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PReS-FINAL-2086: In vitro investigation of the sustained therapeutic effect of etanercept loaded microspheres on human rheumatoid arthritis fibroblast-like synoviocytes

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Introduction

Anti-TNF α treatment has become an important part of our systemic treatment in chronic inflammatory arthritis. Local application to the joint produces transient clinical improvement since the drug quickly leaves the joint.

Objectives

We aimed to develop a sustained release system for an anti-TNF α drug in treatment of chronic inflammatory arthritis. A novel form of intra-articularly injectable etanercept (ETN) loaded poly(ϵ -caprolactone) (PCL) or methoxy poly(ethylene glycol)-poly(ϵ -caprolactone)-methoxy poly(ethylene glycol) (MPEG-PCL-MPEG) microspheres (patent pending) were prepared to provide long term controlled release of ETN with a sustained anti-inflammatory effect as a local treatment approach.

Methods

Size, surface morphology, encapsulation efficiency, and in vitro release profiles of γ -sterilized microspheres loaded with ETN were determined. Treatment efficacies of free and microsphere loaded ETN were evaluated by determining changes in cell number and viability of fibroblast-like synoviocytes (FLS), in protein levels of pro-inflammatory cytokines (TNF α , IL-6, IFN γ , IL-17) and MMPs (MMP-3 and MMP-13) and in mRNA expressions of TNF α , IL-6, MMP-3 and MMP-13.

Results

Microspheres possessed a rough surface and had a mean particle size around 5 μ m. MPEG-PCL-MPEG microspheres had higher drug encapsulation efficiency than PCL microspheres. Total amounts of biologically active ETN released from MPEG-PCL-MPEG microspheres were significantly higher than that from PCL microspheres at each time point during the four weeks study period. FLS viability significantly decreased in the free drug group at first week whereas no significant decrease was observed in microsphere groups. ETN loaded microspheres significantly decreased the levels of pro-inflammatory cytokines TNF α , IL-6, IFN γ , IL-17 and MMPs in FLSs. However, there were no significant variations in the gene expressions of pro-inflammatory cytokines and MMPs among groups.

Conclusion

ETN loaded microspheres provide a sustained release, which resulted with a significant decrease in pro-inflammatory cytokines and MMPs levels. This study showed that MPEG-PCL-MPEG and PCL microspheres are promising and safe systems for an effective local treatment approach in chronic inflammatory arthritis.

This study is a part of patent pending invention (PCT No: PCT/TR2012/000148).

Disclosure of interest

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