Introduction: Osteoset® (medical grade alpha-hemihydrate calcium sulfate) (Wright Medical Technology, Arlington, TN) is known as a synthetic bone graft substitute. It can be used either alone or in combination with other naturally occurring materials to fill bone voids or gaps1,2,3. Moreover, the efficiency of calcium sulfate as a vehicle for drug delivery for local antibiotic treatment has also been demonstrated4,5. Several reports and studies have shown that calcium sulfate has osteoconductive properties6.

The surgical created bone defects left after the arthroscopic ACL (anterior cruciat ligament) reconstruction with bone-ligament-bone grafting (both in patella and the tuberosity of tibia) will usually never be filled with new bone completely. In this prospective randomized human trial we have investigated the effects of Osteoset® pellets on bone healing and on anterior knee pain.

Materials and Methods: 20 patients undergoing a standard ACL reconstruction were randomized in to groups with 10 in each. The study was designed as double blinded trial both for patients and clinicians. It was approved by the local ethical comitée. Operation: Two senior surgeons performed the operations by a standardized procedure. During the operation bone-patellar ligament-bone graft was prepared. The defect in tuberositas tibia measured approximately 1x1x2.5cm. The tibial defect in the active group was filled manually with Osteoset® pellets (4.8X3.3mm) to the level of the cortical bone. No graft material was left in the tibial defect in the control group. All the patients followed standard postoperatively rehabilitation program with mobilization at the first day after operation. Computer tomography images (CTI) of the defect were obtained the first day after the operation and at 6, 12 and 24 weeks. Clinical evaluation of the knee and VAS score registration were performed at the same time. According to the double blinded design CTI were read in reverse order when evaluated.

The PICKIR PQ 2000 CT scanner was used to perform CTI. The images were obtained, enlarged and developed by standard procedures. The Sclerotic Digitizer (software Jandel SigmaScan) was used to measure the square of defect on each CTI. The defect volume was calculated by using the formula:

\[ V_{\text{vold}} = \frac{1}{2} \sum_{x_i} x^2 \times t \]

\[ V_{\text{vold}} \] - void volume (mm³),

\[ \sum_{x_i} - \text{sum of the squares (mm²)}, \]

\[ t \] - the step between the each cut images (mm).

Statistics: The data were presented as mean ± std.dev. The data were analyzed using unpaired ANOVA on ranks and pairwisse multiple comparison procedures (Student-Newman-Keuls method). The study was designed to show a difference of 70% between groups with a SD=50%, type I fault=5%, the type II fault=20%.

Results: All 20 patients accomplished the study. There were no intraoperative or postoperative complications. No side effects of Osteoset® pellets have been observed. It was not possible to distinguish remnants of pellets from the new bone on CTI at 6 weeks, whereas no pellets were visible after 12 weeks. The most considerable defect volume decrease was demonstrated during the first 6 weeks after the operation. At that time the defect volume decrease became statistically significant in both groups (p<0.05, fig. 1). Afterwards no significant changes happened either in Osteoset® or in control group.

The decrease in defect volume was greater in Osteoset® group than in control group at 6 weeks, (p=0.035, t test) but no differences were shown between the groups at 12 and 24 weeks. No one defect was filled with bone tissue completely. 51.1%±12.1 of defect volume was filled with Osteoset® pellets. The defects better filled with Osteoset® pellets had greater volume decrease at 6 weeks than the poor-filled ones (correlation coefficient r =-0.78, p=0.005), no significant correlation was found at 12 and 24 weeks.

The anterior knee pain registered both related to gait and lying on knee. The patients in Osteoset group had less pain both related to gait and lying on knee than the patients in the control group. However the difference was not statistically significant (VAS lying on knee, p=0.63, VAS gait, p=0.092).

Discussion and Conclusion: Animal studies have demonstrated significant effect of Osteoset® on bone healing. However in this randomized prospective study we found moderate effect of Osteoset® on bone healing in humans. We have observed that the decrease in defect volume seems to be higher at 6 weeks and the new bone formation seems to be more visible in the defects with Osteoset® pellets. It can be due to the osteoconductive properties of Osteoset® but it can be remnants of pellets which can be very similar to the new bone tissue on CTI. There were no statistically significant differences between the Osteoset® and control groups. It might be due to limited efficacy of Osteoset®, because of insufficient contact between bone and pellets. Moreover it might be explained by rapid resorption of the pellets. Nadkami et al 2000 reported better bone formation on calcium sulfate composites augmented with calcium phosphate, which had decreased the resorption rate6.

The tibial defects in our study was much bigger than in animal trials and it can be one of the reasons why none of the defects was completely filled with a new bone. The persisting knee pain might be explained by remaining bone defect. However other factors than the bone defect might cause anterior knee pain7. Further investigations of Osteoset® with less rapid resorptions characteristics might be interesting. The combination of bone substitute and bone growth factors in large bone defects are indicated to find the best suitable graft material for humans.

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