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Impact of Topical Tacrolimus and DMSO on Ischemic Flaps: A Gross and Histological Study in a Rodent Model

Purpose: Flap necrosis is a common surgical complication. Our prior studies in rodent models have shown that topical tacrolimus significantly improves ischemic flap survival. Topical dimethyl sulfoxide (DMSO) has recently been highlighted for its potential to reduce ischemia in mastectomy flap patients. This study aims to directly compare the efficacy of topical tacrolimus versus DMSO in the treatment of ischemic flaps. **Methods:** A 3 × 10-cm cranially based dorsal skin flap was raised and reinset on 24 Sprague Dawley rats. Rats were randomized to the tacrolimus or DMSO group, 0.2 g of either topical was applied after flap surgery and then twice daily. On postoperative day 7, rats were sacrificed, and two blinded reviewers marked each flap for areas of healthy, reversible ischemic and necrotic tissue. Biopsies from six rats (three per group) were stained with H&E, and analyzed by a blinded dermatopathologist.

Results: Average area and percentages of healthy, ischemic, and necrotic tissue in the tacrolimus group were 20.80cm (64.89%), 5.02 cm (15.93%) and 6.15cm (19.27%) respectively , versus 15.37cm (51.82%), 4.86cm (16.27%) and 9.53cm (32.71%) in the DMSO group. The tacrolimus group had a significantly greater area of healthy tissue compared to the DMSO group (p=0.026), and a lower percentage of necrotic tissue (p=0.043). Histological analysis showed that the tacrolimus group had a higher density of viable microvessels per mm² in reversible areas and demonstrated increased neovascularization and granulation tissue formation compared to the DMSO group.

Conclusions: Topical tacrolimus significantly increased healthy tissue and reduced necrosis compared to DMSO, with histology showing greater microvessel density and neovascularization. This study continues to reinforce that topical tacrolimus leads to improved outcomes in postoperative ischemic flaps.