

Stimulation of orthopedic implant fixation – investigations of osteogenic growth factors and topical delivery systems

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ABSTRACT

The studies leading to this PhD dissertation were performed at the Orthopedic Research Laboratory at the University Hospital of Aarhus, and at the Midwest Orthopedic Research Foundation in Minneapolis, Minnesota, USA.

The general purpose of the studies was to investigate possible adjuvant therapies for the fixation of bone to metal without using bone cement. To avoid early loosening of the joint replacement prosthesis it is essential that it is fixated by bone and not fibrous tissue.

Three experimental animal studies were performed. In the first two studies we coated the experimental implants with the osteogenic growth factors Transforming Growth Factor beta 1 (TGF- β 1) and Insulin-like Growth Factor 1 (IGF-1), dissolved in a biodegradable polymer Poly(D,L-Lactide), PDLLA.

The animals carried the implants for four weeks, after which the implants were harvested and examined by mechanical and quantitative histological tests.

The third study investigated chitosan, a substance fairly novel to bone research, which is a derivative of the polysaccharide chitin. We made a scaffold of the chitosan directly on the implant surface. The purpose of the study was in part to investigate whether chitosan as a scaffold could increase the bone healing, and in part to evaluate whether it would be suitable for a drug carrier to use in further studies.

The results are very promising for the combination of TGF- β 1 and IGF-1 in PDLLA. There was a significant increase in bone healing and mechanical fixation provided by the growth factors.

For chitosan the results are hardly as encouraging. There was a thick layer of fibrous tissue covering the implants where the chitosan scaffolds had been, causing very poor mechanical fixation.

The combination of TGF- β 1 and IGF-1 in PDLLA is promising as potential adjuvant therapy for uncemented joint replacement prostheses. TGF- β 1 and IGF-1 are not yet approved for human use, so it is far too early to predict the effect in humans. The cost of these growth factors is immensely high, so if they are going to be used in joint replacement therapy, it will probably be for those patients whose healing potential can be identified as reduced.

The potential for chitosan in prosthesis surgery is unresolved.

Further research will concentrate on testing the growth factor combination in more advanced models, such as the revision model.