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ROLE OF APROTININ IN MODERATE AND SEVERE BURNS

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SUMMARY

The role of Aprotinin (Antagosan) in moderate and severe thermal burns has been studied. Patients were randomised in two groups; both receiving same treatment with the exception that patients in trial group received Aprotinin in addition. 2000,000 *K.I.U. (Kallikrein inhibition units) Aprotinin was given I.V. stat, followed six hourly, for three days. Mortality was* 27.08 *percent in trial group and* 47.92 *percent in control group* ($p < 0.05$). *Aprotinin is believed to be helpful in reducing mortality in burns.*

Werle (1958), isolated a proteinase inhibitor. It inhibits several biological enzyme systems. W.H.O. named it Aprotinin. Ever since, the drug has been used extensively in different shock states with satisfactory results. It has also been found useful in acute pancreatitis (Pollock, 1959; Skyring, 1965; Trapnell, 1974). The present study has been undertaken with the objective of assessing its utility in the management of moderate and severe burns.

Material and Methods

The study was conducted at L.L.R. Hospital, Kanpur. Patients with more than 20 percent thermal burns (second and third degree) were taken up for study. Patients were randomized into two groups, a trial and a control group. Patients were alternately allocated to these groups. Case numbers 1, 3, 5 and so on went in the trial group, whereas case numbers 2, 4, 6 etc. were in the control group. A detailed history taking and physical examination were done. Depth of burn and extent of burn were mapped on a chart. Investigations included haemoglobin percent, total leucocyte count, differential leucocyte count, urine examination, urine flow rate, bleeding time, coagulation time, prothrombin time and platelet count. Investigations were repeated as and when required.

Careful monitoring of vitals was done. The patient was said to be in shock, when:

(a) Pulse rate was more than 100 per minute,
(b) Systolic blood pressure less than 90 mm of mercury, and
(c) Urine flow of less than 20 ml per hour.

All patients received similar treatment in the form of I.V. fluids (according to Brooke's formula), antibiotics, analgesics and other supportive measures. Blood transfusion and vasopressors were given whenever indicated. Patients in trial group (group A) received in addition injection Aprotinin 200,000 units intravenously stat and was repeated six hourly for three days. Careful monitoring and frequent reappraisal of haemodynamic state was done. Changes in clotting time, prothrombin time and platelet count were recorded. Due to administrative and technical reasons tangential excision and immediate skin grafting was not feasible. Delayed split skin grafting after separation of eschar was carried out. Any complication occurring during the course of treatment was noted and appropriately managed.

Observations

A total of 96 patients have been studied. They were equally divided in group A (Trial) and group B (Control). Most of the patients were in the second and third decade of life (Table 1). There were 61 females and 35 males.

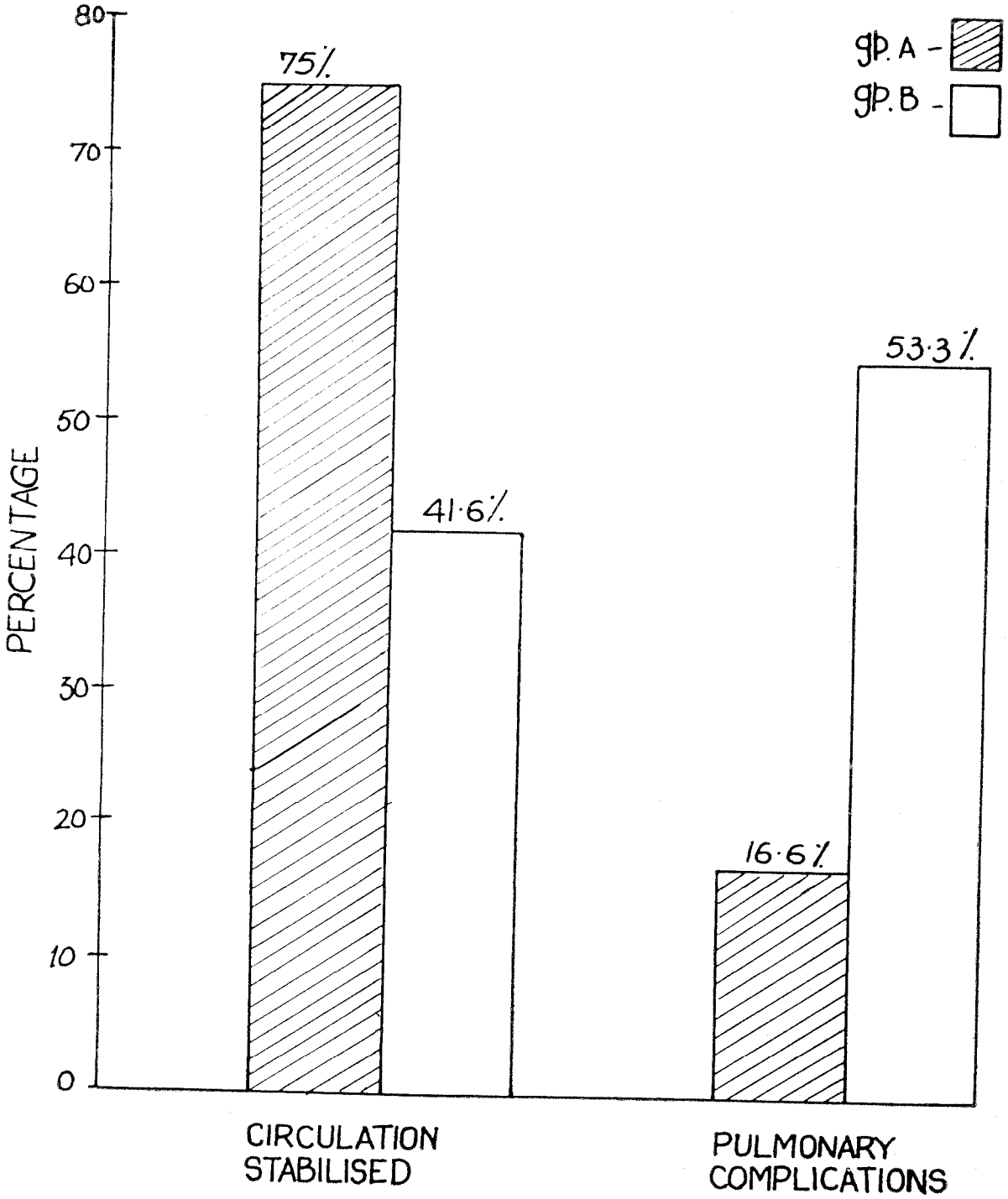

Fig. 1. Showing haemodynamic stabilization and pulmonary complications in both groups.

Table 1. Showing age distribution of patients

Age in years	No. of cases	
	Group A	Group B
0-15	4	3
16-30	13	15
31-45	20	16
46-50	7	10
51-65	3	4
65 & above	1	—

Table 2, shows the body surface area involved (Rule of nine). Most of the patients were in the 30 percent to 50 percent range.

Table 2. Showing extent of burns in both groups

Percent area burn	Group A No. (%)	Group B No. (%)
21-30	6 (12.5)	5 (10.4)
31-40	8 (16.7)	13 (27.1)
41-50	10 (20.8)	11 (22.9)
51-60	13 (27.1)	9 (18.7)
61-70	7 (14.6)	8 (16.7)
71 & above	4	2 (4.2)

Changes in clotting time, prothrombin time and platelet counts have been recorded in both the groups (Table 3).

Table 3. Showing changes in clotting time, prothrombin time and platelet counts in both groups

Group		Clotting time (min.)	Prothrombin time (sec.)	Platelet count per cu. mm.
Trial (A)	mean	−2.9	−2.0	29,100
n=48	S.D.	±0.2	±0.6	±12,228
Control (B)	mean	1.09	0.6	−9,126
n=48	SD	±0.8	±0.5	±7,708
	't'	2.5	3.4	2.67
	'p'	<0.05	<0.01	<0.05

The mean clotting time decreased by 2.9 min. in the Aprotinin treated group (Group A) while it increased in control group by 1.9 min. ($p<0.05$). Mean prothrombin time fell by 2.0 sec. in the trial group and increased by 0.6 sec. in the control group ($p<0.01$). The mean platelet count improved by 29,100 per cu. mm. in the trial group and deteriorated by 9,126 per cum mm. in control group ($p<0.05$).

Improvement in shock state was observed in many patients. 75 percent (36 cases) in group A became stable with Aprotinin therapy. The comparable figure for control group is 41.66 percent (20 cases) as shown in Fig 1. Pulmonary complication in the form of respiratory distress was observed in 8 patients of group A (16.66 percent). In group B the incidence of this complication was 53.33 percent (28 cases).

Overall mortality in group A (Trial) was 27.08 percent (13 cases), while in group B (Control) was 47.92 percent (23 cases). This was statistically significant ($p<0.05$).

Discussion

Second and third degree burns involving more than 20 percent of body surface area, cause systemic changes as well. Larger the area of burn, more profound are the changes, and there are more chances of shock. Damaged body tissues produce pathophysiologically active enzymes, viz. kalikreins, plasma trypsin and certain other proteineases liberated from leucocytes and damaged tissues. They are liberated due to tissue hypoxia. Further capillary damage causes increased permeability leading to loss of fluid from the intravascular compartment. It reduces the effective blood volume.

Plasma kinins act on kininogens, liberating vasoactive polypeptides called kinins. Kinins are highly potent pharmacologically active substances. They cause vasodilatation, increased capillary permeability and oedema. Increased kinin levels are seen in burns. Apro-

tinin inhibits the formation of kinins.

Aprotinin also inhibits plasmin and plasminogen activators, thereby inhibits fibrinolysis and fibrinogenolysis. This prevents further formation of fibrin and fibrin degradation products (FDP), which act as anticoagulants and interfere with polymerization of fibrin monomer.

Results of our study show that there has been significant reduction in prothrombin time. It is in conformity with those of Daftery and Agarwal (1983). Aprotinin with methyl prednisolone has been used in patients with septic shock and found to give significantly better results. Clotting time is also reduced (though not statistically significant).

Some degree of thrombocytopenia occurs after burns. However, a marked reduction of thrombocytes ($>100,000$ per mm^3), especially during the first 24 hours, is a clear sign of impending development of severe respiratory insufficiency. It is due to trapping of thrombocytes in the lungs. Supplementary Aprotinin treatment decreased the degree of thrombocytopenia. This corroborates with the findings of Rosengarten et al. (1981) who observed it in patients with multiple trauma.

Stabilisation of the haemodynamic state was achieved in 75 percent of patients in trial group, compared to 41.66 percent in the control group. Besides preventing capillary injury. Aprotinin attenuates the action of myodepressant factor (MDF) produced in burns and other hypoxic states.

Pulmonary complications were less in the group receiving Aprotinin. In shock state release of a peptide has been described, which can raise the pulmonary arterial pressure and produce morphological lung parenchymal changes. The peptide is inhibited by Aprotinin (Schnells, 1980).

The overall mortality in group A (Trial group) was lower than the group B (Control group) which received similar treatment, except for Aprotinin. It is statistically significant at 'p' values <0.05. The distribution of patients in trial and control groups is comparable (Tables 1 and 2). The difference in mortality is perhaps due to the administration of Aprotinin (Antagosan) in trial group. Gandhi and Nandi (1982) have emphasised on earliest possible administration of Aprotinin in adequate doses.

Conclusion

In this preliminary clinical study the following conclusions are drawn. Aprotinin therapy in burn patients,

1. Improves clotting time,
2. Improves prothrombin time,
3. Improves platelet count,
4. Helps combating shock,
5. Reduces, incidence of pulmonary complications, and
6. Brings down mortality.

However, further controlled clinical trials are warranted to substantiate our observations.

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