THE SPINE JOURNAL
Official Journal of the North American Spine Society

The Spine Journal
Volume 14, Issue 3 , Pages 416-423, 1 March 2014

Investigating the role of DNA damage in tobacco smoking-induced spine degeneration

Luigi A. Nasto, MD, Kevin Ngo, BS, Adriana S. Leme, PhD, Andria R. Robinson, PhD, Qing Dong, MS, Peter Roughley, PhD, Arvydas Usas, PhD, Gwendolyn A. Sowa, MD, PhD, Enrico Pola, MD, James Kang, MD, Laura J. Niedernhofer, MD, PhD, Steven Shapiro, MD, Nam V. Vo, PhD

Received 20 November 2012; received in revised form 15 July 2013; accepted 23 August 2013. published online 08 November 2013.

Abstract

Background context

Tobacco smoking is a key risk factor for spine degeneration. However, the underlying mechanism by which smoking induces degeneration is not known. Recent studies implicate DNA damage as a cause of spine and intervertebral disc degeneration. Because tobacco smoke contains many genotoxins, we hypothesized that tobacco smoking promotes spine degeneration by inducing cellular DNA damage.

Purpose

To determine if DNA damage plays a causal role in smoking-induced spine degeneration.

Study design

To compare the effect of chronic tobacco smoke inhalation on intervertebral disc and vertebral bone in normal and DNA repair-deficient mice to determine the contribution of DNA damage to degenerative changes.

Methods

Two-month-old wild-type (C57BL/6) and DNA repair-deficient *Ercc1*$^{-/\Delta}$ mice were exposed to tobacco smoke by direct inhalation (4 cigarettes/day, 5 days/week for 7 weeks) to model first-hand smoking in humans. Total disc proteoglycan (PG) content (1,9-dimethylmethylene blue assay), PG synthesis (^{35}S-sulfate incorporation assay), aggrecan proteolysis (immunoblotting analysis), and vertebral bone morphology (microcomputed tomography) were measured.

Results

Exposure of wild-type mice to tobacco smoke led to a 19% increase in vertebral porosity and a 61% decrease in trabecular bone volume. Intervertebral discs of smoke-exposed animals also showed a 2.6-fold decrease in GAG content and an 8.1-fold decrease in new PG synthesis. These smoking-induced degenerative changes were similar but not worse in *Ercc1*$^{-/\Delta}$ mice.

Conclusions

Short-term exposure to high levels of primary tobacco smoke inhalation promotes degeneration of vertebral bone and discs. Disc degeneration is primarily driven by reduced synthesis of proteoglycans needed for vertebral cushioning. Degeneration was not exacerbated in congenic DNA repair-deficient mice, indicating that DNA damage per se does not have a significant causal role in driving smoke-induced spine degeneration.

Keywords: Tobacco smoking, Intervertebral disc degeneration, Matrix proteoglycans, Aggrecan, Matrix metalloproteinases, DNA damage repair

FDA device/drug status: Not applicable.

Author disclosures: ***LAN:*** Nothing to disclose. ***KN:*** Nothing to disclose. ***ASL:*** Nothing to disclose. ***ARR:*** Nothing to disclose. ***QD:*** Nothing to disclose. ***PR:*** Nothing to disclose. ***AU:*** Nothing to disclose. ***GAS:*** Royalties: UpToDate (A), Speaking and/or Teaching Arrangements: Cytonics (A), Trips/Travel: Cytonics (A), Research Support (Investigator Salary, Staff/Materials: NIH/NCCAM (E, Paid directly to institution), Grant: NIH/NCCAM (E, Paid directly to institution). ***EP:*** Nothing to disclose. ***JK:*** Grant: Stryker Research Grant Synthes Grant (F). ***LJN:*** Nothing to disclose. ***SS:*** Nothing to disclose. ***NVV:*** Grant: NIH (F, Paid directly to institution).

The disclosure key can be found on the Table of Contents and at www.TheSpineJournalOnline.com.

Supported by the 2010 ORS Collaborative Exchange Award (to NVV, PR) and National Institutes of Health grants AG033046 (to NVV) and ES016114 (to LJN).

PII: S1529-9430(13)01481-2

doi:10.1016/j.spinee.2013.08.034

Published by Elsevier Inc.

« Previous

The Spine Journal
Volume 14, Issue 3 , Pages 416-423, 1 March 2014

Next »