Repeat use of rhBMP-2 at an adjacent lumbar level: An assessment of efficacy and immunologic response

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Introduction: The spine literature suggests a 10-20% re-operation rate in the years following lumbar fusion surgery. Little research has been performed on the immunoreactivity of rhBMP-2 in the context of its re-use in revision fusion spinal surgery. The purpose of this study is to determine whether rhBMP-2 elicits an immune response during its re-administration thereby reducing its rate of fusion in revision spinal surgery.

Materials and Methods: Thirty-three New Zealand White rabbits underwent posterior intertransverse process fusion at L5-6 with the use of rhBMP-2/ACS (2.58 mg/level). Baseline serologic studies (Type I bovine collagen and rhBMP-2 protein antibodies) were obtained pre-operatively and at two-week intervals. At ten weeks, postero-anterior radiographs were obtained confirming solid fusion masses in all rabbits. The 32 rabbits were randomly separated into two groups of sixteen. Baseline serologic studies (Collagen/rhBMP-2 Ab) were re-obtained and all rabbits subsequently underwent an adjacent level (L4-5), bilateral intertransverse process arthrodesis with either rhBMP-2/ACS (2.58 mg/level) or bilateral iliac crest. Serological studies (Collagen/rhBMP-2 antibodies) were obtained at two-week intervals. All animals were euthanized at 10 weeks and the lumbar spines were excised. Spine fusion was assessed via manual palpation and postero-anterior radiographs by blinded observers. Fusion masses were evaluated histologically and with computed tomography.

Results: At the completion of stage I (10 weeks) all thirty-two rabbits obtained a successful radiographic fusion at L5-6 with rhBMP-2 (n=32/32, Grade V). At final euthanization (20 weeks), solid radiographic fusion at the adjacent L4-5 level (Grade IV/V) was greater with rhBMP-2 (n=15/16, 94%) than iliac crest (n=13/16, 81%) (p < 0.05). Manual palpation also revealed a substantially increased fusion mass (Grade IV) in the adjacent level with rhBMP-2 (n=15/16, 94%) as compared to iliac crest (n=11/16, 69%). (Figure 1) Eight rabbits (n=8/32, 25%) developed collagen antibodies with seven rabbits developing antibodies after the first exposure (average 4.4 weeks, range 2-7) and one rabbit developing antibodies after the second exposure (16 weeks). Four rabbits (n=4/32, 13%) developed both rhBMP-2 and collagen antibodies. Of these four rabbits, two rabbits developed anti-rhBMP-2 antibodies after the first surgery (2 and 4.4 weeks) and two developed antibodies after the second exposure (12 and 14 weeks). (Figure 2) There was no correlation between antibody response and radiographic or manual palpation fusion quality (p < 0.05). No fusion mass demonstrated the presence of inflammatory cells upon histological analysis. No rabbits suffered any anesthetic or wound related complications. One rabbit was euthanized secondary to a hind limb paralysis sustained after the index procedure.

Discussion: rhBMP-2 appears to be a successful arthrodesis agent in primary and revision surgical environments with an increased fusion rate as compared to iliac crest. The development of antibodies to rhBMP-2 and Type I bovine collagen occurs without a predictable time course suggesting that host immunological variation may play a role. Further studies are needed to evaluate immunologic response to dosage and host factors such as the presence of systemic inflammatory conditions and pregnancy.