British Journal of Plastic Surgery (1980), **33**, 430 433
0007-1226/80/0086-0430 $02.00

THE ROLE OF HEPARIN IN RESTORING THE BLOOD SUPPLY IN ISCHAEMIC SKIN FLAPS: AN EXPERIMENTAL STUDY IN RABBITS

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In recent years many attempts have been made clinically and experimentally to improve the blood supply in ischaemic flaps and minimise or prevent completely the impending tissue necrosis. Kiehn and Des Prez (1960) stressed the role of cooling. Stark and De Haan (1959) used histamine iontophoresis and other techniques such as hyperbaric oxygen (McFarlane and Wermuth, 1966), topical dimethylsulphoxide (Adamson *et al.*, 1966), low molecular weight dextran (Grabb and Oneal, 1966; Goulian, 1967), high doses of corticosteroids (Mendelson and Woods, 1978) and α and β adrenergic blocking agents (Myers and Cherry, 1968; Norberg and Palmer, 1969; Barisoni and Veall, 1969; Palmer, 1972; Johnson *et al.*, 1975; Jurrell and Johnson, 1976; Finseth and Adelberg, 1978) have been tried experimentally with some success.

This present study investigates the role of heparin in preventing ischaemic flap necrosis experimentally in rabbits.

METHOD AND MATERIALS

Albino rabbits (weight 1 to 2 kg) were premedicated with intramuscular atropine sulphate and anaesthetised with open ether. Standard flaps 2 cm wide and 6 cm long were raised on the side of the trunk with the base of the flap at the mid-dorsal line in front of the hind limbs. The flaps were raised by incising the skin and panniculus carnosus and then sutured back in the same position. These flaps consistently developed necrosis at the distal end. Indeed after raising these flaps it was our practice to check their vascularity using an injection of bromophenol blue dye and only to include the flap in our study if the dye showed definite visual evidence of ischaemia.

Two methods were used to check and assess the vascular efficiency of the experimental flaps:

1. The distribution and pattern of skin staining in the flap after the i.v. injection into an ear vein of bromophenol blue dye 2·5 per cent solution in physiological saline buffered at pH 7·4. The definitive assessment was made 30 minutes after the intravenous injection.
2. The clearance of radioactive iodine I^{131} injected intradermally at two sites in the flap itself (2 cm from the base and 1 cm from the tip of the flap). These isotope studies were carried out under basal sedation with diazepam 0·5 mg-/kg body weight.

The amount of radioactivity was counted using a specially calibrated

scintillation counter and charts were compiled to plot the $T\frac{1}{2}$ clearance which indicated the "vascular efficiency" at the site of injection.

All the flaps in this study were kept under observation for seven days and the extent of the flap necrosis was recorded. The experimental animals were allotted to 3 groups:

Group I. Controls (10 rabbits). The flaps were raised, the vascularity checked by bromophenol dye injection and isotope clearance: the flaps were then replaced in position. No heparin was given to any animal in this group.

Group II. 30 rabbits injected with i.v. heparin, shortly after raising the flap. Divided into 3 subgroups of 10 rabbits each:

1. Heparin given 6 hourly intravenously into an ear vein in a dose of 50 units/kg body weight.
2. Heparin given 6 hourly intravenously in a dose of 100 units/kg body weight.
3. Heparin given 6 hourly intravenously in a dose of 200 units/kg body weight.

In all these groups the blood clotting time was checked at regular intervals over a period of 7 days.

Group III. 10 rabbits were given the first dose of heparin 6 hours after raising the flap in a dose of 100 units/kg given 6 hourly.

Observations

Controls: Group I. Immediately after intravenous injection of the dye bromophenol blue, bluish discolouration extended into the flap over a distance of 1·67 cm and this increased to 3·7 cm after an interval of 30 minutes. The dye *never* appeared in the remainder of the flap. The radioactive clearance studies ($T\frac{1}{2}$ clearance) showed some improvement at the base of the flap within 24 hours, but a very significant reduction in the rate of clearance at the distal end of the flap.

After 7 days, only 73 per cent of the total length of the flap survived.

Group II.

1. With intravenous heparin in the dosage of 50 units/kg, the clotting time increased by a factor of 2. The radioactive clearance $T\frac{1}{2}$ showed highly significant improvement over 24 hours both at the base and the tip of the flap (from 55 and 80 minutes to 32 and 60 minutes respectively). After 7 days 88 per cent of the length of the flap survived.
2. With intravenous heparin in the dosage of 100 units/kg the clotting time increased to 2·7 times the normal range. The radioactive clearance ($T\frac{1}{2}$) from the base and the tip of the flap improved in 24 hours from 50 to 80 minutes to 33 and 37 minutes respectively.

After 7 days the whole length of every flap had survived.

3. With an intravenous heparin dosage of 200 units/kg, the clotting time was increased by a factor of 3·6. The $T\frac{1}{2}$ clearance was dramatically increased from the base and tip of the flap from 32 and 60 minutes to 17 and 23 minutes respectively. After 7 days, the full length of every flap had survived (Fig. 1). There was, however, significant bleeding from the flap in one animal.

Group III. When heparin was given intravenously 6 hourly starting 6

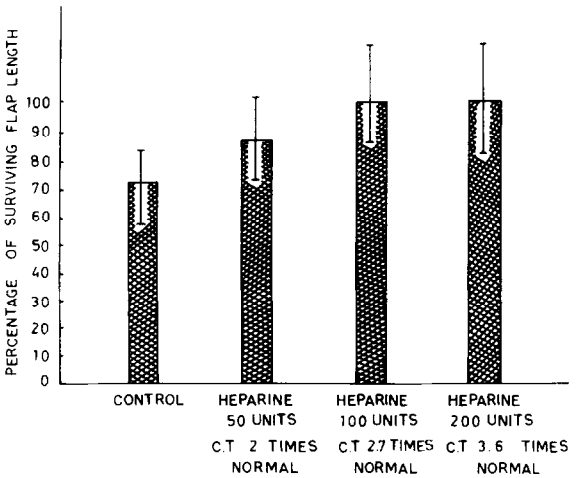

FIG. 1. Shows comparison of surviving length of flaps with or without varying dosage of heparin, administered immediately after raising flaps.

hours after elevation of the flaps in the dosage of 100 units/kg, the clotting time was increased by a factor of 2·25. The $T\frac{1}{2}$ clearance from the base and tip of the flap in 24 hours improved from 35 and 60 minutes to 22 and 45 minutes respectively. After 7 days 96·6 per cent of the length of the flap survived (Fig. 2).

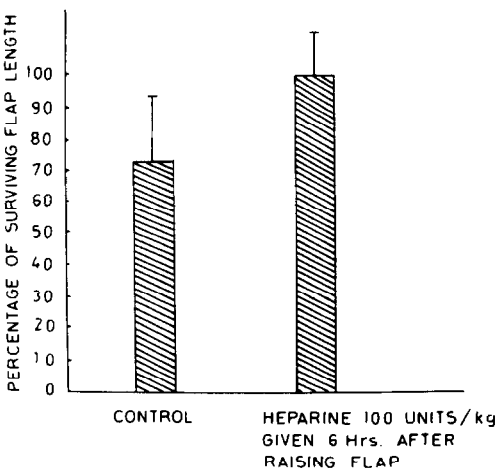

FIG. 2. Showing comparison of surviving length of flaps with heparin administered immediately or 6 hours, after raising flaps.

DISCUSSION

When a disproportionately long random pattern flap 2 × 6 cm was raised in the rabbit, there was always a significant reduction in the blood supply visible clinically to the naked eye and capable of confirmation by the injection

intravenously of the dye Bromophenol Blue and radioactive clearance studies using I^{131}.

There did not appear to be a direct relationship between the surviving length of the flap and the length of the flap which showed dye staining on the first day. Indeed the surviving length of the flap observed at 7 days was always greater than the length in which dye was noted 30 minutes after injection. This could be explained *in part* by improvement of the circulation in the flap over the first 24 hours since the $T\frac{1}{2}$ clearance did show some improvement at the base of the flap. On the other hand, it must be remembered that intravital dyes given intravenously may vary considerably in the pattern of staining of the tissues and perhaps this part of the experiment should be repeated with other dyes.

Administration of heparin intravenously shortly after elevation of the flap and repeated 6 hourly for 7 days, very significantly increased the survival of the flap: so much so that with doses of 100 units heparin/kg or over to maintain a clotting time of 2·7 times or more than the normal level necrosis of the flap was completely averted in every case. This dramatic effect was obvious to the naked eye and confirmed by the $T\frac{1}{2}$ clearance studies.

Equally impressive was the observation that the intravenous administration of heparin even after a delay of 6 hours, was able to protect the potentially ischaemic flap from necrosis almost as effectively. These observations would appear to have considerable relevance to clinical practice.

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