ROLE OF XANTHINOL NICOTINATE IN AUGMENTING VASCULAR SUPPLY IN ISCHEMIC SKIN FLAPS.

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Necrosis to a variable extent is infrequently seen in disproportionately long and ischemic random pattern skin flaps. Attempts have been made from time to time to improve vascularity of such flaps by various means i.e. cooling (Kiehan 1960) Hyperbaric oxygen (Macfarlane 1966) low molecular weight dextran (Grabb 1966 and Goulin 1967) Histamine iontophoresis (Stark 1959) and topical dimethylsulphoxide (Adamson 1966). In addition various pharmacological agents i.e. high doses of corticosteroids (Medelson 1978) and α and β adrenergic receptor blocking agents (Myers 1968, Norberg 1969, Barisoni 1969 Palmer 1972, Jonsson 1975, Jurell 1976 and Finseth 1978) have also been recently tried with some success.

We report here our findings on the role of xanthinol nicotinate (complamina) in augmenting vascular supply in ischemic flaps.

Methods and Materials

The study was conducted in albino rabbits weighing 1-2 kgs. Potentially ischemic flaps 2 cm$\times$6 cm were raised on the side of trunk with base 2.5 cm from mid line dorsally and situated 2.5 cms in front of hind limbs, and sutured back. The vascular efficiency was demonstrated by :—

(i) administration of bromophenol dye (2.5 percent in physiological solution buffered at pH. 7.4) intravenously into ear vein and recording the distribution of the dye in the flaps over a period of time.

(ii) Studying the clearance of isotope sodium iodide^{131} (B.A.R.C. code 10 M-1) from the flap after intradermal injection (immediately after raising and 24 hours later). The amount of radioactivity at the site of injection was monitored immediately and then continued for 30 minutes with the help of a suitably collimated Nai (Tl) scintillation counter having crystal size 50 cm diameter $\times$ 2.5 cm thick (Nuclear enterprises NE-4601) connected to a rate meter and linear strip chart recorder (Beckman recorder). Counts collected in 10 seconds at the instant of injection and at frequent intervals for 30 minutes were also recorded. $T\frac{1}{2}$ clearance was then found. As the rate of isotope clearance depends on the efficiency of circulation in flaps $T\frac{1}{2}$ clearance gave an indirect indication of the vascular efficiency of the flap at injection site.

The flaps were observed for 7 days at the end of which the extent of distal flap necrosis was noted.

The study was carried out in three groups.

Group I. Controls. (10 rabbits).

Group II. Complamina (Xanthinol Nicotinate).

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injected soon after raising flap (30 rabbits 10 in each sub-group).

(i) Sub-group A. Soon after raising the flaps, complamina 40 mgm/Kg was given intravenously into ear vein and repeated every 12 hours.

(ii) Sub-group B. The dose of complamina was increased to 80 mgm/kg 12 hourly.

(iii) Sub-group C. The dose of complamina was increased to 160 mgm. 12 hourly.

Group III. (10 rabbits.

The experiments were repeated as above but the first dose of complamina 80 mgm/kg was administered 6 hours after raising the flap so that its effect is studied after ischaemic changes had set it.

Observations :

Group I Controls :—

After injection of bromophenol blue, the dye immediately appeared all over the body as indicated by bluish discolouration, but in the flap it extended for 1.67 cm from the base on an average. After 30 minutes it extended further down to the extent of 3.7 cms. No dye was seen in the distal part of the the flap. $T\frac{1}{2}$ clearance of the isotope from the base and tip of the flaps averaged 45 minutes and 72 minutes respectively on the first day and 35 minutes and 120 minutes respectively after 24 hours. The clearance improved from the base but was significantly reduced from the flap tip. After 7 days only 72.8% of the flap length survived on an average.

Group II. Complamina group.

(i) Subgroup A. After injection of complamina, 40m gm/kg, 12 hourly $T\frac{1}{2}$ clearance of isotope from base and tip of the flap was 42 minutes and 68 minutes respectively on the first day and 35 minutes and 110 minutes respectively after 24 hours. The clearance improved from the base but was significantly reduced from the tip after 24 hours ($P<0.05$).

After 7 days it was found that only 65% of the flap length survived.

(ii) Subgroup B. After dose of complamina was increased to 80 mgm/kg 12 hourly there was significant improvement in $T\frac{1}{2}$ clearance from base and tip of flaps i.e from 22 minutes and 65 minutes respectively to 7 minutes and 35 minutes respectively on an average ($P<0.05$). When observed for 7 days. There was significant reduction in flap necrosis ($P<0.01$) and 90% of flap length survived.

(iii) When dosage of complamina was further increased to 160 mgm/kg 12 hourly none of the animals survived for more than 24 to 48 hours. Perhaps the dosage was much higher than could be tolerated (Figure 1).

Group III.

When complamina was administered 6 hours after raising the flaps. There was no improvement in $T\frac{1}{2}$ clearance from base and tip of the flaps i.e. being 42 minutes and 70 minutes immediately after raising of flaps and 35 minutes and 125 minutes respectively after 24 hours on an average. After observing for 7 days, 60% of the flaps were found to have survived.

Discussion

The study shows that Xanthinol Nicotinate in dosage of 80 mgm/12 hourly when administered soon after raising ischemic flaps

was capable of increasing the surviving length of the flap though not able to completely prevent flap necrosis. The dosage lower than this was ineffective and that higher than this was perhaps very toxic as all the animals died following its administration. The increasing in surviving length may be explained by improvment in peripheral circulation as indicated by improvement in $T\frac{1}{2}$ clearance. If however, the drug was administred after 6 hours had elapsed and ischemic changes had set in, the drug was ineffective in reversing or counteracting ischemic changes as there was no increase in surviving length of flap.

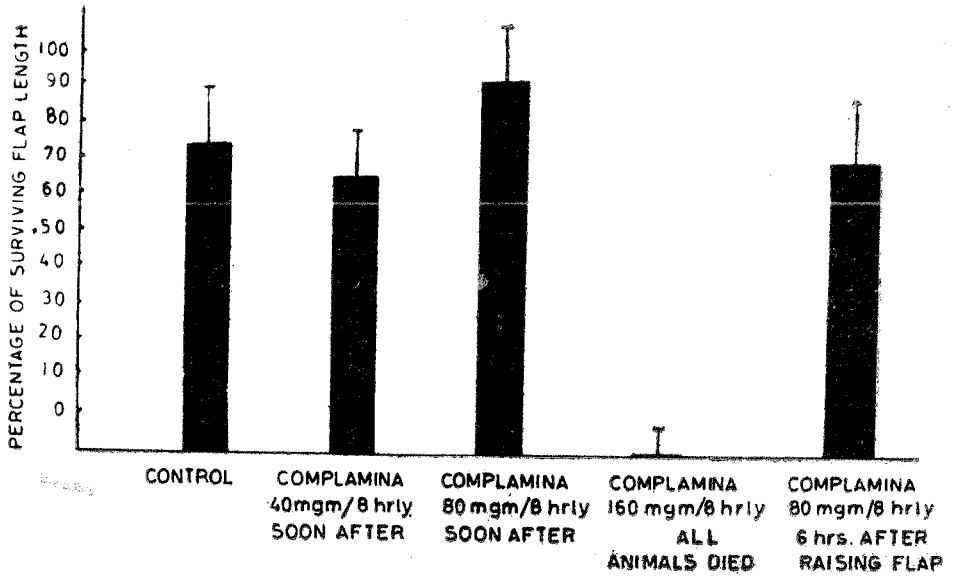

Fig. 1. Showing comparison of surviving flap lengths between control and those administered different doses of Xanthinol Nicotinate immediately after raising flaps or a lapse of 6 hours.

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