Matrix Metalloproteinase and Pressure Ulcers: Is the Ratio of MMP-8 and TIMP-1 a Predictor of Wound Healing?

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INTRODUCTION:
Matrix metalloproteinases (MMPs) play a major role in wound healing: they can degrade all components of the extracellular matrix. In pressure ulcers there is an excess of MMP-8 and a decrease of the tissue inhibitors of MMPs (TIMP-1). This imbalance is probably one cause of impaired healing. However, little is known about changes in MMP-8 during wound healing. This study was conducted with an aim to find the level of MMP8 and TIMP-1 protein in pressure ulcers by RT-PCR and to correlate its association with healing of pressure ulcers.
METHODS:
Fifty-nine subjects with grade III and grade IV pressure ulcers were recruited. Wound tissue was collected three times (at weeks 0, 3, and 6) during the 6-week follow-up period, for measurement of MMP-8 and TIMP-1. Results were analyzed by the degree of wound healing: good healers (defined by a reduction of at least 82% in initial wound surface at 4 weeks) and poor healers (reduction of less than 82% in wound surface at 4 weeks).
RESULTS:
The mean MMP-8 expression of subjects at 0, 3, and 6 wk were 4.14 ± 0.18, 2.64 ± 0.15, and 1.84 ± 0.11 respectively. The mean MMP-8 expression decreased linearly with time at both 3 and 6 wk as compared to 0 wk. Moreover, it also decreased significantly ($p<0.001$) at 6 wk as compared to 3 wk. Furthermore, the mean TIMP-1 marker expression (RT-PCR) of subjects at 0, 3, and 6 wk were 1.98 ± 0.11, 2.63 ± 0.15, and 3.53 ± 0.18 respectively. In contrast to MMP-8 expression, the mean TIMP-1 expression increased linearly with time. The mean TIMP-1 was significantly ($p<0.01$ or $p<0.001$) higher at 3 and 6 wk as compared to 0 wk. Moreover, it was also significantly ($p<0.001$) higher at 6 wk as compared to 3 wk. Comparison of difference in the mean between time periods showed that MMP-8 expression (fold change) lowered significantly ($p<0.001$) at 3 and 6 wk as compared to 0 wk in both the non-healing and healing groups. Further, in healing group, it also lowered significantly ($p<0.05$) at 6 wk as compared to 3 wk. In contrast, in both groups, TIMP-1 expression (fold change) was significantly ($p<0.001$) different and higher at 6 wk as compared to 0 wk. Further, in non-healing group, it was also significantly ($p<0.01$) higher at 3 wk as compared to 0 wk. Conversely, in healing group, it was also significantly ($p<0.01$) higher at 6 wk as compared to 3 wk.
DISCUSSION AND CONCLUSION:
The expression of MMP-8 significantly decreased with healing at each follow up whereas expression of TIMP-1 in healing group showed significant increase at week 6 than baseline.