ENHANCING POSTEROLATERAL SPINAL FUSION WITH rhBMP-6 EXPOSED OSTEOPROGENITOR CELLS

INTRODUCTION: The nonunion rate after posterolateral fusion has been reported to be as high as thirty-five percent, even with the use of autogenous iliac crest bone graft (ICBG) [4]. Accordingly, alternative techniques for expanding or stimulating the spinal fusion process are actively being investigated [1].

For the past several years we have been developing a strategy for stimulating marrow-derived osteoprogenitor (OP) cells by exposure to a cell-derived osteoinductive matrix containing rhBMP-6. Our preliminary data suggests that this exposure induces osteoblastic differentiation [4] and that the induced cells are capable of increasing new bone formation in the New Zealand white rabbit (NZW) posterolateral intertransverse fusion model [6].

In this study we have expanded our prior work [6] to assess the osteogenic capacity of two different concentrations of rhBMP-6 exposed osteoprogenitor cells.

METHODS: With IACUC approval, single level lumbar intertransverse process fusions were performed in sixty-seven skeletally mature NZW rabbits as previously described [4, 6].

In each rabbit, the L5-L6 intertransverse area was exposed bilaterally and the dorsal surface of the pars interarticularis and transverse processes were decorticated with a burr. Following decortication, the rabbits were assigned to one of five experimental groups. In Group I, the L5-L6 dorsal aspect was decorticated on both sides of the spine. In Group II, each decorticated fusion bed was grafted with 2.5 cc guanidine extracted demineralized bone matrix (gDBM) carrier [2, 3]. In Group III, each fusion bed was grafted with 2.5 cc of morselized iliac crest bone graft ICBG.

Prior to the spine surgery in groups IV and V, rhBMP-6 induced OP cells were generated in the following manner. Approximately 1 cc of bone marrow was harvested from both the right and left femur; the OP cells were then isolated, cultured and expanded for 3 weeks on a cell-derived osteoinductive matrix containing rhBMP-6. Our preliminary data suggests that this exposure induces osteoblastic differentiation [4] and that the induced cells are capable of increasing new bone formation in the New Zealand white rabbit (NZW) posterolateral intertransverse fusion model [6].

Animals received an autograft of 30M OP cells (15M/side) in Group IV and 60M OP cells (30M/side) in Group V.

RESULTS: Fifty-one rabbits were included in the study. 16 (23%) of the animals were excluded due to perioperative morbidity and mortality.

Radiographic Results [Figure 1] There was homogeneous new bone growth in the ICBG and OP cell-treated animals (Groups III, IV, V). The fusion masses were less prominent in the DBM group (Group II) and absent in the decortication only group (Group I).

Palpation Results [Table I] The fusion rate of the decortication/gDBM group (Group II) was inferior to the decortication/ICBG group (Group III) and superior to the decortication only group (Group I). The animals which received BMP-6 OP cells/gDBM (Groups IV and V) had the highest fusion rate.

Mechanical Testing Data [Figure 2] The fusion masses in animals treated with OP cells (Groups IV and V) had significantly higher peak load (p < 0.05) and energy to failure (p < 0.05) compared to the other treatment groups. There was no significant difference in stiffness among the five groups.

DISCUSSION: This study demonstrates that rhBMP-6 exposed autologous osteoprogenitor cells have potential as an alternative to ICBG for spine fusion. The groups treated with rhBMP-6 exposed cells had more new bone formation, a higher fusion rate, and stronger fusion masses than any of the other three treatment groups. With further refinement this technology may have applicability in spinal fusion surgery as a graft substitute/expander.

REFERENCES

ACKNOWLEDGEMENTS: Funded by the RIH Orthopaedic Foundation and University Orthopaedics, Inc. Scott McAllister.