Low back pain with vertebral body endplate (Modic) changes:
use of antibiotics

A randomised controlled trial has found an improvement in chronic low back disability and pain in patients with new Modic type I changes following disc herniation who received 100 days’ treatment with co-amoxiclav. However, confirmatory studies are required, particularly in other populations, before any changes are made to UK practice. Healthcare professionals should continue to follow NICE guidance on low back pain.

Overview and current advice

NICE has published a clinical guideline on early management of persistent non-specific low back pain. The full guideline notes low back pain probably affects around one third of the UK adult population each year, of whom about 1 in 5 will consult their GP. Typically, pain and disability improve rapidly during the first month, with little further improvement being observed after 3 months. One year after a first episode of back pain 62% of people still have pain and 16% of those initially unable to work are not working after 1 year. (The NICE guideline was reviewed in July 2013 and will be updated.)

Modic changes are vertebral body endplate changes observed on MRI, classified as type I, II or III. Type I Modic changes indicate bone marrow oedema and inflammation. Infection with anaerobes such as Propionibacterium acnes has been suggested as a cause of Modic type I changes. A systematic review of prevalence studies found that the median prevalence of any Modic change was 6% in the general population and 43% in people with low back pain. However, the prevalence of the particular types of Modic changes in the population with back pain was not reported.

See the NICE Evidence topic page on low back pain and the Clinical Knowledge Summary for a general overview of the condition. The NICE Pathway: low back pain brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.
New evidence

Following encouraging results from a pilot study, Danish researchers investigated the use of antibiotic therapy in a randomised controlled trial (RCT)\(^1\).

The study included people with previous disc herniation (L3/L4, L4/L5 or L5/S1) found on MRI within the preceding 6–24 months, and lower back pain of more than 6 months' duration (score of 6 or more on a lower back pain [LBP] scale of 0–10, with higher score indicating greater pain). Patients were included regardless of previous surgical or non-surgical treatment and the presence or absence of neuropathic pain or sciatica.

Of the 347 patients originally recruited, 51% were excluded because a second MRI at screening identified no new Modic type I changes adjacent to the previously herniated disc, or only Modic type II changes. After other potential participants also dropped out (e.g. because of a planned pregnancy), 162 patients (mean age 45 years, 58% female) entered the study. They were randomised to receive 1 co-amoxiclav tablet (amoxicillin 500 mg/clavulanate 125 mg) 3 times a day, 2 co-amoxiclav tablets 3 times a day, or 1 or 2 placebo tablets 3 times a day for 100 days. Allocation was concealed. The study was stated to be double-blind and it was powered and analysed for the comparison between the pooled antibiotic and pooled placebo groups. The baseline characteristics of the antibiotic and placebo groups were similar, except that more people in the placebo group than the antibiotic group had Modic changes that were graded as minute (affecting the endplate only): 28.8% compared with 10.4%, \(p=0.007\).

The primary outcome was the change in Roland Morris Disability Questionnaire (RMDQ) and LBP. The RMDQ is a patient-rated scale with a range of 0–24, with higher scores indicating worse symptoms. Statistical analysis was confined to those who completed 1 year follow-up (86% of those randomised to antibiotics and 93% of those randomised to placebo).

In the antibiotic group, the RMDQ score decreased from a median of 15.0 at baseline to 7.0 at 1 year, compared with a decrease from 15.0 to 14.0 in the placebo group \((p=0.0001)\). The median LBP score similarly reduced from 6.7 to 3.7 in the antibiotic group and remained unchanged at 6.3 in the placebo group \((p=0.0001)\). There were also statistically significant improvements in the antibiotic group compared with the placebo group for a number of other outcomes relating to symptoms and quality of life, but although there was a numerical reduction in days with sick leave in favour of antibiotic therapy, this was not statistically significant.

A **clinically important** change was defined as a 30% or greater reduction from baseline in RMDQ. The proportion of patients in each group with this response was not reported but the number needed to treat (compared with placebo) in the lower-dose antibiotic group was 4 (95% CI 3 to 12) and in the higher-dose group it was 3 (95% CI 2 to 6). The between-dose difference was not statistically significant but the study was not powered for this comparison.

At 1 year follow-up, 13% of the antibiotic group and 15% of the placebo group had no Modic changes on MRI: the statistical significance of this difference was not reported. There was a statistically significant decrease in the volume of Modic changes in the antibiotic group from baseline, where changes of volume 2–4 (up to 25% to more than 50% of the vertebrae) were reduced to volume 1 (affecting the endplate only; \(p=0.05\)), This reduction was not observed in the placebo group.

The authors note that the extent to which these results can be generalised to people with other types of Modic changes is unknown.
Adverse effects were more common in the antibiotic group than the placebo group (65% of people compared with 23%). Most adverse effects were low-grade gastrointestinal adverse effects, but 4 people in the antibiotic group (4.4%) dropped out of the study because of side effects, compared to none in the placebo group.

**Commentary provided by Professor Martin Underwood, Warwick Medical School**

Professor Underwood was chair of the Guideline Development Group for the NICE clinical guideline on early management of persistent non-specific low back pain

Albert and colleagues have produced interesting preliminary data suggesting that long-term antibiotic treatment may be helpful in some individuals with chronic low back pain. Identifying these individuals would require a major change to current practice. Participants all had back pain for at least 6 months and a current MRI showing new Modic type I changes adjacent to a herniated disc shown on an MRI 6–24 months previously.

Although the acquisition cost of co-amoxiclav is modest there may be substantial additional costs incurred identifying those who might benefit. Current NICE guidance advises against imaging for non-specific low back pain. Few people will have had the baseline scan required. New episodes of low back pain, with or without radicular pain (sciatica) are common and the prognosis is generally good. Thus many additional baseline MRI scans, on people who will subsequently recover, would be needed to identify people who could benefit. It is too soon to change clinical practice to identify those who might benefit. If these findings are replicated in different populations, and there is evidence for cost-effectiveness of the overall approach to diagnosis and treatment required, they may have important implications for the approach to managing low back pain.

**Commentary provided by Dr Paul Chadwick, consultant medical microbiologist, Salford Royal NHS Foundation Trust**

Recent studies have reported isolation of bacteria from disc material in patients with disc herniation and have raised the interesting possibility that infection with low virulence skin commensals may contribute to the aetiology of chronic low back pain. This should be distinguished from our understanding of vertebral osteomyelitis and discitis, where infection is most commonly due to *Staphylococcus aureus*, streptococci or enteric Gram-negative bacilli. Although co-amoxiclav may be a reasonable choice for some patients with spinal infections, microbiologists would typically recommend a 6-week course, extending to 12 weeks for extensive disease or where a significant undrained collection is present. In this context, some of the antimicrobial-related decisions in the Albert study are perhaps unexpected.

The authors imply that co-amoxiclav was chosen to cover both *Propionibacterium acnes* and *Corynebacterium propinquum*. It is not clear why co-amoxiclav was preferred to amoxicillin to cover these species. The reason for including the higher dose of co-amoxiclav is also unclear. Increasing the dose of the clavulanate component above 125 mg 3 times daily is generally thought to be unnecessary and could potentially increase unwanted drug effects.

The authors conclude that antibiotics could be considered for a highly selected subgroup of patients with chronic low back pain when all other treatment options have failed. Confirmatory work is warranted and should include a consideration of shorter course therapy, together with biopsy and culture of the study patients to directly correlate the microbiological findings (and susceptibility results) with clinical outcomes. In addition, if there were to be non-selective use of broad-spectrum antimicrobial agents for a wider group of patients with
chronic low back pain, concerns about widespread use contributing to antimicrobial resistance and Clostridium difficile infection would arise.

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**References**


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