The Effects of Doxorubicin on Spinal Fusion: An Animal Model
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Introduction. Malignant spinal lesions may require surgical excision and segmental stabilization. The decision to perform a concomitant fusion procedure in part by the patient’s anticipated survival and the need for adjunctive chemotherapy. Based on our review of the literature, no information exists regarding the effect of chemotherapy on spinal fusion healing. The purpose of this study, therefore, was to determine the effect of a standard chemotherapeutic agent, doxorubicin, on posterolateral spinal fusion.

Methods. Thirty-two New Zealand white rabbits underwent posterior intertransverse process arthrodesis at L5-6 with the use of iliac autograft. Rabbits randomly received either intravenous doxorubicin (2.5 mg/kg) via the central vein of the ear at the time of surgery (16 animals) or no treatment (16 animals) (the control group). The animals were killed at five weeks and the spines were denuded of soft tissues. Spine fusion was assessed by manually palpating (by observers blinded to the treatment group) at the level of arthrodesis, and at the adjacent levels proximal and distal. This provided similar information to surgical fusion assessment by palpation in humans. Fusion was defined as complete absence of motion. Postero-anterior radiographs of the denuded spines were graded in a blinded fashion using a five-point scoring system (0-4) devised to describe the amount of bone observed between the L5-6 transverse processes. Grade zero indicated no bone, Grade one indicated only scattered islands of bone, Grade two indicated bridging bone with two or more discontinuous regions or one large gap, Grade three indicated bridging bone with only one narrow line discontinuity, Grade four indicated complete bridging bone at the motion segment. Power analysis conducted prior to initiation of the study indicated that an allocation of 16 animals to each group would permit detection of at least a 20% difference in fusion rates with statistical significance at p=0.05.

Results. Sixty-nine percent (11) of the 16 spines in the control group and 38% (six) of the 16 spines in the doxorubicin group fused. This difference was statistically significant (p=0.03). There was no significant correlation (p>0.05) between the radiographic grade of bone formation (0-4) and fusion as determined by palpation. There were four wound infections in the control group and four in the doxorubicin group, however solid fusions were palpated in three of four spines in both the control and treatment groups.

Discussion/Conclusion. Doxorubicin administered intravenously at the time of surgery appears to play a significant inhibitory role in the process of spinal fusion. Our data suggests that doxorubicin should not be administered perioperatively to patients in whom a spinal arthrodesis has been performed. Further investigation should elucidate whether delaying doxorubicin administration results in improved fusion potential and whether bone morphogenetic proteins could overcome these inhibitory effects.