CLINICAL APPLICATION OF RESORBABLE POLYMERS IN GUIDED BONE REGENERATION

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Introduction

Long segmental diaphyseal bone loss often results from high energy trauma like blast injury, osteomyelitis or wide excision of malignant conditions. Treatment of this long segmental diaphyseal defects remain a difficult clinical problem. In the literature, many authors have reported that bone loss more than 2.5 cm always require bone grafting. This is probably the critical size defect in human. Non-vascularized bone graft frequently fails if the defect is longer than 6-7 cm. 2.5 cm is probably the critical size defect is human and 7 cm is likely the critical size for non-vascularized bone graft. Various treatment methods are adopted currently to address this problem, including vascularized bone graft, distraction osteogenesis and massive allograft. However, all these methods are associated with a lot of problems.

Successful guided bone regeneration has been achieved in skull bone and jaw bone using resorbable allograft. Bone regeneration in long segmental defect and relatively small defect in tumour excision has been achieved using resorbable polylactide scaffolds.

Methods and materials

10 patients with bone defect of sizes up to 6 cm due to various causes including benign tumour, osteomyelitis & fractures were treated with resorbable polylactide scaffold impregnated with marrow blood which contains stromal cells. In cases with infection, antibiotics was also loaded into the scaffold and in this situation, the scaffold also served as a drug delivery device. The patients have assessed regularly with X rays and clinical symptoms.

Results

Serial X ray evaluation and clinical evaluation revealed presence of bone regeneration. The limbs enjoyed satisfactory function and there was minimal donar site morbidity and major surgery can be avoided.

Discussion

Selected cases are treated with guided bone regeneration which would be treated otherwise by conventional technique. Vascularized bone transfer has limited supply and involves a major operation. There is always a chance of vascular complication and there is donor site morbidity. Distraction osteogenesis has a limitation of length that can be lengthened and requires a prolonged placement of external fixation. There is a high chance of traction injury to nerve and other soft tissues. Massive allograft requires a prolonged period, in terms of decades, for complete creep substitution. There is also a high incidence of disease transmission and infection. Therefore there is a constant demand for bone substitute which can bridge long segmental defect effectively with minimal morbidity and can heal in reasonable time frame. The affected limb can be rehabilitated and bear weight for functional restoration as early as possible. These early results are promising.

INJECTABLE POLYURETHANES FOR THE TREATMENT OF THE OSTEOPOROTIC SKELETON

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Introduction

Bone loss resulting from osteoporosis increases the risk of fractures. The "at risk" population is estimated to be 28 million in the US and 100 million worldwide. Among fractures of osteoporotic bones compression fractures of the vertebral body are the most demanding to treat. Common treatment involves injecting of methylmethacrylate (MMA) cement into the vertebral body to restore the height of a collapsed vertebra (vertebroplasty, kyphoplasty).

Both procedures have several drawbacks including leakage of MMA cement outside of the vertebra, soft tissue damage, pressure on nerve roots and/or the spinal cord resulting in pain, paralysis necessitating cement removal, migration of cement to the lungs, which may cause pulmonary embolism, respiratory and cardiac failure, and even death. Increased stiffness of the segments resulting from the presence of injected cement, often leads to fractures of the vertebrae adjacent to those treated. The MMA cements have high rigidity and, in consequence, there is a mismatch in Young's moduli between cement and osteoporotic bone. Tissue necrosis due to high polymerization temperature of MMA and high monomer toxicity can be yet another problem.

A possible solution to these problems could be the use of new injectable polymeric materials that set at lower temperatures, possibly based on nontoxic monomers and having lower moduli than those of poly(methylmethacrylate) (PMMA) cements. The latter property can be achieved, for example, by incorporating an elastic component in the polymer chain or by developing porous structure in the setting cement. In addition, such injectable materials could be loaded with antiresorptive drugs preventing further bone loss and osteogenic drugs promoting new bone formation.

If the osteoporotic bone of the vertebrae possesses potential to regenerate, it might be beneficial to use biodegradable cements, allowing new bone to fill the space formed by degrading cement.

Candidate materials for such injectable cements are seg-

mented polyurethanes, which can be synthesized with a broad range of mechanical and biological properties.

Injectable polyurethane cements can potentially be prepared in two ways. In the first approach the linear polymer is dissolved in an appropriate solvent to obtain solution with viscosity suitable for injection. The second route is similar to that of MMA cements, i.e. two or more monomers are premixed and subsequently injected into the vertebrae where polymerization is completed as a result of catalysis.

This study reports on the process of designing new biocompatible injectable materials for the treatment of the osteoporotic skeleton, based on linear segmented polyurethanes and/or hybrids consisting of these polymers and nanosize calcium phosphate salts.

Experimental

Polymers: Experimental linear polyurethanes with a molecular weight in the range of 70.000 - 110.000 dalton, designed for cancellous bone graft substitutes and for tissue engineering. The polymers were based on aliphatic noncarcinogenic diisocyanates, ε-caprolactone diol, polysaccharide diol and biocompatible catalyst. The hard segment contents of these materials were 60 and 70%, respectively.

Polymer solutions for injection: Injectable polyurethane solutions were prepared by dissolving the polymers in dimethyl sulfoxide (DMSO) and/or methyl-2-pyrrolidone (NMP). Both solvents are allowed by the FDA allowed for contact with tissues (PMP - permited daily exposure = 48.4 mg/day). Nanosize CaP salt was hydroxyapatite (HA) with broad particle-size distribution (Merck, Germany).

Materials characterization: Polymerization kinetics: calorimetry, infrared spectroscopy. Cement setting temperature: calorimetry. Composition: infrared spectroscopy. Absolute HA content: thermogravimetry. Cement structure: SEM. Mechanical properties: compressive strength and Young's moduli at 10% deformation. Water uptake: gravimetric. In vitro degradation: phosphate buffer, 37°C, pH changes. Mass loss upon degradation: gravimetric. Additional tests: extractables, degradation products, cytotoxicity, biocompatibility.

FIG. 1. Nanosize HA crystals in various solvent systems.

FIG. 2. Porous structure developing in PU - nanosize HA hybrids in an aqueous environment.

Solvent systems	Initial concentration of HA (%)		
	2	6	8
DMSO	1.08	4.58	6.44
NMP	1.05	4.50	6.20
EtOH	0.51	2.67	4.10
Water	0.49	2.45	4.40
DMSO/NMP 50/50	0.98	4.57	6.23
DMSO/NMP 20/80	0.86	4.49	6.16
DMSO/NMP 80/20	0.96	4.61	6.20

TABLE I. Stability of HA suspension in various solvents after 24 hr of storage.

Results

For the polymers used in the study the concentrations of solutions suitable for injections were 20 wt-% for the poly-

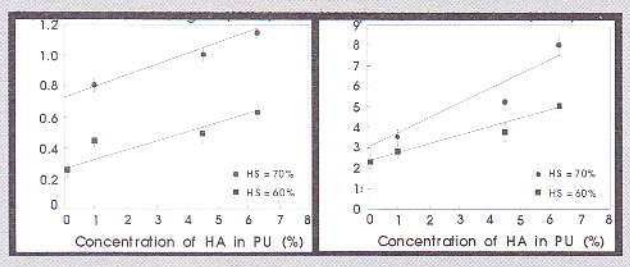

FIG. 3. Mechanical properties of injectable polyurethane materials.

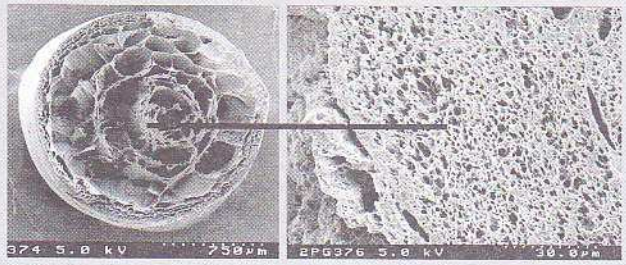

FIG. 4. Porous tubular scaffolds for nerve regeneration.

mer with a hard segment content of 60%, and 16 wt-% for the polymer with a hard segment content of 70%. Stable suspensions of nanosize hydroxyapatite HA could be obtained by using suitable high-viscosity, high-boiling point solvents (TABLE I).

Injectable hybrid materials can be produced by dissolving new biocompatible polyurethanes of varying elasticity in the suspensions of nanosize hydroxyapatite crystals in such solvents. The total amount of HA that can be loaded into the polyurethane solution depends on the stability of the HA suspension, i.e. the quality of the solvent. The hybrid materials solidify in an aqueous environment as a result of solvent replacement by water. Solidification is accompanied by the development of porous structure of varying pore size and geometry (FIG. 2).

Due to highly porous structure, the mechanical properties of the PU materials and the PU - HA hybrids are far from those required for the treatment of osteoporotic bone (FIG. 3).

Mechanical properties can be enhanced by reducing the pore-to-volume ratio in the hybrid, increasing the hard segment content in the polyurethane, and/or increasing the HA load in the hybrid. The injectable materials based on polyurethane solutions and nanosize hydroxyapatite may have limited applications in vertebroplasty due to the amount of solvent required to permit injection of the material. These solutions are, however, excellent systems for the preparation of porous scaffolds for tissue repair and regeneration (FIG.4).

Conclusions

Injectable polyurethane and polyurethane - nanosize calcium phosphate cements for vertebroplasty should be based on systems consisting of two or more monomers that are premixed before injection and solidify in the vertebrae as a result of a catalytic process.

EXPERIMANTAL WAY TO DETERMINE EFFICIENTY OF ACUPUNCTURE AND ANALOGOUS TREATMENT IN ALLOGENIC RHINOPLASTY

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Aesthetic surgery of innate and acquired nose pathology takes 58,90% of the total amount of aesthetic operations made in cranio-maxillofacial area. Grate attention in plastic surgery is pied to the stimulation of reparative and compensatory processes which are turned to the quickest rehabilitation of connective body structures, as well as in rhinoplasty.

Aim

of this abstract deals with making of experimental model for determining efficiency of acupuncture and analogous treatment application in allogenic rhinoplasty.

Materials and methods

Experiment was performed on 36 rabbits "Chinchilla". Line slit of nasal bone, moving under periosteum of first sterilized ear allogenic transplant taken from an other animal were performed under intravenous anesthesia of thiopentali-natrium (0,2 mg/kg) and local infiltration anesthesia (Novocaini 0,5% - 5 ml). Allogenic transplant was sterilized and conserved first with water Sol. Farmalini 0,5% within 3 days. The wound was closed in layers with atraumatic needle and materials (vicrilum). Animals were divided into 3 groups. Acupuncture stimulation of the acupoint GI4 was applied for the animals of the 1-st group. Local acupoints in the nose bone region were stimulated for the animals of the 2-nd group. Acupoint GI14 was irritated as well as local acupoints closed to the region of postoperative wound for the animals of the 3-rd group. Acupuncture treatment course have been lasted 10 days. Strong brake method has been applied for acupuncture irritation.

Results

Tissue infiltration in postoperative scar region of the 3-rd group animals was authentically less expressed five days postoperatively in respect of 1 and 2 groups ($p<0,01$ and $p<0,01$ correspondingly). That gives to take conclusion that to make experimental model of determining efficiency of acupuncture and analogous treatment application in allogenic rhinoplasty it is advisable to use acupuncture treatment model applied for the 3-rd group animals.