

## Role of Pentoxifylline in Preventing Keystone Flap Necrosis

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### Abstract

Flaps are important in covering defects caused by trauma, tumour excision, lower limb vascular ulcer, or diabetes mellitus. Distal flap necrosis is one of the most common postoperative complications for flaps, leading to increased morbidity, prolonged hospital stay and need for repeat surgery. Pentoxifylline (PTXF) is a vasoactive agent that improves the flow of blood by reducing its viscosity. In our patient, we studied the usefulness of pentoxifylline as an adjuvant to prevent flap necrosis.

**Keywords:** Pentoxifylline, flap necrosis, flap, keystone flap.

## INTRODUCTION

Flaps are important in covering defects caused by trauma, tumour excision, lower limb vascular ulcer, or diabetes mellitus.<sup>1-3</sup> Distal flap necrosis is one of the most common postoperative complications for flaps, leading to increased morbidity, prolonged hospital stay and need for repeat surgery.<sup>4,5</sup> The main mechanisms of flap necrosis are insufficient blood perfusion, venous return disorder, and ischemia reperfusion injury. It is of utmost importance to improve local neovascularization and increase the blood supply

to ischemic tissues to prevent flaps from getting necrosed.<sup>6</sup> Angiogenesis in skin flaps is an intricate process involving the coordination of various cells and cytokines.<sup>7</sup> Various strategies have been developed recently to prevent flap necrosis, including reduction of oxidative stress,<sup>8</sup> inhibition of apoptosis,<sup>9</sup> and vasodilators.<sup>10</sup>

Pentoxifylline (PTXF) is a vasoactive agent that improves the flow of blood by reducing its viscosity.

## MATERIALS AND METHODS

This study was conducted in a tertiary care hospital after obtaining approval from department scientific and ethical committee. This is a prospective, descriptive, observational case study. Informed consent was obtained from the patient. This case report is about a 45 year old male who sustained electrical burn injury by 220 volts alternating current to the vertex region of the scalp (entry zone) and the left leg (exit zone). The patient was disoriented and unconscious at the time of admission with a Glasgow score of 12 and was intubated. Multiple second-degree superficial burns were present over the face, neck, chest and

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anterior aspect of abdomen, bilateral arms, bilateral thighs and second-degree deep burns involving frontoparietal region of scalp at the vertex (figure 1). CT skull showed small ill-defined hypodense area with loss of grey white differentiation noted in the left frontal region- suggestive of left frontal infarct. He was resuscitated with the standard WHO burn protocol. Serum electrolytes, urea and creatinine, urine analysis, and electrocardiogram were normal, urine myoglobin negative. Patient was asymptomatic with no seizures, syncope, focal neurological deficits. He was managed conservatively with prophylactic antiepileptic Phenytoin. The patient was extubated after three days of intensive care. According to the manual muscle test, both upper and lower extremities were normal. Sensory function was intact, muscle stretch reflexes were normoactive, no pathological reflexes were identified, and all the other cranial nerve and cerebellar functions were normal. Debridement of scalp wound was done after demarcation of necrotic patch. Non-viable necrotic tissue was debrided without damaging the normal tissues in both horizontal and vertical planes with dermabrader. After debridement, regenerative therapies like biological human amniotic membrane, collagen scaffold dressing, Low level laser therapy, Negative pressure wound therapy was done to enhance granulation over the scalp bone and wound bed preparation was done. Once the wound bed showed healthy granulation, perforator-based type 4 keystone flap was done. Pentoxifylline was given orally twice daily for five days to prevent flap necrosis.

## RESULTS

In our patient, pentoxifylline was found to be useful to prevent flap necrosis.(fig. 2)



**Fig.1. Scalp electrical burn wound at presentation**



**Fig.1. Scalp electrical burn wound at presentation**

## DISCUSSION

Pentoxifylline (PTXF) is a vasoactive agent that improves the flow of blood by reducing its viscosity. It is FDA approved for the symptomatic treatment of claudication. The other off label indications are venous ulcers, severe alcoholic hepatitis, given prophylactically to prevent flap necrosis. Pentoxifylline and its metabolites decrease blood viscosity and improve blood flow and peripheral tissue oxygenation. The precise mechanism of action by which it leads to symptom improvement remains yet to be determined. However, several pathways are likely involved.

- Pentoxifylline increases red blood cell flexibility by increasing erythrocyte ATP and cyclic nucleotide levels.<sup>11</sup> It reduces the viscosity of blood by decreasing erythrocyte aggregation and stimulating fibrinolysis to reduce plasma fibrinogen concentrations.<sup>12</sup> All these effects enhance the ability of blood to flow through peripheral vessels (hemorheological action).
- Pentoxifylline is a phosphodiesterase (PDE) inhibitor. By blocking the membrane-bound phosphodiesterase, it increases the concentration of cyclic AMP. It also inhibits thromboxane synthesis and increases prostacyclin synthesis. These actions result in reduced platelet aggregation. Further, pentoxifylline has demonstrated decreased adhesion of platelets to the vessel wall in patients with circulatory disorders.

- Pentoxifylline exerts vasodilation in the skeletal muscle vascular bed by inhibiting PDE and increasing the cAMP.<sup>13</sup>
- Pentoxifylline inhibits the leukocyte-derived free radicals generated during peripheral ischemia in patients with peripheral vascular disease. It has been shown to reduce the impairment of the filterability rate of unfractionated leucocytes, limiting ischemia-related tissue damage.<sup>14</sup>
- Pentoxifylline has immunomodulatory effects. The drug improves leukocyte deformability and chemotaxis. It depresses neutrophil degranulation, decreases endothelial leukocyte adhesion, and lowers the sensitivity of leukocytes to cytokines. Besides, pentoxifylline can inhibit the production of inflammatory cytokines.<sup>7</sup>

The keystone flap is made up of two V-Y advancement flaps that face each other. The migration of these advancement flaps results in the availability of additional tissue adjacent to the defect, allowing for main skin edge approximation. Younger surgeons can simply replicate this method because it is straightforward. In order to follow the chosen nourishing vessels for a short tract into the muscle belly or into the septa, microsurgical expertise is frequently required during the vasculature dissection phase of loco regional flaps, which should be performed under loupe magnification. There is also aesthetic morbidity in the donor area of loco regional flaps due to skin grafts. In loco regional flaps, preoperative Doppler flow is frequently used to locate perforator arteries in the anatomical area. The location of the perforating vessels is operator dependent, time demanding, and not always exact. Donor site morbidity is low with the keystone flap. Only one of our instances required a little skin graft. The donor locations were mostly closed in the remaining cases.<sup>15,16</sup>

### *Types of Keystone Island Flaps*

- Type I:** Standard flap design with no deep fascia segmentation.
- Type II:** The convex side of the flap's deep fascia is separated to improve mobilisation. The secondary defect is closed predominantly in Type II a, and the secondary defect is closed with a splint skin graft in Type II b.
- Type III:** Two keystone flaps, one on each side of the defect, are designed to aid closure.

**Type IV:** The flap is undermined up to two-thirds of the way. The mobilisation of the flaps is maximised.

In regions where skin expansibility is limited, such as around the knee, ankle, elbow, plantar aspect of foot, and palmar aspect of hand, the keystone flap should be used with caution. We had to raise the distal end of the flap to cover a defect below the knee in our patients since there was less skin laxity.<sup>4</sup> We incised the flap's edges through deep fascia on a regular basis. This will make it easier for the flap to move around and fill the defect. The flap's mobility is equivalent to that of a tree top, and it's only achievable after cutting the deep fascia all the way around the flap's convex border. In situations where the deep fascia was not incised, we saw shearing of the flap and increased strain in the suture line. We did not incise the skin over the central part of the convex surface of the flap to retain more vascularity in the flap when closing smaller defects and in the presence of sufficient laxity, but we did incise the deep fascia underneath the skin to retain more vascularity in the flap when closing smaller defects and in the presence of sufficient laxity. Splints were worn for 3-4 days to aid soft-tissue healing in the upper and lower limbs. In cases when skin grafting has been performed, physiotherapy will be required.<sup>5</sup> In none of the patients was long-term splinting used. As a result, bilateral limb surgeries can be completed in one session. Traditional skin grafts, whether with or without a local flap, result in substantial scarring, post-operative immobility, prolonged physiotherapy, graft pressure therapy, and other complications. We operated on an instance of a raw region over the knee joint on the right side of the knee. Four days following surgery, the patient was advised to move his lower limb. Within 9 days, the wound was completely healed. However, unlike a free flap, key stone flaps have minor limitations such as lengthy scars beyond the defect's bounds and a limited arc of rotation. It's critical to make sure the keystone flap's blood supply hasn't been harmed by either cancer ablation surgery or radiation therapy.<sup>17</sup> Despite these drawbacks, keystone flaps provide primary wound healing for a wide range of abnormalities with minimum pain, a sensitive cover, and great cosmetic results. It's been utilised to treat malformations in the head and neck, as well as parotid and trunk deformities. This method can eliminate the requirement for microsurgical flaps. When compared to perforator flaps and microvascular free flaps, the keystone flap has a shorter learning curve. This flap could be a valuable tool in the hands of a plastic surgeon.

## CONCLUSION

Pentoxifylline (PTXF), a vasoactive agent a useful adjuvant to improves the flow of blood and prevent flap necrosis.

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