood pressure, artificial rupture of membranes and oxytocin drip. The time of onset of uterine contractions was noted, and the interval between this and the time of delivery determined.

Blood samples were drawn at the time of delivery and after 6 hours and again subjected to the investigations mentioned above.

(B) Trial group: The cases in this group were those who even after having undergone artificial rupture of membranes and attempts at induction by oxytocin drip, showed evidence of uterine inertia. Uterine inertia was diagnosed when repeated vaginal examination at intervals of two hours, showed no progress in cervical dilatation over a period of six hours.

Such patients were given inj. Aprotonin 200,000 KIU intravenously followed by an infusion of 200,000 QIU in 500 ml of glucose adjusted so as to give 50,000 units/hour i.e. 34 drops/min.

Onset and progress of uterine activity were monitored. Blood samples were drawn at delivery and after 6 hours for the investigations mentioned above.

Observations and Results

Out of the 40 cases studied 20 served as controls and 20 were given the drug under consideration.

Table I shows the average latent period after which uterine contractions started and the time taken for delivery in both groups of cases.

The results show that in the trial group, uterine contractions started earlier, and the time taken till delivery was considerably shortened (53.25%) as compared to the control group. Also the number of patients who had to undergo caesarean section in the Aprotonin treated group

TABLE I

Average Latent Period of Starting Uterine Contractions and Time Taken for Delivery

Control		Time after which contractions started hrs.	Time taken for delivery hrs.	No. of Pts. delivered by LSCS No.	%
Conrol (10)	Mean	3.55	11.50	8	75
	S.D.	± 0.3237	± 0.8396		
Trial (10)	Mean	1.13	7.46	2	25
	S.D.	± 0.6245	± 1.536		
Percentage Decrease		69.23	53.25		
't'		9.06	5.55		
'p'		<0.01	<0.01		

was considerably less (25%) in trial group and (75%) in control group.

Blood samples were drawn at three times for estimation of coagulation status in cases of abruptio placentae on admission, at delivery and six hours after delivery, here after referred to as stage 1, stage 2 and stage 3.

The changes in the parameters between stage 1 and stage 2 are represented in Table II and between stage 2 and stage 3 in Table III.

The results showed that the Aprotonin treated group showed a decrease in clotting time, decrease in prothrombin time, increase in platelet count and increase in plasma fibrinogen. The changes in all these parameters were significant. Clinical improvement in the Aprotonin treated patients was noted in the form of stoppage of bleeding from various sites including-gums, various puncture sites, haematemesis, epistaxis and haematuria etc. None of the patients treated with Aprotonin had post partum haemorrhage.

Discussion

The cause of fibrinogen depletion following abruptio placentae can be explained by the escape of placental or decidual thromboplastins into the maternal blood stream. This converts prothrombin to thrombin, which in turn converts fibrinogen to fibrin, the latter being deposited

TABLE II

Changes in Coagulation Parameters in Cases of Abruptio Placentae—Stages 1 & 2

Group		Changes from normal values			
		CT (min)	PT sec	PC/C.mm	PF mg%
Control	Mean	+ 1.5	+ 0.6	— 5200	— 5.8
	S.D.	± 1.025	± 0.6633	+ 6223	± 4.238
Trial	Mean	— 2.1	— 1.2	13800	13.8
	S.D.	± 2.47	± 0.8718	± 10720	± 9.518
't'		4.035	4.93	4.599	5.644
'p'		<0.01	<0.01	<0.01	<0.01

TABLE III

Changes in Coagulation Parameters in Cases of Abruptio Placentae—Stages 2 & 3

Group		Changes from normal values			
		CT (min)	PT (secs)	PC/C.mm	PF mg%
Control	Mean	0	+ 0.7	— 6409	— 1
	S.D.	± 1.183	± 1.005	± 9989	± 8.27
Trial	Mean	— 3.1	— 1.1	23400	16
	S.D.	± 2.508	± 1.64	± 18950	± 13.58
't'		3.355	2.807	4.175	3.208
'p'		o<0.01	<0.05	<0.01	<0.01

over a very large vascular surface some times producing serious visceral lesion. Other possible mechanisms are loss of fibrinogen into the retroplacental haematoma and primary activation of the fibrinolytic enzyme systems leading to hyperplasminemia. Aprotonin acts by stabilising the fibrinolytic system, leading to an improvement in the status of consumptive coagulopathy.

The probable mechanism of uterine inertia in abruptio placentae was explained by Basu (1955) who suggested that fibrinogen degradation products (FDP) had a direct inhibitory action on myometrial activity. Aprotonin, by bringing about a decrease in FDP levels, brought about reversal of uterine inertia.

Our results compared favourably with Sher (1975, 1977, 1981) and Daftary and Agarwala (1983) who also noted a significant improvement in the status of consumptive coagulopathy in patients of abruptio placetae treated with Aprotonin. We observed no side or toxic effects with the use of this drug.

Conclusion

Our study revealed that Aprotonin could be of considerable help in the treatment of abruptio placentae complicated by disseminated intravascular coagulation.

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