AUGMENTATION EFFECT OF CERTAIN VASODILATORS ON SKIN FLAP VIABILITY—AN EXPERIMENTAL STUDY

* V. Bhattacharya, M. S., M. Ch.
* S. K. Bhattacharya, M. D.
* J. M. Das, M. S., M. Ch.
* J. K. Sinha, M. S., F. R. C. S.
* F. M. Tripathi, M. S., M. Ch.

Summary

The effect of some drugs, inducing vasodilatation, was noted on skin flap survival in rats. 6-hydroxydopamine, which induces chemical sympathectomy, produced marked survival of the flaps. Isoxsuprine and salbutamol, the beta-2 receptor agonists, also induced significant augmentation of flap survival. All these drugs were more effective than the surgical delay procedure. Reserpine did not enhance skin flap survival. Since 6-HD, isoxsuprine and salbutamol produce marked vasodilatation, they may prevent skin flap necrosis by enhancing cutaneous blood flow.

Introduction

Despite a better understanding of cutaneous vasculature, the failing skin flap continues to be an enigma and a challenge to the plastic surgeon. Attempts have been made to salvage the failing skin flap experimentally, by using drugs which augment blood flow (Jurell and Jonsson, 1976; Finseth, 1979; Jurell et al., 1983), alter the rheology of blood (Takayanagi and Ogawa, 1980) or increase tolerance to ischaemia (Mendelson and Woods, 1978). The results of these studies are often conflicting and therefore difficult to interpret (Kerrigan and Daniel, 1982). Clinical studies on the treatment of failing skin flaps are also based primarily on isolated cases (Kerrigan and Daniel, 1982).

In view of the equivocal reports on drug induced salvage of the failing skin flap, a systematic experimental study has been undertaken involving the autonomic and autacoid systems affecting microcirculation. In this report we present the effect of some drugs, which affect the sympathetic nervous system, on the survival of the skin flap.

Material and Methods

Male Charles-Foster (250-300 gm) were used. They were housed in colony cages at an ambient temperature of 25±2°C, with free access to food (Hind Lever Chow) and water. The rats were anaesthetised (pentobarbitone sodium, 40 mg/Kg, ip). The dorsum was depilated by a hair remover and cleaned with normal saline. Bilateral cranially based random skin flaps, 1 cm wide and 3.5 cm long, were raised on either side of the dorsal spine, starting at the level of the lower border of the scapula. The entire flap, including the panniculus carnosus, was raised from the dorsal muscle fascia and fastened back with interrupted stitches on either side. Following the surgical manoeuvre, each rat was kept in a separate cage and obscr-
ved daily for signs of flap necrosis, characterised by initial discoloration, darkening and hardening of the tissues followed by sloughing. Generally necrosis of the flaps was observed from the fifth post operative day and was complete by the tenth day. Final observation was, therefore, carried out on the tenth postoperative day. The degree of necrosis was measured using a caliper and scale at three levels and the mean was recorded.

In the surgical delay group, ten bipedicile flaps of similar dimension were raised by making two parallel incisions and undermining the total length of the flap above the deep fascia. The margins were then stitched back. Seven days later the caudal end of the flap was divided and the flap was raised and observed along with the control and drug treated groups.

**Drug treatment**

The following drugs were used: reserpine (0.5 mg/Kg), isosuprime (5 mg/kg), salbutamol (1 mg/Kg), and 6-hydroxydopamine (50 mg/Kg).

All the above drugs except 6-hydroxydopamine (6-HD) were administered one day prior to the flap operation and then daily till the ninth postoperative day. 6-Hydroxydopamine was administered once 48 hours before surgery. Control animals received equivalent volume of sterile normal saline, intraperitoneally, starting one day before surgery and then each day till the ninth postoperative day.

**Statistics**—Results are expressed as means survival length as percentage of the total length of the flap ± St. Statistical analysis was done by the student’s t test for unpaired varieties.

**Results**

The results are summarised in the Table 1.

In the control group marked necrosis of the flap was noted, flap survival ranging from 1 to 1.2 cm (31.32%±0.60).

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Experimental group</th>
<th>% of mean survival in cm ± S.E.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Control</td>
<td>31.42±0.60</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Surgical delay</td>
<td>70.20±3.75</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3.</td>
<td>Reserpine</td>
<td>32.83±1.41</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>4.</td>
<td>Isoxsuprine</td>
<td>88.08±0.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5.</td>
<td>Salbutamol</td>
<td>79.71±2.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6.</td>
<td>6-Hydroxydopamine</td>
<td>100.00±0.00</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

N = 10

In the surgical delay group, no evidence of necrosis was found during the delay procedure. Even after the flaps were raised on the seventh day, the survival length of the flap varied from 1.9 to 3.1 cm (70.2%±3.75). The results being highly significant as compared to the control group (Fig. 1).

![Fig. 1. Showing the comparative survival length in the surgical delay and control group.](image)

In the reserpine treated group, there was no augmentation of flap survival as compared to the control, survival being 32.83%±1.41. The flap survival was significantly less than that achieved by surgical delay. Furthermore, the rats of this group suffered from diarrhoea, decreased food intake and loss of weight. Both
isoxsurpine and solbutamol enhanced flap survival significantly (Fig. 2), the survival length ranging from 2.8 to 3.2 cm (88.08% ± 0.98) and 2.4 to 3.2 cm (79.71% ± 2.53). The flap survival induced by these two drugs was significantly more than that achieved by surgical delay (Fig. 3). Pretreatment with 6-HD, completely protected the flap against necrosis, flap survival being 100% in all cases.

Discussion:

A skin flap, prepared as in the present study, is deprived of most of its blood supply since the blood vessels supplying the flap are severed. In addition, most of the nerve supply, including sympathetic nerves, are also cut (Palmer, 1970). The nerve endings, severed from central connection, degenerate leading to release of noradrenaline between 6 to 24 hours after the surgical manoeuvre (Jurell and Hjemdahl, 1983). This released noradrenaline is believed to induce vasoconstriction and augment metabolism, which impede skin flap survival (Jurell and Jonsson, 1976). Necrosis usually starts at the tip of the flap because the vascularity is most severely embarrassed at this point (Jurell and Jonsson, 1976).

In the present study, there was minimal evidence of necrosis during the surgical delay in contrast with the marked evidence of necrotic changes noted in the flaps of the control group. Even when the flaps were raised on the seventh post operative day, the survival of the flaps were more than doublic than that seen in the control group. These findings stress the importance of severence of the vascular and nerve supply to the skin flap. This also emphasise that surgical trauma has minimal per se effect on flap survival unless the flap is raised so as to severe vascular and neural connections.

During the past few years, a number of investigations have been aimed at prolonging skin flap survival, by employing drugs acting on the sympathetic nervous system (Kerrigan and Daniel, 1982). However, results are often equivocal. In the present study, reserpine was found to have no effect on skin flap survival, contrary to earlier observations (Jurell and Jonsson, 1976; Cutting et al., 1970) but confirming the finding of Kennedy et al., 1976).
Reserpine is known to induce depletion of neuronal noradrenaline and induce vasodilatation. However, the drug has other diverse pharmacological actions as well, including depletion of serotonin and cholinergic effects. It is quite possible that, though vasodilatation is induced by reserpine, the net effect on skin flap survival is determined by its actions on other systems as well. It may be mentioned that the reserpine treated animals became progressively debilitated and this may well be a contributory factor in the ineffectiveness of the drug to prolong skin flap survival.

6-Hydroxydopamine is known to induce chemical sympathectomy inducing marked reduction of sympathetic activity with intense and persistent vasodilatation (Tranzer and Thoenen, 1968). Pretreatment with 6-HD induce a marked increase in skin flap survival, confirming earlier reports (Finseth and Adelberg, 1978; Reinisch, 1974). The findings stress the importance of vasodilatation as a target for inducing skin flap survival. Apart from alpha-adrenoceptor blockers (Jurell et al., 1983), direct vasodilators (Finseth and Adelberg, 1978), have been shown to aid survival of skin flaps.

Both isoxsuprline and salbutamol are beta-2 adrenoceptor agonists, the latter being more specific in nature. Stimulation of these receptors in blood vessels, lead to vasodilatation. Both these drugs, significantly augmented skin flap survival to almost equal extents. This finding emphasizes the importance of vasodilatation as an impedance to skin flap necrosis. Isoxsuprline has been reported to enhance (Finseth and Adelberg, 1978) or to have no effect (Sasaki and Harii, 1980; Kerrigan and Deniel, 1982). The effect of Salbutamol has not been studied earlier.

Pharmacological manipulation of the cutaneous microcirculation has been attempted by various workers in efforts to salvage the failing skin flap. The sympathetic nervous system, which maintains the tonicity of blood vessels, was the primary target. However, past attempts have not been consistently successful (Kerrigan and Deniel, 1982). There is a general consensus that skin flaps fail because of arterial insufficiency resulting in ischaemic necrosis. Treatment of the failing flap is therefore, directed towards enhancing the circulation of the flap. Venous congestion, secondary to impaired circulation, may also be a major contributory factor. The present findings tend to suggest that use of vasodilators will prolong skin flap survival, by enhancing circulation through the still intact blood vessels. The use of Salbutamol and other beta-2 receptor agonists deserves a fair trial.

References


