

# **The Role of Cyclooxygenase-2 in Lumbar Disc Herniation**

## **Spine**

**November 15, 2002; Vol. 27, Issue 22, pgs. 2477-2483**

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FROM ABSTRACT:

**Study Design.**

The expression of cyclooxygenase-2 was studied immunohistologically in specimens from lumbar disc herniation.

The cultured disc cells also were examined to evaluate the significance of cyclooxygenase-2, which might be involved in the pathogenesis of lumbar disc herniation (LDH).

**Objective.**

To investigate whether cyclooxygenase-2 might be involved in the pathogenesis of lumbar disc herniation.

**Summary of Background Data.**

Prostaglandin E2 is one of the most important mediators contributing to pathogenetic components of lumbar disc herniation.

Cyclooxygenase-2 is the rate-limiting enzyme of prostaglandin E2 synthesis, has been identified extensively in other inflammatory diseases.

**Methods.**

Fifteen specimens from patients with lumbar disc herniation and five control discs from traumatic burst fracture were harvested.

The expression of cyclooxygenase-2 was evaluated immunohistologically.

The ability of cultured disc cells to produce prostaglandin E2 with inflammatory stimulus in the presence or absence of a selective inhibitor of cyclooxygenase-2 was investigated.

**Results.**

Immunohistologically, the expression of cyclooxygenase-2 was observed only in the lumbar disc herniation specimens.

The cultured cells had a strong ability to produce prostaglandin E2 coinciding with cyclooxygenase-2.

A selective inhibitor of cyclooxygenase-2 inhibited this prostaglandin E2 production in a dose-dependent manner.

Conclusion.

Cyclooxygenase-2 might be involved in the pathogenesis of lumbar disc herniation through upregulation of prostaglandin E2 production. **[IMPORTANT]**

THESE AUTHORS ALSO NOTE:

Investigations have showed that the biochemical effects of inflammation, which the herniated disc itself possesses, "may be the pivotal contributors to the pathogenesis of LDH". [IMPORTANT, 10 references]

"The herniated disc might have the capacity to produce a strong mediator such as prostaglandin E2 (PGE2), and it may play an important role at the site of LDH."

"Arachidonate cascade, the pathway of PGE2 production, has a rate-limiting enzyme, cyclooxygenase-2 (COX-2)." **[Remember, arachidonic acid is an omega-6 fatty acid and is the precursor to PGE2]**

"COX-1 is constitutively expressed in almost all types of cells and appears to be responsible for the PG production that is important for homeostatic function."

"COX-2 is the inducible product of an 'immediate-early' gene that is upregulated just during inflammation."

"COX-2 plays a pivotal role through upregulation of PGE2 synthesis in the pathogenesis of other inflammatory-related diseases such as rheumatoid arthritis and osteoarthritis."

This study was designed to investigate the role of COX-2 in the pathogenesis of LDH through upregulation of PGE2 synthesis.

Using immunohistochemistry, the authors evaluated the inflammatory granulation tissues found in 15 herniated discs and compared the results to 5 control discs.

## DISCUSSION

Inflammation is an important pathogenetic component in the pathogenesis of LDH.

The nucleus pulposus has the capacity to induce inflammation, and its "inflammatory property might play a pivotal role in causing symptoms of LDH"

Lumbar disc materials can produce inflammatory mediators such as PGE2, nitric oxide, and inflammatory cytokines.

PGE2 is the principal mediator related to the induction of sciatica and low back pain.

"PGE2 possesses the capability of causing pain or enhancing sensitivity to pain-inducing substances such as bradykinin."

High concentrations of PGE2 have been extracted from herniated lumbar discs.

"PGE2 provokes ectopic firing of nerve roots, indicating that it might play a part in the chemical irritation of nerve roots."

Dorsal root ganglion neurons can be sensitized by PGE2.

"COX-2 is a rate-limiting step in the arachidonate cascade, the process in which PGE2 is synthesized."

Phospholipase (PL) A2 releases arachidonic acid from membrane fatty acids.

Once released,

COX-2 is the "pivotal rate-limiting enzyme for the production of PGE2 in the inflammatory condition."

PGE2 and COX-2 presence coincided with osteoarthritis-affected cartilage.

In this study, the control discs showed no obvious COX-2 activity.

"This data suggest the involvement of COX-2 in the pathogenesis of LDH."

"This study also showed that not only the cells constituting the inflammatory granulation that infiltrated along the disc, but also the chondrocytes included in the disc material were apparently positive for COX-2 in LDH specimens."

"This study has suggested that COX-2 may play a role in the pathogenesis of LDH through upregulation of PGE2 synthesis."

#### KEY POINTS FROM AUTHORS

- (1) Immunohistochemical examination showed the expression of cyclooxygenase-2 (COX-2) in the specimens of lumbar disc herniation.
- (2) Few expressions of COX-2 were observed in the control specimens.
- (3) Herniated lumbar disc-derived cells produced a high amount of prostaglandin E2.
- (4) "It is suggested that COX-2 may be involved in the pathogenesis of lumbar disc herniation through upregulation of PGE2 production."

## KEY POINTS FROM DAN MURPHY

- (1) Arachidonic acid is an omega-6 fat that is a precursor to PGE2.
- (2) Arachidonic acid is converted to PGE2 primarily by COX-2 enzymes.
- (3) PGE2 is pro-inflammatory and causes pain.
- (4) PGE2 is involved in the pathogenesis of lumbar disc degeneration and herniation.
- (5) Blocking the conversion of arachidonic acid to PGE2 by inhibiting COX-2 protects the disc.

[This is the theoretical basis being COX-2 inhibiting drugs, like Vioxx and Celebrex. However, both Vioxx and Celebrex are froth with serious side effects, including gastrointestinal damage, kidney damage, and cardiovascular risks.]

[As we have seen in other articles, stopping the conversion of arachidonic acid to PGE2 is very effectively accomplished by the supplementation with omega-3 fatty acids, and this is accomplished with no side effects.]

[It is also important to reduce one's intake of omega-6 fatty acids because they are converted to arachidonic acid. Omega-6 fatty acids are vegetable oils. I have found that an easy way to reduce omega-6 ingestion is to read labels and eat nothing with "partially hydrogenated" oils, as they are always omega-6 oils. Hydrogenation converts these omega-6 oils into trans-fatty acids, which we have seen are very harmful to the body. There is no safe level of trans-fatty acids in the diet.]