"Mechanism of Intervertebral Disc Degeneration Caused by Nicotine in Rabbits to Explicate Intervertebral Disc Disorders Cause by Smoking"

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Study Design. The effects of nicotine on intervertebral discs in rabbits were studied experimentally.
Objectives. To investigate the effects of nicotine on the vascular buds in rabbits for elucidating the mechanism of nicotine-induced vertebral disc degeneration.
Background data. Several groups have suggested that cigarette smoking is associated with low back pain, but the exact mechanism is not yet fully understood.
Methods. The pump was filled with a diluted nicotine solution, then implanted under the skin of rabbits for 8 weeks. This model was designed to maintain blood nicotine concentration at approximately 110 ng/ml. Rabbits receiving physiologic saline were used as control animals.
Results. Nicotine treatment resulted in necrosis and hyalinization of the nucleus pulposus in all rabbits. The annulus fibrosis showed a disturbance of the pattern of overlapping laminae with and without clefts and separation. There resulted in changes indicative of stenosis of vascular buds and perivascular calcification. Nicotine treatment resulted in hypertrophy of vascular walls, necrotic changes in endothelial cells, and narrowing of the vascular lumen. Nicotine treatment resulted in delineation of vascular buds in the vicinity of the vertebral end-plate and a reduction of their numbers. However, the control animals showed a dense vascular network. The number of vascular buds decreased in nicotine treatment.
Conclusion. The authors believe that both reduction in the density of vascular buds and narrowing of the vascular lumen result in decreased oxygen tension, leading to decreased synthesis of proteoglycan and collagen, thus facilitating degeneration of the disc.

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Editor's Comments

Spine surgeons are often curious about the causes of maladies they evaluate and treat. The spine problems that have a traumatic etiology do not cause as much consternation as those labeled "lumbar degenerative" and present with a chronic complaint of low back pain. Back pain specialists are often queried by patients and families on "what they should do" to reduce their symptoms and improve their spine health, as well. Iwashashi et al, the authors of this article, have done a study to see the effect of infused (non-inhaled) nicotine on the spine of experimental rabbits.

Their model utilized 20 rabbits (controls or experimental). Their spines were studied using light microscopy, electron microscopy, and transparent vascular preparations. All analyses were aimed at studying the vascular buds, composed of capillaries and mesenchymal cells, at the end of the vertebral endplates or surrounding the annulus fibrosis. These buds have been considered responsible for the flow of nutrients and ions into the avascular adult disc. The experimental model produced approximately the same blood levels of nicotine that humans demonstrate smoking about 1.5 packs per day (32.7 cigarettes per day with average amounts of nicotine per cigarette). The rabbits were exposed to 8 weeks of subcutaneous infusion with blood levels measured each week. There was no "surgical model" or group that had undergone an attempted spinal fusion to examine the effect of this infusion on that type of group. This study was to examine vascular bud changes and not cytotoxic or other possible effects of nicotine. They referred to another study in pigs, where the animals had been exposed to tobacco smoke and demonstrated acute contraction of vascular buds. Hence, this study continues down that path.

The study does not utilize a large number of animals, and the coterie of analyzed animals in some categories is small. The animals were not chronically exposed to nicotine before the eight

weight study period, and, therefore, some conclusions may be criticized on that basis—not knowing whether chronic habituation to nicotine may worsen or ameliorate the exposure during the eight week study period. Nevertheless, the study produced some very interesting findings.

Light microscopic and electron microscopic evaluations were done on the en bloc preparations of 5 exposed rabbits and 5 controls in each group. The findings with light microscopy in exposed rabbits included: necrosis and hyalinization of the nucleus pulposus, disturbance of the annulus with overlapping laminae with and without clefts, stenosis of and a significant reduction in the number of vascular buds, and perivascular calcification. E/M findings showed enlargement of vascular endothelial cells, hypertrophy of vascular walls, necrotic changes in endothelial cell, and narrowing of the vascular lumen. The E/M changes were NOT statistically different, just obvious in the nicotine-exposed group. In the transparent or vascular preparation animals, the vertebral body vasculature was studied in 3 exposed and 3 control animals. The findings included reduction of vascular buds in the vicinity of the vertebral endplate with many showing signs of interruption with dead-end blood vessels near the endplate. The vascular buds aggregates were adjacent to the endplates suggesting, as has other studies, that the buds provide nutrition.

The authors provide demonstrative photomicrographs of their findings and one cannot but be impressed at the micro-structural changes that occur in the rabbits exposed to constant infusion of nicotine. They raise the issue that nicotine not only disrupts the vascular nutritive support to the annulus but to the vertebral endplates, both of which comprise the probable nutritive support for the intervertebral disc after age three years. The authors make reference to other articles that suggest that some of these vascular obstructions may come from the increase in white blood cells in the peripheral circulation that may obstruct these channels when the blood vessels react to nicotine. Hence, the question of whether the dead-end vessels seen occur from which process, both of which incriminate nicotine. The authors, though, lean to the effect of nicotine on the blood vasculature and vascular buds.

This study raises questions for spine surgeons and those treating spine related diseases: how much does smoking contribute to degenerative disc disease; in a spine surgical patient contemplating discectomy or spinal fusion, should there be a “preoperative no smoking period”; and, are nicotine-embedded skin patches as harmful as smoking in spine-effected patients. There are other questions that can be raised, as well.

The authors are to be complemented for this study. Medical professions attempt to prevent or reduce the occurrence of degenerative spine disease. Further studies on the effects of non-traumatic etiologues on spine disease and spine surgery would be worthwhile.

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