

In vivo use of human fibrin glue under the subperiosteal and subcutaneous planes in Holtzman Rats.

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Abstract:

Background: Commercial fibrin sealant has been increasingly used off-label in the United States for aesthetic surgical procedures to minimize postoperative drainage, hematoma and seroma collections, ecchymosis, and edema. Objective: We sought to determine the optimal concentrations of thrombin and fibrinogen to extend the sealant adhesion time and to maintain the maximal glue strength, respectively, in subperiosteal and subcutaneous planes in Holtzman rats. Methods: Three preparations of 2-component fibrin sealant from the Hemaseel APR kit (Haemacure Corp., Sarasota, FL) were formulated: standard fibrin sealant (fibrinogen 75-115 mg/mL, thrombin 500 IU/mL), half fibrinogen concentration (fibrinogen 37.5-57.5 mg/mL, thrombin 500 IU/mL), and 1/100 thrombin concentration (fibrinogen 75-115 mg/mL, thrombin 5 IU/mL). In 6 rats, paired standardized subperiosteal scalp pockets and subcutaneous abdominal pockets were elevated, leaving a retained septum between each pair. In experiment 1, 1 of the 3 fibrin sealant preparations was instilled into 1 side of each paired subperiosteal and subcutaneous pockets in 2 of the 6 rats, leaving the adjacent pocket as a control flap. Changes in force of flap displacement and in setup time for adherence within the treated and matched control flaps were measured at intervals over an hour. In experiment 2, the duration and strength of adherence in flaps treated only with the standard fibrin sealant preparation and their paired control flaps in 34 rats were measured weekly over 6 weeks. One of the 34 rats was sacrificed each week to examine the histologic changes at the tissue-glue interface. Results: In flaps treated with the half-concentration of fibrinogen, the grams of force needed to displace the scalp flaps by 5 mm and the abdominal flaps by 10 mm were significantly reduced

compared with values obtained in similar flaps treated with the standard fibrin preparation over 1 hour of interval measurements ($P < 0.05$). In flaps treated with the 1/100 concentration of thrombin, the setup times before flap adherence were significantly extended to about 1 minute compared with the 15-second setup times observed in flaps treated with the standard fibrin preparation ($P < 0.05$). The use of the standard fibrin preparation in 34 rats resulted in up to 6 weeks of tissue adherence in the subperiosteal scalp flaps and up to 2 weeks of tissue adherence in the subcutaneous abdominal flaps over the paired control flaps, as measured weekly on the basis of force of flap displacement. Histologic examination demonstrated that glue material was absent at about 5 to 6 weeks in the subperiosteal space and 2 to 3 weeks in the subcutaneous space. Conclusions: Any decrease in fibrinogen concentration from that found in the standard fibrin sealant results in suboptimal strength of adherence of flaps. The standard thrombin concentration (500 IU/mL) results in a rapid onset of adherence within 15 seconds that may prevent the surgeon from massaging the glue evenly throughout the pocket and may produce a premature seal on opposing surfaces, leading to a seroma cavity. A reduced thrombin concentration (5 IU/mL), on the other hand, extends the onset time to a minute before adherence occurs, optimizing the sealing of the surgical cavity.