INTRODUCTION

Elderly patients with hip fractures have generally undergone cemented or cementless hemiarthroplasty for early rehabilitation and preventing the complications due to immobilization on bed. In spite of intraoperative complications, including death, associated with cemented hemiarthroplasty, it is still popular. Cementless hip arthroplasty is safer in elderly patients, however, even hydroxyapatite(HA)-coated implants showed a lower implant fixation in osteopenic condition in our previous study. Therefore we have tried to develop a cementless hip implant with stable fixation in osteopenic rat model. We consider that a combination of a drug, improving the osteopenia, can increase the osteoconductive effect of HA.

Prostaglandins E2 (PGE2) has the two functions, i.e. bone formation and resorption. PGE2 exerts its effects through interaction with G protein -coupled cell surface receptors including EP1, EP2, EP3, EP4. Drugs acting specifically at EP4 have induced bone formation in vivo and are beneficial in bone formation in osteoporosis.

In the previous study we demonstrated that the synergy of EP4 agonist and HA can enhance the HA-coated implant fixation in ovariectomized(OVX) rats. In the previous study, HA-coated implants had the smooth surface, so, we did not investigate the effect of EP4 agonist to implant fixation of rough surfaced implants. This time we developed the HA/Ti composite to induce the bone ingrowth for rat model. In this study, we investigated the effect of EP4 agonist to the fixation of HA/Ti composite in OVX rat femur.

MATERIAL AND METHODS

Twelve-weeks female rats were divided into two, bilaterally ovariectomized (OVX) and control sham-operated rats. Twenty-four weeks after operation, femora of all rats were implanted intramedullary with either Ti or HA/Ti composite-coated implants (23 mm length and 1.4 mm diameter). Both control and OVX rats were further divided into drug and saline-treated sub-groups and were injected subcutaneously with EP4 agonist, ONO4819, (30 microgram/Kg body weight, dissolved in saline) and saline only, respectively, for 4 weeks. Then, all animals were sacrificed and their femora were excised. All animal procedures were approved by review board of Hara Doi Hospital.

For measurement of bone-implant shear strength, after removal of soft tissues from femora and fixing them in a wooden base, the shear strength of bone-implant interface was measured by applying vertical load to the implant. For observation of osteogenic profiles, the implanted and non-implanted femoral tissues from OVX group were processed and stained using standard methods. The results were calculated as the mean +/-SEM. ANOVA was used to determine the effect of drug and HA-coating.

RESULT

In the OVX group, the shear strength of rats administration EP 4 agonist significantly greater than those rats administration saline only, in each of Ti and HA composite implant. The shear strength was significantly improved by using HA implant compared with those Ti implant in both Control and OVX groups administration saline only. Although the shear strength of OVX-HA-saline group was still about 30% less than Control-HA-saline group, OVX-HA-EP 4 agonist group showed great tendency than Control-HA-saline group.

DISCUSSION

HA-coated THA showed an excellent clinical results, however, all studied cases were patients with osteoarthritis and comparatively younger(50s) than patients with hip fractures. The major problem is weak bone-implant attachment strength in elderly patient with severe osteoporosis which limits HA-coated cementless implants. In our previous study, EP4 agonist augmented HA-coated implant fixation in ovariectomized rats femur. However, we investigated the HA-coated implants with smooth surface and have not analyze the effect of EP4 agonist to the bone ingrowth for the implants.

REFERENCES

We could not manufacture the small implants with beads, fiber mesh, and titanium spraying by arc spraying method for rats model, but large implants applied for rabbits or dogs. However, the osteoporosis model is not established for rabbits or dogs. This time we developed the HA/Ti composite implant to induce the bone ingrowth for rat model. The cross-sectional microstructure of the HA/Ti composite coating displayed a lamellar structure which was composed of Ti and HA splats. The composition of the HA/Ti composite coating was regulated so as to change gradually from Ti-rich at the bottom layer to HA-rich at the top.

In this study HA/Ti composite of OVX rats in saline group showed a 30% lower push-out strength than normal rats. EP4 agonist enhanced the HA/Ti composite fixation in OVX rats femur and compensated this shortage. Interestingly, EP4 agonist enhanced the non-HA/Ti composite of OVX rats. In addition, the non-HA/Ti composite of OVX in EP4 agonist group showed a higher push-out strength than HA/Ti composite of OVX in saline group. HA/Ti composite of OVX in EP4 agonist showed a much higher push-out strength than HA-coated implants with smooth surface of OVX in EP4 agonist group of previous study.

The effect of EP4 agonist and HA/Ti composite to enhance the bone ingrowth seem to confirm the stable fixation of hip implant for elderly patient.

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