—Short Communications—

An experimental study on wound healing in hypothyroidism

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Since the question of wound healing related to thyroid function attracted attention, the close relation between hypothyroidism and the delay in wound healing has been discussed¹⁾. In fact, various symptoms suggesting that hypothyroidism adversely influences wound recovery, such as refractory fistula after drastic laryngectomy have been reported^{1,2)}. So far, there have been several basic studies that T4 administration fosters wound healing in hypothyroidism^{3,4)}. However, these clinical phenomena still remain obscure. In this study, we examined the healing of wounds using rats with experimentally developed hypothyroidism.

Methimazole at a dose of 3 mg/body was subcutaneously administered to male Wistar strain rats weighing about 300 g every day for 14 days to create a model of hypothyroidism (MMI group hereafter). Blood samples were collected from the femoral artery, and thyroid function was evaluated by monitoring T4 and TSH levels preoperatively and 1 week and 2 weeks postoperatively. To obtain tissue samples, 4-cm-long upper median incisions were made in the abdominal wall of the rats and interrupted sutures were made under ether anesthesia creating primary suture wounds two weeks after initial MMI administration. Two round open wounds measuring 6 mm in diameter were also made on the dorsal skin. A similar procedure was carried out on untreated rats, which were used regarded as the control group. Fifteen rats were used in each group for this experiment. Skin samples measuring 6 mm in width were collected from the center of the wounds 1 week and 2 weeks after surgery. In addition to pathological examination focusing on the microscopic recovery of granulation of suture wound and macroscopic progressive recovery of the punched out lesions, the amount of hydroxyproline indicating the amount of collagen from the open wound area was examined for comparison between the MMI group and the control.

The thyroid functions expressed as TSH and T4 were respectively 2.2 ng/ml and 4.6 µg/dl in the control group while they were 4.8 ng/ml and 2.8 µg/dl in the MMI group, indicating the development of preoperative hypothyroidism in the latter group (Fig. 1). The amount of hydroxyproline per mg wet weight of the wound skin in the control group was 31.9 nmol in the first week and 27.7 nmol in the second week, whereas the values for the MMI group were respectively 20.2 nmol and 29.8 nmol, indicating a lower first week value for the latter group (Fig. 2). The microscopic findings of the suture wounds in hypothyroidism indicated stromal edema and relatively poor amount of fibrous connective tissue compared with control group. In macroscopic recovery, the average open wound width was 4.2 mm² in the first week and 0.2 mm²

Fig. 1 Pre and postoperative thyroid function expressed by TSH in rats. TSH level was elevated compared with the control group preoperatively and 1 and 2 weeks postoperatively, indicating the development of hypothyroidism by administration of MMI.

Fig. 2 Quantitative analysis of hydroxyproline in primary suture wounds. The amount of hydroxyproline from suture wounds in the MMI group is lower than that of the control group 1 week after surgery, indicating poor fibroblast function in hypothyroidism during this period. This result suggests that wound healing is badly influenced in hypothyroidism.

in the second week for the control group, and 3.8 mm² and 0.11 mm² respectively in the MMI group, showing no significant differences between the two groups.

In the process of wound healing, the major constituent of the tensile strength of the wound is collagen fiber produced by fibroblasts. The tensile strength increases remarkably 6-7 days after the injury⁵. In our study, the lower amount of hydroxyproline found in the prepared wounds in the first week in the MMI group indicates a lower content of collagen. This suggests that the function of fibroblasts is not fully displayed in hypogroups regarding the open wound area, it is assumed that reduced thyroid function does not adversely influence epithelial regeneration or wound contraction.

In conclusion, we postulate that hypothyroidism plays a role in delaying wound healing by suppressing fibroblast function.

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