Summary of dissertation thesis

WOUND REPAIR AND DIABETIC WOUND DEFECTS.

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Impaired diabetic wound healing is an important current medical issue, mainly concerning patients recovering from complicated operations or patients with ulcers on their feet.

Hyaluronan (HA) plays an important role in the repair of damaged skin and has been used for the treatment of wounds. A mixture of high molecular weight HA with the antiseptic iodine complex KI_3 (Hyiodine) was reported to accelerate wound healing in patients with diabetes and patients after surgery. We investigated how this mixture affects wound contraction, granulation tissue (GT) and wound edges in excision skin wounds in rats. Hyiodine was applied to full-thickness wounds made on the back of rats. The areas of the contracting wounds were calculated from digital photographs. The migrating edges of the wound were studied by histological methods. The properties of GT were studied in wounds in which contraction was prevented by the insertion of plastic rings. The effects of Hyiodine were compared with those of high molecular weight HA, low molecular weight HA and KI_3 solution. Hyiodine accelerated wound contraction significantly in the first 5 days of healing. On day 3, Hyiodine-treated wounds had reduced to 63% of the original area, whereas the wound area in saline-treated animals was 75% of the original size. The proliferating epidermis was thicker in Hyiodine-treated animals on day 7. In the wounds with inserted rings, Hyiodine caused little change in GT, but the weight of the exudate with crust formed on the top of the wound was increased by 351% compared with only minor changes caused by the Hyiodine components alone. Hyiodine may support wound healing by stimulating wound contraction and epidermal proliferation.

Obese Zucker Diabetic Fatty rat, with a mutation in leptin receptors, may be a good choice for studying impaired wound healing. Male and female rats were fed a diabetogenic high-fat diet. Wound size changes of excisional 2 cm circular wounds, were measured until sampling on day 10 in air-exposed wounds and until complete wound closure in bandaged wounds Wound tissue was analyzed morphologically, histologically, immunohistochemically. Hydroxyproline content in the granulation tissue (GT) was determined. mRNA expression was assayed by DNA-array analysis and realtime RT-PCR. Wound size changes were retarded in diabetic rats and differed between the sexes. Diabetic wounds were characterized by impaired contraction, abundant crust production, increased inflammation and pus formation. On day 10, the GT contained significantly increased amount of intercalated fat tissue and showed irregular arrangement of collagen fibres. Interestingly, the length of new epithelium was increased in diabetic wounds. The concentration of hydroxyproline in the GT of diabetic animals was significantly decreased to about one half when compared with non-diabetic controls. The expression of interleukin-6, myeloperoxidase, stromelysin-1, collagenase-3 was increased in the GT of diabetic rats on day 10, while the expression of type I collagen and elastin was decreased. Taken together, Zucker Diabetic Fatty rats exhibited impairments in wound size reduction, inflammatory response, tissue organization and connective tissue turnover and thus are proposed as a new model for studying impaired repair.