Regenerative medicine in urogynecology

An experimental study in rats of MPEG-PLGA scaffolds, trophic factors, muscle-derived cells and muscle tissue

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Introduction:

Synthetic, permanent implants are extensively used in the surgical treatment of pelvic organ prolapse (POP) in order to improve outcome. However, robust data on efficacy are tenuous, and safety issues have emerged. Safer alternatives are therefore needed. Regenerative medicine based on biodegradable scaffolds and autologous muscle tissue is a novel concept for the treatment of urogynecological disorders including POP. A newly developed synthetic, biodegradable biomaterial, methoxypolyethyleneglycol-poly(lactic-co-glycolic acid) (MPEG-PLGA), was chosen as a scaffold in this study, which was conducted in a rat model.

Aims:

To investigate and compare biocompatibility and tissue regeneration of three preparations of MPEG-PLGA: pure, enriched with extra-cellular matrix or estrogen.

To investigate if MPEG-PLGA seeded with either autologous *in vitro* cultured muscle cells or autologous fresh muscle tissue could be of potential use in regenerative medicine.

Materials, methods and results:

Study I: The tissue reaction was investigated 3 and 8 weeks after implantation of MPEG-PLGA (pure, enriched with extra-cellular matrix (ECM) or estrogen). The MPEG-PLGA and surrounding tissue was explanted and routinely processed for standard stains for histopathology. Histopathological assessment of organization, inflammation, vascularization, and thickness of the regenerated tissue was undertaken.

All three preparations of MPEG-PLGA had a high degree of biocompatibility. Those enriched with ECM had significantly higher inflammatory scores compared to pure MPEG-PLGA at 3 weeks. At 8 weeks neither of the parameters differed significantly among the three preparations and no trace of the MPEG-PLGA remained.

Study II: The tissue reaction was investigated 3 and 8 weeks after implantation of MPEG-PLGA seeded with either autologous *in* vitro cultured muscle-derived cells (MDC) or autologous fresh muscle fiber fragments (MFF). Growth pattern of MDC and MFF was assessed by immunohistochemistry and biocompatibility was assessed by histopathology.

At 3 weeks, both scaffolds with MDC and MFF were present. At 8 weeks, striated muscle tissue was generated from the MFF whereas the scaffolds and the MDC had vanished. The MPEG-PLGA had a high degree of biocompatibility whether delivering MDC or MFF.

Conclusions:

- The MPEG-PLGA was very biocompatible and left virtually no traces behind
- The MPEG-PLGA alone, or combined with ECM or estrogen, is hardly a candidate implant for reinforcement in pelvic reconstructive surgery
- *In vitro* cultured muscle-derived cells were compatible with the MPEG-PLGA, but disappeared when the scaffold was degraded
- Striated muscle tissue was created by using autologous fresh muscle fiber fragments seeded on MPEG-PLGA
- Tissue engineering using MPEG-PLGA as a scaffold for fresh muscle fiber fragments may be a promising new concept for pelvic floor regenerative medicine