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Efficacy of Antibiotic Therapy in Those Diagnosed With Chronic Lower Back Pain

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by

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ABSTRACT

Chronic back pain affects approximately eight percent of the American population, yet no treatment has been agreed upon universally. Recent studies suggest that between 20-30 percent of lower back pain cases are caused by a low-virulence bacterial infection of the intervertebral disks in those who suffered disc herniation. This scholarly project is to investigate: In patients with chronic lower back pain and Modic changes after disc herniation, what is the effect of antibiotic therapy on reducing pain symptoms compared to placebo. This literature review used the following electronic databases: ClinicalKey, Cochrane Library, Embase, and PubMed. Keywords and mesh terms refined searches to the most recent and relevant literature. The articles were then analyzed and refined, revealing 10 for critical review. The studies included are peer-reviewed and include a double-blind randomized control trial, pilot study, systemic literature reviews, literature reviews, monocentric study, and cohort study. A majority of the research presented shows evidence that *Cutibacterium acnes,* formerly known as *Propionibacterium acnes* presence in intervertebral discs, is not from contamination but rather is an infectious process that occurs after disc herniation. The research suggests that antibiotic treatment in those with chronic lower back pain and Modic changes after disc herniation is beneficial. Additional studies are required, but antibiotic therapy appears efficacious in reducing pain symptoms in those with chronic lower pain and Modic changes after disc herniation.

Keywords: Low virulence bacteria and back pain, antibiotics back pain, bacteria modic changes, intervertebral disk herniation low virulence bacteria.

Introduction

Chronic lower back pain affects approximately eight percent of the American population, yet no treatment has been agreed upon universally. Recent studies suggest that between 20-30 percent of lower back pain cases are caused by a low-virulence bacterial infection of the intervertebral discs in those who have suffered a disc herniation (Albert et al., 2013a; Albert, Sorensen, Christensen, & Manniche, 2013b). If this is the case, can antibiotics cure or reduce lower back pain symptoms if a bacterial infection is present? The initial research shows promising results when using Amoxicillin-Clavulanic acid 500mg/ 125mg for 100 days in those who suffered disc herniation, resulting in chronic lower back pain and Modic changes.

The Problem

Chronic lower back pain has crippling effects on performing daily living activities while also reducing one's overall quality of life. Chronic pain can negatively influence personal, romantic, and work relationships. Narcotic drugs have treated pain for centuries, and long-term use can produce adverse effects, including addiction and death. Thus, narcotics are a controversial treatment that is not appropriate for all patients. Chronic lower back pain can have many causes. However, it is often due to an injury that leads to a disc bulge or herniation. It is believed that when disc herniation occurs, low-virulence bacteria infect the injured disc leading to chronic lower back pain (CLBP) and Modic changes (Modic changes are pathogenic bone marrow edema that is visible on magnetic resonance imaging).

In the past, CLBP was treated with narcotic pain killers. However, suppose a bacterial infection is causing the pain. In that case, narcotics are only a temporary fix that does not treat the pain's underlying cause. If a non-addictive alternative pill were available to take for a three-month regimen that would cure or reduce a lifetime of pain, it would be groundbreaking.

Antibiotics could be a cost-effective treatment that may reduce the need for invasive procedures and costly surgeries for those suffering CLBP with Modic changes after disc herniation.

Research Question

In patients with chronic lower back pain with Modic changes after disc herniation, what is the effect of antibiotic therapy on reducing pain symptoms compared to placebo?

The Methodology

This literature review involved defining keywords and mesh terms to represent results related to CLBP with Modic changes, *Propionibacterium acnes,* and the efficacy of antibiotic therapy in those with CLBP. Three-fourths of articles reviewed were published within the last five years, while the other one-fourth were not. The electronic databases used to compile data included: ClinicalKey, Cochrane Library, Embase, and PubMed. The keywords and mesh terms refined searches to the most recent and relevant literature. The patient population is specific to males and females who are 17 and older that suffer from chronic lower back pain with and without sciatica and Modic changes. The literature compiled is comprised of a randomized double-blind control trial, systemic literature reviews, literature reviews, a monocentric study, and a cohort study. Search results were systematically refined, revealing 35 peer-reviewed articles. Ten were selected for critical review because they provided high-quality studies and data.

Literature Review

After a thorough review of the literature, conflicting views were found on whether low-virulence bacteria cause chronic lower back pain (CLBP). However, compelling evidence shows that low-virulence bacteria are highly associated with Modic changes that may lead to CLBP.

Disc Herniation Leading to Infection

Albert et al. (2013a) conducted a study that tried to find how often the nucleus pulposus of herniated lumbar discs become infected with anaerobic bacteria leading to Modic changes (bone marrow edema) in the adjacent vertebrae. In this study, the patients were 18-65 years of age and had a disc herniation at a single level that required surgery. A confirmatory magnetic resonance image (MRI) was used to confirm nuclear tissue infiltration into annular fibers. All participants were immunocompetent and have never had an epidural steroid shot or back surgery. Anyone who took antibiotics within two weeks of surgery were dismissed. MRIs were taken at baseline, 1-year follow up, and 2-year follow up.

Strict antiseptic technique and protocols were employed by Albert et al. (2013a) to avoid specimen contamination. Participant's intervertebral disc (IVD) biopsies were split into five pieces after being harvested. New sets of sterilized instruments were used to handle each section. Once a sample was placed in a collection vile, it was immediately frozen to -112° and was not thawed until the examination took place. After sample collection, patients received an intravenous (IV) antibiotic (Albert et al., 2013a, p. 692).

To culture samples, Albert et al. (2013a) placed them in Columbia blood agar. They were incubated for seven days at 98.6° in both anaerobic and aerobic conditions. After seven days of incubation, colonies were sub-cultured and incubated for another 24 hours at 98.6°. Colonies believed to be *Cutibacterium acnes* (C. acnes), formerly known as *Propionibacterium acnes,* underwent 16SrDNA polymerase chain reaction (PCR) and analytical profile index (API) biochemical analysis to be further identified.

Fisher’s exact test and odds ratio calculations were used to interpret statistical data and examine associations between the anaerobic bacteria cultured and new Modic changes. Initially,

67 patients began the study, but only 61 finished. Of those who did not finish the study, three patients had nuclear tissue that was unable to be harvested, and three patients did not show at the 1-year follow-up. So they were not included in the study (Albert et al., 2013a, p. 692). The remaining 61 participants consisted of 28% (17/ 61) females and 72% (44/ 61) males (mean age 46.4; SD 9.7 years) (p. 693).

Albert et al. (2013a) found that tissue cultures were bacteria positive in 46% (28/ 61) of participants, and 43% (26/ 61) of the positives were anaerobic bacteria. There were 26 positive anaerobic cultures in which 7% (4/ 26) had both anaerobic and aerobic bacteria, with 3% (2/ 28) being aerobic bacteria. Of the patients with positive anaerobic growth, 80% had bacteria isolated in the discs nucleus pulposus with new Modic changes to the adjacent vertebrae (OR=5.6, 95% CI=1.51-21.95). This study found a significant (p=0.00038) association between anaerobic culture and new Modic changes. No patients with aerobic only bacterial growth developed new Modic changes.

A significant association (p=0.00038) between anaerobic cultures and new Modic changes was found by Albert et al. (2013a). However, he does not discuss why some patients develop Modic changes while others do not. The study mentions that C. acnes was the predominant bacteria isolated in the IVDs, suggesting that bacterial colonization caused the Modic changes. A limitation of this study is the modest sample size. It also has no randomized control, which can lead to contested results. A weakness I found was that the tissues surrounding the IVDs were not sampled and cultured, so it is unclear if some of the disc samples were contaminated. This study concludes that disc herniation with colonization most likely leads to Modic changes in adjacent vertebrae.

Bacteria and Lower Back Pain

A study by Fritzell et al. (2019) performed a surgical, prospective, observational, comparative, multicenter, and multidisciplinary study to investigate other literature findings that *Cutibacterium acnes* (C. acnes), formerly known as *Propionibacterium acnes,* has been found in painful degenerative intervertebral discs (IVDs), leading to the suggestion of initiating antibiotic therapy in those patients. This study investigated the presence of low-virulence bacteria in IVDs by collecting samples from adult patients with lumbar disc herniation (LDH) and lower back pain (LBP). The lumbar disc herniation groups (LDH) data will be compared to the control group made up of adolescents diagnosed with scoliosis and degenerative disc disease who may or may not have LBP and sciatica. Additionally, Modic signs were assessed and graded preoperatively by magnetic resonance imaging (MRI).

Patient samples were cultured at an independent university laboratory, and bacterial DNA was analyzed at two separate independent university laboratories. Staff at the centers participating were shown a video before surgery that described all protocols and procedures involved. All centers received the same universal video from the research nurse who was present and involved in the initial sample collection surgery at each center. Surgery centers received the research nurse's contact information for if issues or questions arise (Fritzell et al.,2019).

The samples taken by Fritzell et al. (2019) were from the skin, surgical incision, disc, and vertebrae of 40 adult patients suffering from LDH and LBP. There were 23 males and 17 females (median age of 43; IQR 33-49) who underwent spinal surgery. The control group consisted of 20 adolescents with scoliosis (7 males and 13 females with a median age of 17; IQR 15-20) undergoing spinal surgery. The tissue samples were screened for C. acnes and isolates using

16SrRNA based polymerase chain reaction (PCR) screening. All patients received antibiotics just prior to surgical incision.

All samples were collected using sterile procedures and strict protocol, then transported for culture and examination accordingly. Fritzell et al. (2019) found that both groups' skin and subcutaneous tissues cultured several bacteria species. The study found that the tissue from discs and vertebrae almost exclusively grew C. acnes bacterium. 75% (15/20) of the control (scoliosis) group and 65% (26/40) of the LDH group had discs and vertebral tissues cultured negative for C. acnes. 15% (9/60) of participants had all sample tissues culture negative. Of those who cultured negative, 15% (6/40) were from the LDH group, and 15% (3/20) were from the control (scoliosis) group. 72% (29/40) of the LDH group and 70% (14/20) of the scoliosis group had positive cultures of C. acnes. Of those who cultured positive, 43% (13/ 29) of the LDH group and 29% (4/14) of the control (scoliosis) group had C. acnes present in the disc and vertebral tissues (p. 2983-2984).

MRI analysis of the LDH group was at the surgical level of disc herniation. The control group’s MRI analysis was at the surgical biopsy level. Fritzell et al. (2019) found that the LDH group exhibited Modic changes in 58% (23/40) of patients. 10% (2/ 20) of the control group’s participants did not have an MRI before surgery. Among those in the control group who did receive a pre-surgical MRI, only 6% (1/ 18) had Modic changes. The control group’s one participant with Modic changes had their disc and vertebral tissues cultured negative for bacteria. Modic changes were not present in any patients with a positive C. acnes culture of their disc or vertebral tissues.

Deoxyribonucleic acid (DNA) analysis found that 98% of the disc and vertebral samples of participants were negative for bacteria presence. One sample from the LDH group had a

positive bacterial culture and 16SrRNA PCR for C. acnes (Fritzell et al., 2019). No tissue samples from the control group had a positive 16SrRNA PCR for C. acnes. The bacteria *Cutibacterium acnes,* formerly known as *Propionibacterium acnes*, is a normal flora of the skin and could cause contamination of tissue samples during surgery. Tissue sample contamination is a possibility because the control group had samples culture a similar amount of C. acnes, and almost all had no preoperative Modic changes. The protocols used for collecting samples and analyzing them were strict and uniform, which reduces the chance of contamination, false positives, and false negatives. Nevertheless, there are many variables to consider since multiple centers and multiple staff were involved in collecting samples (Fritzell et al., 2019).

This study suggests that contamination plays a role in positive disc and vertebral C. acnes cultures due to PCR being negative in almost all samples collected. The study potentially limited themselves by using universal non-C. acnes specific PCR for analysis, which may lack the sensitivity and specificity required to detect C. acnes strains. Fritzell et al. (2019) wanted a broad PCR to detect all the potential bacteria present. This study has several strengths, including a control group of adolescents. This allows a benchmark to be established for analysis and creates an understanding between the groups. The study was unique because a minority of disc and vertebral samples were positive for C. acnes. Because of antibiotic resistance, there should be clear evidence of infection before considering the use of antibiotic therapy in LDH/ LBP patients (Fritzell et al., 2019).

Annular Tears and The Presence of Cutibacterium Acnes

A relationship between lumbar intervertebral disc herniation and their colonization by *Propionibacterium acnes,* which is now called *Cutibacterium acnes* (C. acnes), was investigated by Zhou et al. (2015). Of interest were the effects of disc colonization by C. acnes on adjacent

vertebrae. The study looked for a link between annular tears (fissures) caused by disc herniation and IVD infection by *Cutibacterium acnes* (C. acnes). The internal environment of IVDs are avascular, anaerobic, and considered perfect for C. acnes replication and survival. Because C. acnes is an opportunistic infection and IVDs are avascular. It is believed to gain access to IVDs through angiogenesis initiation due to a ruptured nucleus pulposus caused by an annular tear.

Forty-six people were selected to participate in this study (Zhou et al., 2015). Twenty-five being male and 21 being female (mean age 54.7; range 22-75). Those who participated endured 2-6 months of lower back pain (LBP) or sciatica after lumbar disc herniation, with little to no improvement from conservative treatments. Those who took antibiotics within one month of surgery were dismissed. Baseline images looked for disc herniation, Modic signs, spinal stenosis, tumors, infections, spinal lesions, arthritis, spondylolisthesis, scoliosis, and lumbar disc height (Zhou et al., 2015). The stringent antiseptic protocols used by Yuan et al. (2017) discussed on page 14 of this study were used. Discs included in the study were inspected for annular tears before their removal. Specimens of the annulus, nucleus, and muscle were immediately prepared for culture. Samples were cultured using the same method as Yuan et al. (2017) minus the blood agar.

Values that are of statistical significance are $p = < 0.05$. One way ANOVA was used for mean values of continuous variables and variables abnormally distributed used the Kruskal-Wallis test (Zhou et al., 2015). The Fisher exact and Chi-Square tests were utilized for categorical variables. Zhou et al. (2015) found a significant ($p=0.038$) association between those experiencing sciatica and those who do not. 60.9% of those experiencing sciatica had an annular tear. A significant value ($p=0.038$) was found between the mean age and standard deviation of

those with an annular tear (50.6, SD15.8 years) and those without an annular tear (61.0, SD 5.59 years). Patients with confirmed annular tears had a higher incidence of sciatica.

MRI revealed that 45.6% (21/46) of patients had signs of Modic changes in their lumbar spine (Zhou et al., 2015). Almost all males, 96% (27/ 28), with disc herniation had an annular tear. In comparison, only 50% of females with disc herniation experienced an annular tear. A significant finding (p=0.01) was that 85% (39/ 46) of all participants had an annular tear after disc herniation. Most participants showed no C. acnes in the muscle surrounding IVDs, which reduces the potential for contamination.

Zhou et al. (2015) excluded three patients whose surrounding tissues were infected with C. acnes. They were dismissed because *Cutibacterium acnes* does not grow well in an environment rich with blood/ oxygen, like a muscle. So, if a muscle contains C. acnes, it is considered contamination because the environment is not anaerobic. A total of 43 patients did not have C. acnes in their surrounding muscles. Of those, 21% (9/ 43) had C. acnes present in their IVDs, and *Cutibacterium acnes* was present in 33.3% (9/ 27) of those with annular tears. All participants IVDs without an annular tear were negative for C. acnes.

A limitation of this study by Zhou et al. (2015) was that although a strong correlation between annular tears and C. acnes colonization is present according to 16SrDNA PCR specific C. acnes identification. However, there was no follow-up histological examination and identification, which is considered the gold standard. The study did provide useful insight into how C. acnes potentially gains access to IVDs after disc herniation. Lastly, the study suggests that C. acnes is not a contaminant of herniated discs with annular tears, but original growth.

Microbiologic Identification Using Histologic Examination

There is controversy with studies that link *Cutibacterium acnes* (C. acnes) with intervertebral disc (IVD) disease. According to Yuan et al. (2017), this is due to a lack of histological evidence, which is the gold standard for microbial detection and identification. Yuan et al. (2017) wanted to confirm C. acnes presence in non-pyrogenic IVDs by utilizing histological observation. Therefore, proving C. acnes colonization of IVDs is an infectious process versus contamination.

The methodology used was to harvest intervertebral discs from 76 patients over two years (Yuan et al., 2017). Patients included in the study had lumbar disc degeneration that caused lower back pain or sciatica. The patients selected had attempted conservative treatment but ultimately required spinal surgery. All patients showed no signs or symptoms of discitis and underwent discectomy at a single level with and without lumbar fusion. Surgeons used a standard posterior approach to harvest IVDs. The study excluded patients who had taken antibiotics within one month of surgery. The average age of participants was 55.30, with 39 being male and 37 being female.

Yuan et al. (2017) implemented strict protocols for disc collection to prevent contamination. The participant's skin at the site of incision was sterilized three times using povidone-iodine. 3M Ioban-2 antimicrobial incise drape was adhered to the surgical field to prevent potential bacterial contamination from the dermis or sub-dermis. After the surgical incision, sterile water was used to irrigate the wound two times before the discectomy. Tissue samples were taken from around the IVD to act as markers for surgical contamination. All specimens were handled with new sterilized instruments.

Specimens harvested by Yuan et al. (2017) were placed in tryptone soy broth (TSB) enriched with 10% bovine serum. The enriched TSB samples were then incubated in an anaerobic atmosphere consisting of 80% N2, 10% CO2, and 10% H2 at 98.6° for 14 days. The same medium was incubated without tissue to serve as a blank control to monitor for contamination during culturing. All cultures examined used polymerase chain reaction (PCR) to enhance the 16SrDNA gene to verify C. acnes presence. After PCR testing, cultures positive for C. acnes were then placed onto Columbia blood agar plates and incubated in the same anaerobic conditions previously stated for 48 hours. Then, one colony was selected and placed on another Columbia blood agar plate and cultured for 24 hours to increase bacterial isolation and purification. After culturing, a single colony was chosen and fixed to a slide for Gram staining. Disc samples that were culture positive were fixed and mounted to slides for a histological exam (HE), modified Brown-Breen staining, and Gram staining. Histological examination is more specific than PCR and is considered the gold standard.

The results of this study by Yuan et al. (2017) showed that 26.32% (20/ 76) of IVDs cultured were PCR positive for C. acnes. 20% (4/ 20) of samples that were culture and PCR positive were considered contaminated due to the surrounding tissue being positive for C. acnes. 21.05% (16/ 20) of discs that were culture and PCR positive for C. acnes had surrounding tissue culture and PCR test negative for bacteria. 3.95% (3/ 76) of samples cultured had PCR tests positive for bacteria that were not C. acnes. Furthermore, 69.74% (53/ 76) of participants samples (disc and surrounding tissue) were negative for bacteria. *Cutibacterium acnes* was original growth in 21.05% (16/ 20) of participant's disc samples. Fifteen of those samples were investigated further. To note, one of the 16 patients with positive a C. acnes PCR did not have enough tissue for histological examination.

Out of the 15 samples that were investigated further, 46% (7/ 15), with an overall total of 9.21% (7/ 76) of all samples, had visible C. acnes bacteria after the histological examination (HE) and modified Brown-Brenn staining (Yuan et al., 2017). Seven disc samples were unquestionably original growth. This is because the bacteria were within the tissue samples and growing in clusters, indicating original growth versus bacteria growing on the surface of a sample, which indicates contamination. The surrounding tissues of the seven disc samples found to be original growth tested negative for bacteria. For a control, Yuan et al. randomly selected 15 disc samples with a negative PCR to undergo the gold standard of microbe identification, which is HE and modified Brown-Brenn staining. Of the randomly selected samples, no bacteria were found after HE and modified Brown-Brenn staining. All 15 patients that Yuan et al. identified as positive for C. acnes were diagnosed with non-pyrogenic degenerated intervertebral discs.

This study was the first to utilize histological examination (HE), which Yuan et al. (2017) used to identify C. acnes in IVDs. This study achieved its goal and provided high-quality evidence of original C. acnes colonization of IVDs. A connection between non-pyogenic degenerative IVDs and latent C. acnes infection was identified in this study. Yuan et al. concluded that C. acnes was present in 21% of participant's IVD and was considered original growth. This allowed for the diagnosis of non-pyrogenic degenerated IVDs in the15 participants who had no discitis symptoms but had positive C. acnes presence in IVDs. The studies limitations were its small sample size, and it did not identify the other bacteria that were found.

Modic Changes and Lower Back Pain

A systemic literature review by Herlin et al. (2018) looked at Modic changes, their association with lower back pain (LBP), and individuals' ability to perform activities. The review

utilized MEDLINE, CINAHL, and EMBASE to search for all relevant studies for review. Herlin et al. used:

> Prospective or retrospective cross-sectional cohort studies and case-control studies, including people of all ages from general, working, and clinical study populations were eligible for inclusion. Risk of bias assessment and data extraction for associations and potential modifiers were completed independently by pairs of reviewers. Meta-analysis was performed for homogeneous studies and presented as odds ratios (OR) with 95% CI. (Herlin et al., 2018, para. 2)

Studies excluded in this systemic review by Herlin et al. contained 25 people or less. Herlin et al. (2018) measured the intensity of LBP and the level of activity limitation using the Oswestry Disability Index (ODI) and the Roland Morris Disability Questionnaire (RMDQ). A librarian aided in the systemic search strategy (para. 10). The risk bias assessment tool used was QUADAS-2. The statistical analysis, synthesis, and overall risk of bias used Fischer's exact test. Continuous outcomes could be considered statistically significant ($p=<0.05$) along with dichotomous outcomes ($\neq 1.0$).

The initial search by Herlin et al. (2018) returned 5210 records, which he narrowed down to 31 research articles in which 97% (30/ 31) compared Modic changes and lower back pain (LBP). Of those, 50% found a significant association (1.53 (95% CI 1.02–2.29) to 83.10 (95% CI 4.85–1424.05)) between Modic changes and LBP. One study found a negative association between Modic changes and LBP. And 14 were determined insignificant in their findings by Herlin et al. A statistically significant difference ($p=<0.01$) was discovered in studies using continuous or dichotomous outcomes. Those utilizing dichotomous outcomes all found positive

associations. In contrast, studies that did not use dichotomous outcomes only yielded half of the positive associations.

The systemic review concluded that there is no association between Modic changes and lower back pain due to inconsistent outcomes between studies. A limitation was that the searched material was broad and not restricted, potentially skewing the results. It is also unclear if the studies used in this systemic review contained bias. A strength of this review is that it contained three times as many studies as previous systemic reviews. A strength was the inclusion of a wide variety of literature, almost three times as much as previous reviews.

Discopathy an Infectious Process

A monocenter study by Ahmed-Yahia et al. (2019) explored if disc degeneration associated with Modic changes is an infectious process caused by a slow-growing low-virulence bacteria. The study looked to establish an association between intervertebral disc (IVD) colonization by *Cutibacterium acnes* (C. acnes) and chronic lower back pain (CLBP) caused by disc degeneration and Modic changes. Patients for this study were recruited from orthopedic and neurosurgery units. They were required to be 18 years of age or older. Participants selected underwent lumbar spinal surgery by either anterior or posterior approach.

Intervertebral disc samples collected were separated into two groups by Ahmed-Yahia et al. (2019) based on the surgical approach. Group 1 samples were taken by anterior approach. Group 2 was the control (patients with herniated discs), and the samples were taken by posterior approach. All patients included in the study were given one dose of the antibiotic Cefazoline 30 minutes prior to incision. Skin preparation for surgery used alcoholic povidone-iodine. Extensive efforts were taken to prevent contamination of the IVD specimens.

Identification and testing procedures utilized by Ahmed-Yahia et al. (2019) included molecular detection using commercial universal 16SrRNA polymerase chain reaction (PCR) sequencing assay and microbial media cultures utilizing chocolate agar and Schaedler broth. Highly sensitive C. acnes specific PCR were used to test specimens. The media cultures used for microbial growth included two chocolate agar cultures incubated in different conditions. One chocolate agar plate was incubated for five days and the other for ten days in an anaerobic atmosphere of 5% CO2. Once a specimen reached its incubation time and clouded, then a subculture was taken. To analyze bacteria, Matrix-Assisted Laser Desorption Ionization-Time-of-Flight Mass Spectrometry was used in collaboration with 16SrRNA sequencing to identify microbes present in the agar.

Ahmed-Yahia et al. (2019) collected 77 disc samples from 45 patients. Group 1 (n=26, anterior approach) consisted of 58 disc samples, in which 32 showed Modic changes in the adjacent vertebra and 26 without changes. Group 2 (n=19, control, posterior approach) had 19 disc samples collected with no mention if Modic changes were present or not. Seventy-seven samples were cultured, with 15.6% (12/77; Cl95% 9.0-25.4%) being bacteria positive, in which 13% (10/77) of the positives were C. acnes, with 1.3% (1/77) being *Staphylococcus epidermidis* and 1.3% (1/77) being *Cutibacterium avidum.* The 16SrRNA molecular biology test and the C. acnes specific PCR results did not yield the same results as the bacterial cultures. The 16srRNA test was bacteria positive in 7.8% (6/77) of the samples in which 5.2% (4/77) were *Staphylococcus sp*, 1.3% (1/77) were C. acnes, and 1.3% (1/77) were *Streptococcus sp*. The C. acnes specific PCR was positive in only one sample that was obtained posteriorly. Microbial culture and molecular detection were negative in 75.3% (58/77) of disc samples tested (Ahmed-Yahia et al., 2019).

When comparing the groups' results, a p= <0.05 is considered significant by Ahmed-Yahia et al. (2019). The specimens collected via anterior approach (Group 1) had a positive culture rate of 12.1% (7/58) in which 8.6% (5/58) were C. acnes. Specimens collected by posterior approach (Group 2; Disc herniation) had a 26.3% (5/19) positive culture rate, and all had C. acnes present. Positive C. acnes specific PCR tests between anterior and posterior approaches were (p=0.253) not significant. However, positive C. acnes cultures between the anterior and posterior approaches (p=0.046) were significant. The p-value shows that the posterior approach had significantly more positive C. acnes cultures than the anterior approach. The 16SrRNA PCR detected bacteria in six anterior samples with all posterior samples being negative (p=0.327), which was not significant. The C. acnes specific PCR was negative on all anterior samples and had one positive posterior sample (p=0.253), which was also not significant.

This study found that the posterior approach has significantly more positive C. acnes cultures than the anterior approach. Ahmed-Yahia et al. (2019) believes that it is likely due to contamination since the C. acnes specific PCR only found one positive sample, which was taken by the posterior approach (Group 2). Ahmed-Yahia et al. (2019) concluded that a low-virulence C. acnes infection is most likely due to contamination, and it does not appear to be related to Modic changes. This studies limitation is that it does not state if Group 2 (disc herniation group) had Modic changes. This is a limitation because several other studies suggest that disc herniation leads to C. acnes disc colonization, which leads to chronic lower back pain with Modic changes. A weakness of this study is that the underlying data set is not publicly available. A strength is that Ahmed-Yahia et al. (2019) received no specific funding and declared no competing interests exist, limiting bias.

Original Growth and Latent Infection

Few studies have replicated the results of Stirling et al. (2001), which found that out of 36 patients with severe sciatica, 58% of their intervertebral disc (IVD) samples were positive for *Propionibacterium acnes,* which is now called *Cutibacterium acnes* (C. acnes). Tang et al. (2018) created this study to analyzes intervertebral disc biopsies obtained from patients undergoing disc herniation surgery. They looked for low-virulence bacteria and investigated its association with Modic changes. Close to 70% of previous studies concluded that non-specific lower back pain (LBP) is associated with vertebral bone edema (Tang et al., 2018).

The methodology of Tang et al. (2018) was to take 80 consecutive patients that required discectomy due to lumbar disc herniation and collect IVD specimens to look for bacterial colonization. The study was comprised of 35 male and 45 female participants (mean age 51; SD 14.9 years). All participants had no history of spinal or abdominal surgery and have not received any joint injections. Disc samples were collected from the lumbar region of participants; Ten specimens from L3-L4, 41specimens from L4-L5, and 29 specimens from L5-S1. All participants in the study suffered from severe sciatica with or without lower back pain and exhibited no signs or symptoms of infection. Participants were required to abstain from taking antibiotics for at least one month prior to surgery.

The Pfirrmann system was utilized by Tang et al. (2018) to determine the severity of discopathy. Magnetic resonance imaging (MRI) was used to determine if Modic changes were present. All participants received a prophylactic intravenous dose of the antibiotic Cefazolin while undergoing anesthesia. Strict protocols were followed to prepare, remove, handle, store, transport, and cultivate all participants' tissue samples (Tang et al., 2018).

Samples harvested by Tang et al. (2018) were dissected into five segments using sterile tools. One segment was cultured using MacConkey agar aerobically incubated at 98.6° for 7 and 14 days. The second segment was cultured in chocolate agar incubated at 98.6° with an atmosphere consisting of 5% carbon dioxide for 7 and 14 days. The third segment was placed in horse blood agar and anaerobically incubated at 98.6°for 7 and 14 days. Lastly, the final two segments were placed in a cooked meat broth and incubated at 98.6° for 48 hours than seven days, before being sub-cultured. The first sub-culture was after 48 hours of incubation. Samples were removed from the broth, then placed in blood agar to be anaerobically incubated at 98.6°or into chocolate agar to be incubated at 98.6° with an atmosphere of 5% CO2 for seven days. The decision to choose blood agar versus chocolate agar was random. Bacterial growth was identified using 16Srdeoxyribonucleic acid (DNA) polymerase chain reaction (PCR). The results were then analyzed and referenced with known genes.

To interpret the statistics for categorical and variable comparison, Chi-square and Fisher's exact test was used (Tang et al., 2018). A two-sided Student's t-test was used to analyze the differences between the two groups. P values of $p=<0.05$ were considered significant in this study. Bacteria positive cultures occurred in 32.5% (26/ 80) of IVD samples. However, three cultures were believed to be contaminated during biopsy due to bacteria growth on the outer discs and other surrounding tissue surfaces. Due to contamination, only 28.7% (23/ 80) of IVD samples were considered bacteria positive. *Cutibacterium acnes* (C. acnes) bacteria were found in 26.25% (21/80) of IVD samples, and coagulase-negative *Staphylococcus* was present in 6.25% (5/80) of samples. A significant association ($p= 0.03$) was found when comparing bacteria positive and negative samples. Participants with bacteria positive IVD samples were much younger than those who had negative samples.

Tang et al. (2018) found no significant difference (p=0.162) between the severity of discopathy and bacteria presence. A significant value (p= <0.001) was found, showing an association between Modic changes and the presence of bacteria in IVDs. The MRI found Modic changes in 31.2% (25/ 80) of the adjacent vertebrae to the participant's herniated discs.

This study by Tang et al. (2018) suggests that low-virulence bacteria could be original growth and not from contamination. 28.7% (23/ 80) of herniated IVDs were colonized by low-virulence bacteria leading to a latent infection and Modic changes of adjacent vertebrae of the infected disc. Of the discs positive for bacteria, 26.25% (21/ 80) were identified as C. acnes. A strength of this study is it suggests that low virulence bacteria is an original growth and not from contamination. The data provided by this study adds to the thought that there is a link between Modic changes and latent infection of IVDs. This leads one to believe that antibiotic treatment may be beneficial in this patient population. The studies limitation is that there is no explanation of whether one agar was being disproportionately used more than the other when sub-culturing and not knowing if it skewed the results.

Pathogenic Features of Cutibacterium Acnes

Propionibacterium acnes (P. acnes) name was changed to *Cutibacterium acnes* (C. acnes) because the *Cutibacterium* species creates an advantage for itself by mutating via positive selection, and this is what differentiates it from the *Propionibacterium* species (Chen et al., 2016). *Cutibacterium acnes* is part of normal human flora. “It is a bacterium that is microaerophilic, anaerobic, aerotolerant gram-positive bacilli present on the skin, conjunctiva, intestinal tract, external ear canal, and oral cavity” (Chen et al., 2016, p. 1291).

Researchers, including Chen et al. (2016), found that C. acnes, like many other normal flora on the human body, they have the potential to become a pathogens that can cause an

endogenous infection if the opportunity arises. *Cutibacterium acnes* can cause "a series of complications that include infections of the bones, joints, central nervous system (CNS), and implanted devices along with prostatitis, synovitis, acne, pustulosis, hyperostosis, and osteitis, known as SAPHO syndrome" (Chen et al., 2016, p. 1291).

Cutibacterium acnes is the number one isolated anaerobic organism in bone and joint infections, number two in shoulder infections, and number three in prosthetic joint infections, according to Chen et al. (2016). A strong association between C. acnes and vertebral osteomyelitis, non-pyrogenic discitis, and spondylodiscitis has been long established. *Cutibacterium acnes* colonization of the intervertebral discs (IVDs) in individuals with discitis symptoms is not surprising, but how the bacteria got there is unknown. It is unclear how pathological changes like disc degeneration and bone edema (Modic changes) occur in this study.

One theory proposed by Chen et al. (2016) on how *Cutibacterium acnes* invades IVDs is through the bloodstream from the oral cavity or broken skin. It reaches IVDs via the circulatory system (Chen et al., 2016). *Cutibacterium acnes* is rarely detectable in blood during the infectious process because it has a hard time reproducing and surviving in the aerobic conditions of blood and muscle. IVDs are sealed and not vascularized. A healthy IVD does not provide a suitable home for C. acnes due to the annulus fibrosus outer barrier. Chen et al. (2016) hypothesized that once disc herniation occurs, the annulus fibrosus structure is compromised. Neovascularization will begin to help heal the disc fissure that occurred due to herniation. However, neovascularization also provides a pathway for C. acnes to gain access to and invade the anaerobic environment of both the annulus fibrosus and nucleus pulposus. The environment is ideal for C. acnes to reproduce and thrive, giving rise to a low-virulent latent infection.

Herniated discs have a higher positive C. acnes rate than non-herniated discs. Chen et al. (2016) describes that C. acnes can also gain access to IVDs by invasive spinal procedures like steroid injections or surgery. *Cutibacterium acnes* activates the innate immune system, imitates it, and perpetuates chronic inflammation. Once in an IVD, C. acnes stimulates the immune system to release inflammatory cytokines causing damage to vertebral endplates leading to chronic lower back pain and Modic changes.

The literature review provides readers with information about C. acnes pathogenic features. It argues that C. acnes is an original growth and not from contamination. It describes C. acnes characteristics, including the environment requirements in which it thrives and what is nondutiable. A limitation is Chen et al. (2016) describing a plausible situation in how C. acnes gains access to an anaerobic area like an IVD, since it is not fact. A strength is that this study only provides statistical data about the microbiologic features.

Back Pain and Antibiotic Efficacy

A pilot study by Albert, Manniche, Sorensen, & Deleuran (2007) aimed to see if antibiotic treatment would be beneficial in patients with a lumbar disc herniation that is causing lower back pain (LBP) with Modic (bone edema) changes. The participants in this study already participated in a larger (n=166) randomized control trial (RCT) that was investigating the treatment outcomes of active versus conservative therapy for lumbar disc herniation. Fourteen months into the RCT study, those who had Modic changes and LBP (n=37) were asked by Albert et al. (2007) to participate in this pilot study. Five participants did not meet inclusion criteria and were dismissed from the trial because three did not want to take antibiotics for such an extended time, one spontaneously recovered before the study started, and one could not be located. Of the

32 remaining participants, 29 were able to complete the pilot study, and three left due to severe diarrhea caused by the antibiotic used.

The study by Sterling et al. (2001) was presented to "three independent experts in infectious disease" (Albert et al., 2007, para. 7). Each expert suggested the use of Amoxicillin-clavulanate for 90 days since that is the post-operative treatment for discitis. Participants were given Amoxicillin-clavulanate (500mg/ 125mg) three times daily at eight-hour intervals for 90 days. They were not allowed to receive any other treatments besides mild analgesics if needed. Participants were required to fill out a questionnaire and undergo clinical examination at baseline, end of treatment, and the 1-year follow-up.

Albert et al. (2007) used Global perceived effect, Roland Morris Questionnaire (RMQ), Self-Perceived Function Scale, days with LBP, and LBP Rating Scale to measure outcomes (para. 9). The statistical tests used to compare baseline, end of treatment, and 1-year follow-up were Wilcoxon signed-rank test ($p=<0.5$) with SPSS version 13.0. The participants ($n=29$) were 34% (10/ 29) female (mean age 45.7; SD of 11.1 years) and 66% (19/ 29) male (mean 47.7; SD of 8.2 years).

The outcome measures used by Albert et al. (2007) included disease-specific function, patient-specific function, global perceived health, and LBP Rating, which all showed statistically significant improvement at the end of treatment and the 1-year follow-up. After completion of treatment, no patients reported worsening of symptoms. The Global-Perceived Health Measure found that 52% (15/ 29) of participants reported being cured or having significant improvement, 24% (7/ 29) reported a moderate improvement, and 24% (7/ 29) reported no change.

The Roland Morris Questionnaire (RMQ) was used by Albert et al. (2007) to measure patient improvement in disease-specific function. A RMQ reduction of greater than >30%

(improvement) of baseline or an increase greater than >30% (worsening) of their baseline score was considered significant. 62% (18/ 29) of participants reported >30% reduction at the end of treatment and 1-year follow-up. Only 3.5% (1/ 29) at the end of treatment and 7% (2/ 29) of patients at the 1-year follow-up reported clinical worsening on RMQ. This is significant because an average RMQ score reduction of 30% of baseline would be 2.6 RMQ points. The participants managed a significant reduction of 3.1 RMQ points. This improvement is clinically meaningful because before being given antibiotics, participant's RMQ scores were increasing while waiting for the study to begin. Starting RMQ scores ranged from 5.3 to 8.9 while waiting for the trial to begin, which was an average of nine months. After antibiotic treatment, the mean RMQ score was 5.5 and 5.8 at a 1-year follow-up (mean 10.8 months). All outcome measures showed clinically and statistically significant improvements ($p=0.001$).

Albert et al. (2007) found that almost all participants had improvement in all outcome measures after antibiotic therapy. The results strongly suggest that bacteria play a role in lower back pain with Modic changes due to drastic improvements in all participant's outcome measures. A limitation of this study was that the lab changed their methods for some tests during the study, so some results could not be used because they were tested differently. Another limitation was they did not take biopsies of discs to confirm if bacteria were present or not. The studies strength was that the patients chosen were from a 14-month follow-up RCT study and not from those seeking medical attention for their LBP. Another strength is that patient conditions worsened according to global perceived health measures and improved with antibiotics therapy, suggesting that LBP in this population could be cured with this treatment. This means that it is not likely that the patients recovered spontaneously. Amoxicillin-clavulanate has a minimal anti-inflammatory effect on the body, which is why it was chosen. A weakness is that the association

between low virulence bacteria and Modic changes is not made clear even though it is believed that the bacteria are causing the Modic changes. This study is only a pilot study, but it shows that antibiotics can potentially reduce lower back pain in specific patient populations. This study was approved for a double-blind randomized control trial to see if the results can be duplicated.

Antibiotic Therapy Efficacy Continued

Albert et al. (2013b) found that Modic changes have been associated with lower back pain (LBP) and are present in 46% of the patient population with non-specific LBP versus 6% of the general population. This studies design tests the efficacy of Modic antibiotic spine therapy (MAST) in patients with Modic changes that have previously herniated discs causing chronic lower back pain (CLBP).

This studies inclusion criteria were patients between 18 and 65 with an MRI showing disc herniation between L3 to S1 that occurred within 6-24 months and lead to lower back pain for greater than six months (Albert et al., 2013b). The study included both patients with and without sciatica and neuropathic pain. Both conservative and surgically treated patients were considered. A second MRI was taken of those included in the study. It was interpreted by a radiologist who specializes in grading Modic changes. The radiologist had a perfect kappa score of 1.0 for intra-tester reliability and a near-perfect kappa score of 0.93 for inter-tester reliability (Albert et al., 2013b).

The double-blind random control trial (RCT) conducted by Albert et al. (2013b) included 162 participants. The computer-generated randomized list of the patients was kept at the pharmacy until participants had their 1-year follow-up. The placebo and antibiotic were both packaged in a white box that only had the number that was assigned to each participant. All

patients were asked not to receive any other treatments during the study through and through the 1-year follow-up. The outcome measures used by Albert et al. (2013b):

> Were disease-specific disability Roland Morris Questionnaire (RMDQ) and lumbar pain (LBP Rating Scale). A clinically important change was defined as a 30 % reduction of the individual's baseline score and 2 LBP rating scale points. Secondary outcome measures were global perceived effect, leg pain, hours with LBP during the last 4 weeks, EQ-5D Thermometer, days with sick leave, bothersomeness, constant pain, MRI Modic grading, serum analysis, four test at the physical examination. (Albert et al., 2013b, para. 15)

Amoxicillin-clavulanate (500mg/ 125mg) tablets were given three times daily at 8-hour intervals for 100 days. Albert et al. (2013b) chose the strength and delivery method because it is the treatment of choice for post-operative discitis. The participants were divided into four groups. Group A (n=45) and C (n=45) both received the antibiotic. Group A received one tablet, while group C received two. Group B (n=36) and D (n=36) received a placebo, with group B receiving one tablet and group D receiving two tablets. No other treatments were provided to participants besides mild analgesics during their participation in the trial.

During the study period, the antibiotic group had 13 participants drop out (4-side effects, 3-new disc herniation, 1-did not follow up, 1-had more advanced Modic changes, 2-new cancer diagnoses, and 2-became too old for the parameters set) for various reasons (Albert et al., 2013b). The placebo group had five participants drop out (3-new disc herniation and two did not follow-up). Baseline variables were equally distributed among the placebo and antibiotic groups.

Albert et al. (2013b) found that those who took antibiotics improved on all outcome measures. $P=<0.05$ was considered significant in this study. Both the placebo and the antibiotic

groups reported lower back pain at baseline at the study initiation (100% of participants). At the 1-year follow-up, the antibiotic group had 67.5% of participants still having lower back pain versus 94.0% of the placebo group, which was significant (p=0.0001). All patients (100%) in the placebo group had pain during active flexion of the lumbar spine at baseline versus 96.1% of the antibiotic group. At the 1-year follow-up, 83.6% of the placebo group continued to have the pain, while only 49.4% of the antibiotic group (p=0.0001), which is significant. At baseline, 75.3% of the antibiotic group and 73.1% of the placebo group reported constant LBP. At the 1-year follow-up, 19.5% of the antibiotic group and 67.2% of the placebo group reported constant LBP (p=0.0001), which is significant.

The disease-specific disability RMDQ median employed by Albert et al. (2013b) for the antibiotic group was 15.0 (min-11; max-18) at baseline, 11.5 (min-7; max-14) at 100 days and 7.0 (min-4; max-11) at the 1-year follow up. The placebo group was 15.0 (min-12; max-18) at baseline, 14.0 (min-11; max-18) at 100 days and 14.0 (min-8; max-18) at the 1-year follow up. Albert et al. (2013b) found significant improvement in the antibiotic group (p=0.0001). Both groups rated their back pain from 0-10, with 10 being excruciating and 0 being no pain. The antibiotic group had a median rating of 6.7 (min-5.3; max-7.7) at baseline, 5.0 (min-2.7; max-6.7) at 100 days, and 3.7 (min-1.3; max-5.8) at the 1-year follow up. The placebo group had a median rating of 6.3 (min-4.7; max-8) at baseline, 6.3 (min-3.7; max-7.7) at 100 days and 6.3 (min-4; max-7.7) at the 1-year follow up which showed a significant (p=0.0001) value. The median number of hours with back pain reported by the antibiotic group was 448 (min-364; max-448) at baseline, 180 (min-16; max-136) at 100 days, and 64 (min-4; max-280) at the 1-year follow up. The placebo group's median for hours with back pain was 448 (min-392; max-448) at

baseline, 200 (min-28; max-392) at 100 days, and 448 (min-224; max-448) at the 1-year follow up (p=0.0001) which is significant.

This was the first double-blind randomized control trial experimenting with antibiotic therapy for chronic lower back pain and Modic changes after disc herniation. It is thought that disc herniation leads to bacterial colonization of IVDs. The results of this study are impressive. All participants who received the antibiotic had improvement in all primary and secondary outcome measures established by Albert et al. (2013b) versus those in the placebo group. This provides data that antibiotic efficacy in this patient subgroup may be efficacious. A limitation of this study was having 18 people drop out for various reasons.

Discussion

The preliminary data provided by Albert et al. (2007 & 2013b) suggests that those with a recent lumbar disc herniation who are suffering from lower back pain for more than six months may benefit from antibiotic therapy. Taking Amoxicillin- Clavulanate for 3-months has shown to improve all outcome measures of participants compared to placebo. Even at the 1-year follow-up, those who received antibiotics continue to do significantly better than those in the placebo group.

The conclusion above is promising, but antibiotic stewardship must be considered. Many studies, when combined with their data show roughly that 1/3 of those with lower lumbar disc herniation have a low virulence infection of their intervertebral discs that can be associated with chronic lower back pain and Modic changes (Ahmed-Yahia et al., 2019; Albert et al., 2013b; Albert et al., 2007; Albert et al., 2013a; Chen et al., 2016); Tang et al., 2018; Zhou et al., 2015). Another association was found between Modic changes and lower back pain, but it may not be as significant as the association between Modic changes and intervertebral disc infection, but there

are varying thoughts. Herlin et al. (2018) found that 50% of studies showed a significant association between Modic changes and lower back pain but concluded that there was not enough evidence to confirm the association (para. 3.4).

Another study by Fritzell et al. (2019) concluded that no relationship between Modic changes and bacterial presence in IVDs exist. We initially thought this study would make the argument for an association due to 58% (23/ 40) of the participants with lumbar disc herniation and 6% (1/ 18) of the control group had Modic changes to either one or both sides of the adjacent vertebrae at the herniation level on MRI. Surprisingly only one participant from each group had IVDs positive for C. acnes colonization. Unfortunately, they used a universal bacterial PCR and not a C. acnes specific PCR, which lowered the sensitivity for detecting C. acnes (Fritzell et al. (2019, p. 2985-2986).

C. acnes is a unique normal flora that can infect bones, joints, central nervous system, etc. Chen et al. (2016) describes a strong relationship between C. acnes and vertebral osteomyelitis, non-pyrogenic discitis, and spondylodiscitis. Currently, only theories are available to explain how *Cutibacterium acnes* can travel to and colonize intervertebral discs. IVDs have no blood supply, so it would be hard for C. acnes to reach them. The theories presented by Chen et al. are plausible because of the traumatic nature of disc herniation (p. 1295). If a pathway of infection can be verified, we believe that would be significant because C. acnes would be unquestionably original growth instead of contamination. Fortunately, we found a study that explains the trauma associated with disc herniation. Disc herniation compromises disc integrity, and annular tears expose IVDs anaerobic environment allowing C. acnes access via angiogenesis (Zhou et al., 2015; Chen et al., 2016).

Disc herniation appears to be the one of the key terms used by Ahmed-Yahia et al. (2019), Albert et al. (2013b), Albert et al. (2007), Albert et al. (2013a), Chen et al. (2016), Tang et al. (2018) and Zhou et al. (2015) to show an association between C. acnes colonization of IVDs and lower back pain. After herniation, the nucleus pulposus of lumbar IVDs were colonized by anaerobic bacteria in many of the patients suffering from CLB with Modic changes (Ahmed-Yahia et al., 2019; Albert et al., 2013b; Albert et al., 2007; Albert et al., 2013a; Chen et al., 2016); Tang et al., 2018; Zhou et al., 2015). The anaerobic bacteria found were *Cutibacterium acnes* more often than not (Ahmed-Yahia et al., 2019; Albert et al., 2013b; Albert et al., 2007; Albert et al., 2013a; Chen et al., 2016; Tang et al., 2018; Zhou et al., 2015). According to Albert et al. (2013a), new Modic changes can be related to disc infection by C. acnes (para. 19).

The study by Ahmed-Yahia et al. (2019) disagreed with previous studies and found no difference between those with Modic changes and those without who had positive C. acnes cultures. The study appeared to be looking at different parameters than the others because it was focused on the surgery approach and contamination (p. 2499-2500). The study by Ahmed-Yahia et al. (2019) also used participants with disc herniation as a control group, even though many other studies link disc herniation to C. acnes colonization and LBP with Modic changes (Albert et al., 2013b; Albert et al., 2007; Albert et al., 2013a; Chen et al., 2016; Tang et al., 2018; Zhou et al., 2015). Additionally, Albert et al. (2013a), Chen et al. (2016), Sterling et al. (2001), Tang et al. (2018), Yuan et al. (2017), and Zhou et al. (2015) all believe that C. acnes presence in IVDs is original growth and not from contamination. The original growth is thought to be responsible for Modic changes.

The most substantial evidence we found suggesting that lower back pain is the result of disc herniation leading to C. acnes colonization of IVDs, a low-virulence infection, and chronic

lower back pain with Modic changes is made by two studies conducted by Albert et al. (2007 & 2013b). Based on the initial studies, we believe that antibiotic therapy is efficacious in a select sub-group of patients with chronic lower back pain and Modic changes after disc herniation. Antibiotic therapy has been proven to reduce pain symptoms compared to placebo in this sub-group (Albert et al., 2007 & 2013b). Both studies by Albert et al. (2007 & 2013b) showed that patients with Modic changes and chronic lower back pain improved on all outcome measures, including drastically reducing their pain. We concluded that this improvement is likely because the antibiotic cleared the bacteria from participants IVDs.

We believe additional trials are needed to confirm Albert et al. (2007 & 2013b) results from their studies. With the available data, antibiotic therapy was shown to improved pain symptoms compared to placebo in both studies by Albert et al. (2007a & 2013b). We conclude that additional research is still needed. However, it appears that antibiotic therapy is efficacious in specific patient subgroups suffering from chronic lower back pain with Modic changes after disc herniation.

Applicability to Clinical Practice

The information in this literature review will aid clinicians in making informed decisions on whether to consider antibiotic therapy for patients with chronic lower back pain with Modic changes after disc herniation. Traditional active and conservative therapy should still be the first-line treatment. However, if unsuccessful, antibiotic therapy may be a cost-effective and safer option than narcotics that can potentially improve the lives of those living with chronic lower back pain with Modic changes after disc herniation.

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