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Do LDE-Methotrexate lipid nanoparticles decrease allograft vasculopathy in rabbit transplanted heart ?

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Background

Cardiac allograft vasculopathy is the major fator limiting long term survival after heart transplantion. In a previus study we have shown that LDE binded with placitaxel decreases graft vasculopathy disease in rabbits. The objective of this study is to investigate the influence of LDE-Methotrexate nanoparticle in development of vasculopathy in rabbits tranplanted heart and expression profiles of cellular receptors, inflammatory mediators and metalloproteinases.

Methods

Heterotopic heart transplantation in cervical region was performed in twenty white male rabbits divided in two groups:

1. LDE-Metotrexate group: 10 rabbits treated with intravenous methotrexate particle once a week.

2. Control group: 10 rabbits treated with 3 ml of intravenous saline solution once a week.

All animals were fed with food with 0.5% of cholesterol and receveid 10 mg/kg/day of cyclosporine. After six weeks of observation, the animals were sacrificed.

Results

Inflammation evaluated by macrophage distribution was reduced in animals treated with metotrexate from 27.1% to 6.0% (p= 0.0020), compared to control group. Stenosis of coronary arteries had threefold decrease (p = 0.0010) in LDE-Methotrexate group.

Values of relative gene expression profiles of Low density lipoprotein receptor ; Low density lipoprotein receptor – related protein 1; IL-18; TNFα; VCAM1 (Vascular cell adhesion molecule-1) ; MCP-1 (Monocyte chemotactic protein-1) and MMP-12 (Matrix metalloproteinase 12) were significantly reduced (p< 0.05) in methotrexate group.

Conclusion

Intravenous methotrexate with nanoparticules of LDE-Methotrexate reduced allograft vasculopathy in transplanted hearts and inflamation markers.

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