Skin regeneration with conical and hair follicle structure of deep second-degree scalding injuries via combined expression of the EPO receptor and beta common receptor by local subcutaneous injection of nanosized rhEPO.

Abstract:

Acceleration of skin regeneration is still an unsolved problem in the clinical treatment of patients suffering from deep burns and scalds. Although erythropoietin (EPO) has a protective role in a wide range of organs and cells during ischemia and after trauma, it has been recently discovered that EPO is not tissue-protective in the common ? subunit receptor (?CR) knockout mouse. The protective capacity of EPO in tissue is mediated via a heteroreceptor complex comprising both the erythropoietin receptor (EPOR) and ?CR. However, proof of coexpression of these heterogenic receptors in regenerating skin after burns is still lacking. To understand the role of nanosized recombinant human erythropoietin (rhEPO) in wound healing, we investigated the effects of subcutaneous injections of EPO on skin regeneration after deep second-degree scalding injuries. Our aim was to determine if joint expression of EPOR and ?CR is a prerequisite for the tissue-protective effect of rhEPO. The efficiency in wound regeneration in a skin scalding injury mouse model was examined. A deep second-degree dermal scald injury was produced on the backs of 20 female Balb/c mice which were subsequently randomized to four experimental groups, two of which
received daily subcutaneous injections of rhEPO. At days 7 and 14, the mice were sacrificed and the effects of rhEPO were analyzed with respect to grade of re-epithelialization (wound closure) and stage of epidermal maturation. This was investigated using different histological parameters of epithelial covering, such as depth of the epidermal layer, epidermal stratification, and presence of conical and hair follicle structures. Expression of EPOR, ?CR, and growth hormone receptor at the mRNA and protein levels was demonstrated with reverse transcriptase polymerase chain reaction and Western blot analysis. After rhEPO treatment, the rate of re-epithelialization of the scalding injury was increased and the time to final wound closure was reduced. In addition, the quality of regenerated skin was improved. In this investigation, for the first time, we demonstrated coexpression of EPOR and ?CR at the RNA and protein levels in vivo using a deep second-degree scalding injury mouse model. These results highlight the potential role of rhEPO in the improved treatment of burns patients, which might be crucial for the development of innovative new therapy regimes. Local injection of nanosized rhEPO directly to the injury site rather than systemic administration for deep second-degree scalding injuries achieved complete skin regeneration with conical and hair follicle structure via combined expression of EPOR and ?CR.