

The Effect of Pre- and Post-Surgical Topical Tacrolimus on Pedicled Flap Survival in Rats: A Pilot Study

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BACKGROUND

Our previous rodent studies demonstrated significantly decreased full thickness necrosis in pedicled dorsal skin flaps with topical tacrolimus as compared to petroleum jelly. Histologically, we found that topical tacrolimus was correlated with increased vascular growth in areas more susceptible to ischemic damage. The purpose of this study was to investigate the potential benefits of pre-treatment with tacrolimus. By applying tacrolimus in advance of raising the dorsal skin flaps, we hoped to increase vascularity and thus increase the overall viability of the flaps.

METHODS

18 Sprague-Dawley rats were randomized to four groups based on timing of tacrolimus treatment (pre/post-surgical treatment): Control/Control (C/C), Control/Tacrolimus (C/T), Tacrolimus/Control (T/C), Tacrolimus/Tacrolimus (T/T). Treatments consisted of 0.2g of the control (topical petroleum jelly) and 0.1% topical tacrolimus to the rat dorsum twice per day. After seven days of pre-surgical treatment, a cranially based dorsal skin flap measuring 3 x 10 cm was created. Each rat was treated for a further seven days and sacrificed. Two blinded reviewers marked the total skin flap area as well as areas of viable tissue, reversible ischemia, and full thickness necrosis. Percentage areas were calculated using Fiji:ImageJ and statistical analysis was performed in R.

RESULTS

The average viable areas for C/C, C/T, T/C, and T/T was 31.4%, 31.9%, 35.6%, and 22.6%, respectively. The average reversible ischemic area for C/C, C/T, T/C, and T/T was 53.1%, 54.0%, 54.1%, and 71.5%, respectively. The average necrotic area for C/C, C/T, T/C, and T/T was 15.4%, 14.0%, 10.2%, and 5.9%, respectively. For areas of reversible ischemia, T/T arm had higher areas compared to C/T ($p=0.004$) and T/C ($p=0.044$). There was no significance between treatment arms for areas of viable and necrotic tissue. Interestingly, when compared to C/C, the T/T arm marginally did not reach significance in both reversible ischemia ($p=0.059$) and necrosis ($p=0.062$).

CONCLUSION

We observed higher areas of reversible ischemia for continuous tacrolimus treatment compared to only pre- or post-tacrolimus application. This suggests that tacrolimus application before and after surgical insult may be associated with improved ischemic survival of the skin. Although we did not observe decreased areas of necrosis for tacrolimus treatment compared to control, this was likely due to the limited number of rats available in each arm to reach significance. Further study is needed to fully elucidate the encouraging trends that were observed.

Figure: Percentage Area of (A) Reversible Ischemia and (B) Full-Thickness Necrosis (Boxplot with t-test)

