Macrophages are Essential for Infarct Repair With and Without Stem Cell Therapy

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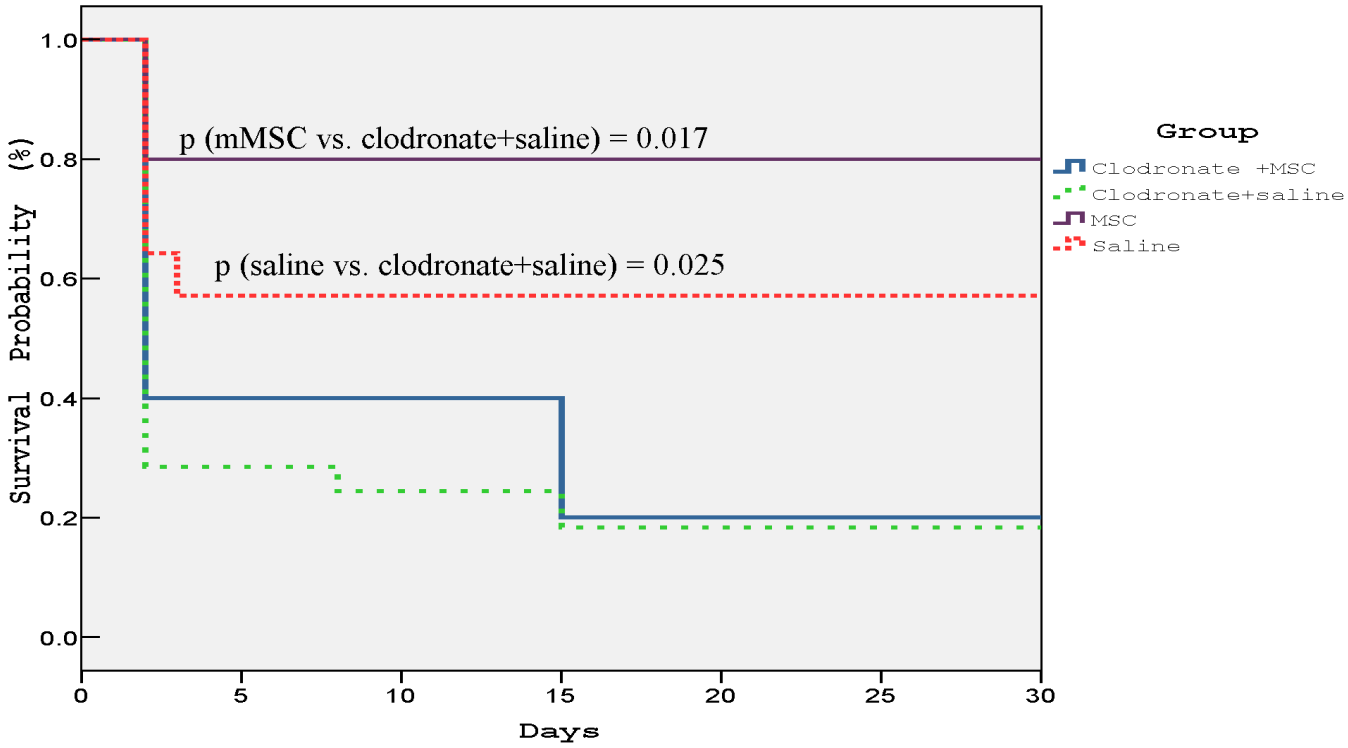
Myocardial healing is impaired in elderly and sick people partially because of defective inflammatory response. The present study aimed to determine the significance of macrophage (MΦ) activity in infarct repair and to test the hypothesis that young MΦ can improve infarct repair in aged mouse.

Methods and Results:

MΦ depletion was induced by clodronate injection (IV or IP) to Balb/C mice. Animals (n=57) with and without MΦ depletion were subjected to MI and randomized to injection of mesenchymal stem cells (mMSC; n=15) into the infarct or saline (n=42). Mortality after MI was significantly higher in MΦ depleted mice, with and without stem cell therapy, compared with controls (Figure1; p=0.02).

Figure 1: Survival curves of the four study groups.



In the next experiment, MΦ were isolated from the peritoneum of young (12w) or aged (8m) Balb/c mouse. The young or old MΦs (50,000) were injected into the infarcted myocardium of aged (8 months) mice (n=9, n=8; respectively) immediately after MI. The control group (n=9) was treated with saline injection. Serial echocardiography studies were performed 1 day and 4 weeks after MI. After 4 weeks, aged animals treated with saline or old MΦ experienced significant increase in infarct thinning and LV dilatation ($p<0.02$), while this variables of adverse remodeling were attenuated in animals treated with young MΦ.

Conclusions:

Macrophages are essential for infarct repair with and without stem cell therapy. The administration of young macrophages to repair MI could be important to sick and elderly people in whom the availability of autologous, functional stem cells is limited.