

[2050-PO] Induction of Fetal-Like Wound Repair Mechanisms In Vivo with a Novel Matrix Scaffolding.

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Conventional diabetic foot ulcer therapy has been unsatisfactory because of the inability to ameliorate the underlying circulatory and neuropathic disease. Current therapies at best facilitate wound closure, without improving underlying disease. A novel injectable scaffolding, E-Matrix, designed to mimic tertiary embryonic connective tissue structure and stimulate fetal wound repair mechanisms, is a copolymer of collagen alpha chains and long chain carbohydrate stabilized with bioadhesives and supplemented with nitric and superoxide inhibitors. This study investigated the ability of E-Matrix to improve wound healing in diabetic dogs and non-diabetic pigs. Wounds treated with E-Matrix were: 6 skin lesions (6 to 29 sq cm) in a spontaneously diabetic dog; 5 full thickness surgical incisions (12-17 cm in length) in diabetic dogs; and 8 full thickness 2.5 x 2.5 cm pig surgical wounds. Treatment was a one time E-Matrix injection into the tissue bed underlying the wounds. Controls were: 3 untreated surgical incisions in dogs; and 16 pig surgical wounds (8 untreated, 8 buffer control). For dogs, gross observations were made to 21 days with biopsies 5 to 6 months and necropsies 6 to 8 months after treatment. Pig wounds were scored for contracture (1 to 4 scale) and scarring (0 to 3 scale) 14 days after treatment immediately before necropsy. E-Matrix treated diabetic dog wounds healed completely after 6 to 21 days with dramatically reduced scarring compared to controls. Histologically, treated lesions had normal skin architecture with blood vessels, hair and reticular extra-cellular matrix. Surgical wounds in normal pigs had less contracture (E-Matrix: 1.9; buffer: 2.8; Untreated: 3.8; $p = 0.006$ by ANOVA), less scarring (E-Matrix: 1.1; buffer: 2.1; Untreated: 2.2; $p = 0.0007$ by ANOVA) and a greater complete re-epithelialization (62% vs 20%). Immunohistochemically, E-Matrix treated pig wound fibroblasts did not react positively for smooth muscle specific actin, whereas in controls they did. In conclusion, E-Matrix stimulates wound healing mechanisms consistent with fetal scarless tissue regeneration. E-Matrix is in human clinical trials to determine its effect on healing diabetic foot ulcers.

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