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Low Back Pain Linked to Bacterial Infection

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May 08, 2013

New research suggests that some 40% of chronic lower back pain (CLBP) could be caused by bacteria, and that a significant percentage of people with lower back pain following a herniated disc and swelling in the spine could find relief by taking an antibiotic.

Investigators from the Research Department of the Spine Center of Southern Denmark, University of Southern Denmark, Odense, led by Hanne B. Albert, PhD, conclude that antibiotics may be considered as a treatment option for patients with chronic low back pain, but with caution.

The authors suggest that long-term antibiotics should not be prescribed "without due consideration." Low back pain is so common in the community that there could be hazards if used indiscriminately, they write.

"However, as many patients, as in this trial, are on sick leave at risk of losing their jobs and have a high analgesic intake, we suggest that antibiotics, when applied along the lines of this MAST [Modic antibiotic spine therapy] protocol may be appropriate in this subgroup, i.e., CLBP with Modic type 1 changes. We do not support the proposition that all patients with lumbar pain should have a trial course of antibiotics."

Their findings, published in 2 papers, 1 a randomized trial of antibiotics for low back pain, are published in the April issue of the *European Spine Journal*.

Positive Cultures

An estimated 80% of Americans have low back pain at some point in their life, the authors write, and back pain is the most common reason for workplace absence.

The first of 2 studies shows that patients with an anaerobic infected disc are more likely to develop Modic change (MC) (bone edema) in the adjacent vertebrae after disc herniation, suggesting a role of bacteria in developing Modic changes.

The study included 61 adults (mean age, 46.4 years; 27% female) who had MRI-confirmed lumbar disc herniation and were undergoing surgery. All patients were immunocompetent. No patient had received a previous epidural steroid injection or had previous back surgery.

Using stringent antiseptic sterile protocols, researchers collected 5 tissue samples from each patient. In total, microbiological cultures were positive in 46% of the patients. Anaerobic cultures were positive in 43% of patients, and of these, 7% had dual microbial infections, containing 1 aerobic and 1 anaerobic culture. No tissue specimens had more than 2 types of bacteria.

The anaerobic microorganism *Propionibacterium acnes* was found in 40% of the total cohort and in 86% of those with positive microbiology. These bacteria typically live in human skin and hair follicles and gums.

The results showed that in the discs with a nucleus with anaerobic bacteria, 80% developed new MC in the vertebrae adjacent to the previous disc herniation. In contrast, none of the patients with aerobic bacteria and only 44% of those with negative cultures developed new MC.

The association between an anaerobic culture and new MCs was highly statistically significant ($P = .0038$), with an odds ratio of 5.60 (95% confidence interval, 1.51 - 21.95).

The authors said that the detected bacteria are unlikely the result of intraoperative skin contamination. They pointed out that the procedures were conducted under the strictest of sterile conditions. As well, if skin contamination was the cause of the infection, a pattern of multiple skin bacteria cultures would be observed, which was not the case.

Why would some patients develop MC when no microorganisms are present in their herniated nuclear tissue? The authors speculate this could be due to a biochemical effect reflecting edema secondary to microfractures and subsequent inflammation, or the result of an inflammatory process from proinflammatory chemicals penetrating through the microfractures from the nucleus pulposus.

Antibiotic Randomized Trial

The second study, a double-blind, randomized trial, showed that an antibiotic protocol was significantly more effective than placebo in reducing pain and disability. This study included 162 adults who had chronic lower back pain that had developed after a previous disc herniation and had lasted more than 6 months.

These patients also had bone edema, as shown by Modic type 1 changes in the vertebrae adjacent to the previous herniation. Such changes in the vertebrae are present in 6% of the general population and 35% to 40% of those with low back pain.

The patients were randomly assigned to amoxicillin-clavulanate (500 mg/125 mg; *Bioclavid*) or identical placebo 3 times daily for 100 days and were blindly evaluated at baseline, end of treatment, and 1 year.

The analysis included 144 patients who completed the 1-year follow-up. The antibiotic group improved on all primary outcome measures, including disease-specific score on Roland Morris Disability Questionnaire (RMDQ), and lumbar pain. The improvement continued from the 100-day follow-up until the 1-year follow up.

The improvements in the antibiotic group were highly statistically significant on all outcomes measured, including secondary outcomes of leg pain, number of hours with pain in the last 4 weeks, global perceived health, and days with sick leave, among others.

For example, at baseline, 100 days, and 1 year, the disease-specific disability-RMDQ scores for the antibiotic group were 15.0, 11.5, and 7.0, and for placebo they were 15.0, 14.0, and 14.0 ($P = .0001$ for the difference between placebo and antibiotic group at 1 year follow up). For back pain, the figures for the antibiotic group were 6.7, 5.0, and 3.7 and for placebo they were 6.3, 6.3, and 6.3. ($P = .0001$ for difference).

For low back pain, which was experienced by all patients at the beginning of the study, 67.5% of the antibiotic group reported this pain after 1 year compared with 94.0% of the placebo group ($P = .0001$ for difference). The percentage of those with constant pain was reduced from 73.5% to 19.5% in the antibiotic group and from 73.1% to 67.2% in the placebo group ($P = .0001$ for difference).

There was a trend toward a dose-response relationship, with double-dose antibiotics being more effective; however, this was not statistically significant because the study was not powered for this comparison.

Adverse events were more common in the antibiotic group (65% of participants) than in the placebo group (23%).

Surgical Setting

In an editorial accompanying the publication, Max Aebi, MD, from the MEM Research Center for Orthopaedic Surgery, Institute for Evaluative Research in Orthopedic Surgery, University of Berne, Switzerland, and editor-in-chief of the *European Spine Journal*, points out that previous studies have shown that MC I occurs 6 times more frequently in the low back pain population than the general population. The relationship may be mechanical, he writes, "but under certain circumstances, low virulent infections may play a key role."

These new papers not only demonstrate that patients infected with herniated nucleus material by anaerobic bacteria in lumbar disc herniation develop new MC I in adjacent vertebrae but also that patients with low back pain and MC I after lumbar disc herniation improved significantly with an antibiotic protocol, Dr. Aebi writes.

"This strongly suggests one cause of low back pain in combination of MC I to be of low-grade infectious nature in case of previous disc herniation," he said.

However, he cautions that it is ethically impossible to take biopsy samples from all of these patients; this could be done only those who have surgery subsequent to disc herniation. The authors ask "the obvious key question" of whether the bacteria found in the nuclear material results from infection or could be due to intraoperative contamination, he writes, and then provide a "plausible" answer as to why such contamination is "highly improbable."

"Nevertheless," Dr. Aebi writes, "further research is necessary to show null what exactly happens in patients with disc herniation who develop MC I and low back pain and who have not been operated on. How could we show that in this fraction of patients there could be the same number of anaerobic infections of the nucleus material? By markers of the anaerobic bacteria or of specific infectious tissue, which could be made visible in imaging? By fine needle biopsy?"

Knowing these answers would make the current study results "even more explosive" in terms of better understanding low back pain and corresponding MRI changes, said Dr. Aebi. "We are keen to wait for further innovative research in this field."

The authors have disclosed no relevant financial relationships.

Eur Spine J. 2013;22:690-696, 697-707, 689. Abstract Abstract Editorial

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Cite this article: Low Back Pain Linked to Bacterial Infection. *Medscape*. May 08, 2013.

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