

trauma. Roughly half of the laryngeal fractures in our series were managed non-operatively although approximately three-quarters required airway intervention ranging from intubation to emergent cricothyroidotomy. Clinicians treating maxillofacial trauma need to be familiar with the signs and symptoms of this injury. A timely evaluation of the larynx and rapid airway intervention are essential for a successful outcome. The Schaefer classification of injury severity and corresponding treatment guidelines were consistent with our study.

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Short and Long Term Effects of Sildenafil on Skin Flap Survival in Rats

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Statement of the Problem: Annually in the United States, approximately 175,000 people sustain severe facial trauma requiring major surgical repair. These injuries often cause significant loss of facial skin, leading to severe aesthetic and functional deficits. Skin flaps are the foundation for reconstructing such defects. The most important factor determining the survival of these flaps is the delivery of oxygen via the circulation. A number of therapeutic modalities have been explored to improve blood flow and oxygenation of flap tissue. One principal approach has been to increase blood flow by vasodilation. However, due to their hypotensive effects, the vasodilators tested thus far have not been utilized in surgical repair of facial skin. Phosphodiesterase (PDE)-inhibitors, which includes the drug sildenafil, are a relatively new class of FDA approved drugs whose effect on tissue viability has not been widely explored. The vasodilatory effects of these drugs have the potential to enhance blood flow to wound sites, improve oxygen supply, and promote wound repair. In this study, we examined whether administering sildenafil intraperitoneally at a dose of 45 mg/kg/d has a beneficial effect on the survival of surgical skin flaps in rats.

Materials and Methods: Surgical skin flaps were evaluated using orthogonal polarization spectral imaging, flap image analysis, and histology at 1, 3, 5, and 7 days. Orthogonal polarization spectral imaging provides high quality, high contrast images of the microcirculation of skin flaps. Areas of normal capillary flow are easily differentiated from areas of stasis and areas completely devoid of vessels. First, rats were assigned to either sildenafil treated (45 mg/kg/day IP), vehicle control, or sham (no injection) groups. Second, caudally based dorsal rectangular (3 x 10 cm) flaps were completely raised

and then stapled closed. Third, spectral imaging was used to determine the distances from the distal end of the flap to the zones of stasis and zones of normal flow. Finally, animals were sacrificed and the flaps removed and photographed. Digital images of the flaps were used to determine the percent of black, discolored (gray/red), and normal tissue.

Method of Data Analysis:

- a. Sample size: N = 152 rats
- b. Duration of study: 3 months
- c. Statistical methods: One-way analysis of variance (ANOVA)
- d. Subjective analysis: No

Results: The orthogonal polarization spectral imaging results showed a significant decrease in the zone of necrosis (no vessels present) in rats treated with sildenafil one and three days after surgery. We also found a significant decrease in the total affected area, which consists of the zones of necrosis and stasis, in treated rats three days after surgery. Digital photography analysis also showed a significant decrease in the area of necrosis (black tissue) at three days. These findings support the results obtained using spectral imaging. No significant differences were found between sildenafil treated and control animals five and seven days after surgery.

Conclusion: These results demonstrated that 45 mg/kg/d IP of sildenafil may have a beneficial effect on skin survivability at the early stages of wound healing. Orthogonal polarization spectral imaging has been proven to predict areas of necrosis more accurately than photographic analysis. This method allowed us to observe differences between sildenafil treated and control rats as early as 24 hours and as late as three days after surgery. Although we did not see any benefit when animals were treated with 45 mg/kg/d IP five and seven days after surgery, we believe that changes in the treatment regimen may enhance long-term flap survivability.

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2005 Straumann Resident Scientific Award Winner

Histomorphometric Assessment of Bony Healing of Rabbit Critical-Sized Calvarial Defects With Hyperbaric Oxygen Therapy

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Statement of the Problem: A critical-sized defect is the smallest osseous wound that will not heal spontaneously with bony union over the lifetime of an animal. Practically, the defect should not heal spontaneously during the experimental period. Hyperbaric oxygen therapy (HBO) is used to improve the healing of a variety of problem wounds. This study evaluated the effect of HBO on the healing of critical-sized defects in the rabbit calvarial model and whether HBO administration can result in the healing of a larger “supracritical-sized” defect.

Materials and Methods: Twenty New Zealand rabbits were divided into 2 groups of 10 animals. Full thickness calvarial defects were created in their parietal bones bilaterally. Defects were critical-sized (15 mm) on one side and supracritical (18 mm) on the contralateral side. Group 1 received a 90 minute HBO therapy session at 2.4 ATA daily for 20 consecutive days. Group 2 served as a control group receiving only room air. Five animals in each group were sacrificed at 6 and 12 weeks postoperatively.

Method of Data Analysis: Data analysis included qualitative assessment of the calvarial specimens as well as quantitative histomorphometric analysis to compute the amount of regenerated bone within the defects. Hematoxylin and eosin stained sections were sliced and captured by a digital camera (RT Color; Diagnostic Instruments Inc, Sterling Heights, MI). A blinded investigator examined merged images and analyzed them for quantity of new bone regeneration. Statistical significance was established with a p value < .05.

Results: The HBO group showed bony union and demonstrated more bone formation than the control group at 6 weeks (p < .001). The control group did not show bony union in either defect by 12 weeks. There was no significant difference in the amount of new bone formed in the HBO group at 6 weeks compared with 12 weeks (p = .309). However, the bone at 6 weeks was more of a woven character, while at 12 weeks it was more lamellated and more mature. Again, in the HBO group both the critical-sized and the supracritical-sized defects healed equally (p = .520).

Conclusion: HBO therapy has facilitated the bony healing of both critical-sized and supracritical-sized rabbit calvarial defects. Since bony healing was achieved early, it is reasonable to assume that an even larger than 18 mm defect (if it were technically feasible) might have healed within the 12 week period of study aided by HBO. Adjunctive HBO, based on histomorphometrics, doubles the amount of new bone formed within both the critical sized and the supracritical-sized defects. It allowed an increase in the critical size by more than 20%.

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Craniofacial Growth Following Cytokine Therapy in Craniosynostotic Rabbits

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Statement of the Problem: Craniosynostosis affects 300-500/1,000,000 births. It has been suggested that an over-expression of Tgf-beta 2 leads to calvarial hyperostosis and suture fusion in craniosynostotic individuals. This study was to test the hypothesis that neutralizing antibodies to Tgf-beta 2 may block its activity in craniosynostotic rabbits, preventing coronal suture fusion in affected individuals, and allowing unrestricted craniofacial growth.

Materials and Methods: Twenty-eight New Zealand White rabbits with bilateral delayed-onset coronal suture synostosis had radiopaque dental amalgam markers placed on either side of coronal sutures at 10 days of age (synostosis occurs at approximately 42 days of age). At 25 days, the rabbits were randomly assigned to three groups: 1) Sham control rabbits (n = 10); 2) Rabbits with non-specific, control IgG antibody (100ug/suture) delivered in a slow release collagen vehicle (n = 9); and 3) Rabbits with Tgf-beta 2 neutralizing antibody (100ug/suture) delivered in slow release collagen (n = 9). The collagen vehicle in groups Two and Three was injected subperiosteally above the coronal suture. Longitudinal lateral and dorsoventral head radiographs and somatic growth data were collected from each animal at 10, 25, 42, and 84 days of age.

Method of Data Analysis: Significant mean differences were assessed using a one-way analysis of variance.

Results: Radiographic analysis showed significantly greater (p < 0.05) coronal suture marker separation, overall craniofacial length, cranial vault length and height, cranial base length, and more lordotic cranial base angles in rabbits treated with anti-Tgf-beta-2 antibody than groups at 42 and 84 days of age.

Conclusion: These data support our initial hypothesis that interference with Tgf-beta-2 production and/or function may rescue prematurely fusing coronal sutures and facilitate craniofacial growth in this rabbit model. These findings also suggest that this cytokine therapy may be clinically significant in infants with insidious or progressive postgestational craniosynostosis.

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