Association of adipose derived mesenchymal stem cells to improve the integration of full-thickness skin graft in murine model

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Abstract

This study aimed to do an evaluation of the effects of adipose derived stem cells (ADSC) on full-thickness skin graft (FTSG) as a wound healing model in ischemic conditions. Two 12 mm diameter FTSGs were harvested and placed onto dorsal recipient beds of twenty-four Wistar rats, in two anatomic regions: cranial and caudal. Rats were randomized into five groups. Before grafting, group E FTSGs received subfascial injection of 1X106 ADSCs diluted in 200 μL of physiologic saline. Group EC FTSGs received only physiologic saline; group B received ADSCs in the recipient bed edges; group C received physiologic saline in the edges; and group EB received the same ADSCs number and volume, half in the graft and half in the edges. Using planimetry, grafts were analyzed for the contraction rate of the grafts (d0, d5, d14), occurrence of epidermolysis and failure rate (d14). FTSGs samples were obtained on the d14 to hematoxylin-eosin and Masson's Trichrome staining for epidermal analysis (hair loss, epidermal thickening, keratosis, acanthosis, hydropic degeneration) and dermal analysis (granulation tissue, inflammatory infiltrate). The obtained results were expressed by mean (n=5). Statistical significance (p<0,05) was calculated using Generalized Estimating Equations. ADSCs treated groups had lower means for failure rate (B=0%, EB=2.81%, E=3.95%) than control (C=5.02%, EC=8.86%), but there were no statistically significant difference. The E group showed epidermolysis only in 30% of grafts while other groups showed 70-90%. Between d5 and d14, the contraction rate of EB (48.47%) was lower than EC (69.01%) (p=0.05). However, the contraction rate between d0 and d5 and d14 were homogeneous. Only the control groups EC and C showed hair loss (30%). There was no thinning of the epidermis in any rat. Considering the thickening of the epidermis, the EB group (4.40) had greater mean than EC (2.80), C (2.60) and E (2.20) groups (p=0.002, p=0.000 and p=0.000 respectively). When acanthosis was evaluated, group E (2.00) showed a lower mean than EB (4.30) (p=0.005), followed by group C (2.60) (p=0.000). Analyzing inflammatory infiltrated in epidermis, group E (0.90) had a lower mean than EC (2.20) (p=0.037), while B (1.20) and C (1.20) had the same values, lower than EB (1.80). In hydropic degeneration, group E (2.00) showed lower mean than EC (3.40) (p=0.021). Considering granulation tissue in dermis, EB (4.50) had a greater mean than C (3.20) (p=0.017) and EC (3.50) (p=0.039). There was no statistically significant difference for keratosis in epidermis or inflammation and collagen deposition in dermis.

In conclusion, our results suggest that the application of ADSCs in subfacial FTSGs decreased the deleterious effects of the ischemic injury by decreasing epithelial thickness, acanthosis, hydropic degeneration and inflammatory infiltrate.

Ethics Committee: Hospital de Clínicas de Porto Alegre. Protocolo 13-0414.