Rheumatoid arthritis, cannabis based medicine eases pain and suppresses disease

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The first study to use a cannabis-based medicine (CBM) for treating rheumatoid arthritis has found that it has a significant effect on easing pain and on suppressing the disease.

Writing in the medical journal Rheumatology [1], the researchers say that although the differences were small and variable in the group of 56 patients they studied, the results are statistically significant and a larger trial is needed to investigate in more detail the effects of CBM on the disease which affects approximately 600,000 people in the UK (1 in 100 of the population).[2]

There is anecdotal evidence that cannabis can provide pain relief for people with rheumatoid arthritis (RA), and in a recent survey 155 (16%) of 947 people who obtained cannabis on the black market for medicinal reasons said they did so to obtain relief from symptoms of RA. However, this study in Rheumatology journal, led by David Blake, Professor of Bone and Joint Medicine at the Royal National Hospital for Rheumatic Diseases (RNHRD), Bath, and the University of Bath, UK, is the first randomised controlled trial to investigate the effect of a CBM on RA. It is published online today (Wednesday 9 November).

In the double-blind trial, the researchers randomised 31 patients to receive the CBM and 27 the placebo. The CBM (brand name: Sativex) was in the form of an easy-to-use mouth spray that patients could administer themselves up to a maximum of six doses a day. The CBM consisted of a blend of whole plant extracts, standardised for content, that delivered approximately equal amounts of two key therapeutic constituents from the cannabis plant: delta-9-Tetrahydrocannabinol (THC) and cannabidiol (CBD). Mouse studies have shown that THC and CBD have anti-inflammatory effects, and that CBD blocked progression of RA and produced improvements in symptoms.

Dr Ronald Jubb, Consultant Rheumatologist, at the University Hospital Birmingham NHS Foundation Trust, UK, said: "Patients had a baseline assessment at the beginning of the trial and then were randomised to receive either the CBM or placebo. Patients only took the doses in the evening in order to minimise possible intoxication-type reactions. The starting dose was one actuation within half an hour of retiring, and this was increased by one actuation every two days to a maximum of six doses according to individual response over a period of two weeks. Stable dosing was then maintained for a further three weeks."

The researchers found that in comparison with the placebo, patients who had taken the CBM had statistically significant improvements in pain on movement, pain at rest, quality of sleep, inflammation (measured by a Disease Activity Score involving 28 joints - DAS 28) and intensity of pain (measured by the Short-Form McGill Pain Questionnaire SF-MPQ).

For instance, on a score of 0-10 where 0 is no pain, CBM patients on average moved from 7 to 4.8 for pain on movement (placebo patients moved from 6.7 to 5.3), 5.3 to 3.1 (placebo 5.3 to 4.1) for pain at rest, and 5.7 to 3.4 (placebo 5.8 to 4.6) for quality of sleep. On the DAS 28 score of 0-10, the CBM patients moved from 5.9 to 5 (placebo 6 to 5.9), and on the SF-MPQ score of 0-100 for intensity of pain at present, the CBM patients moved from 48 to 33, while the placebo patients remained unchanged at 50.

Adverse side effects were mostly mild or moderate (e.g. dizziness, light-headedness, dry mouth, nausea). Of the eight patients who experienced mild dizziness, in four patients this occurred during the initial two-week period when they were gradually increasing the doses, and two occurred two days after this initial period, so these were probably due to patients getting used to the correct dose. No patients taking the CBM had to withdraw from the trial due to adverse side effects, but three did from the placebo group.

Dr Philip Robson, Senior Research Fellow and Consultant Psychiatrist at the Oxford University Department of Psychiatry and Director of the Cannabinoid Research Institute within GW Pharmaceuticals (the manufacturer of Sativex), explained: "Withdrawals from the placebo group were probably due to a psychological effect, a spontaneous occurrence, or a reaction with another medicine."

Dr Jubb said: "The results from the first controlled study of CBM in rheumatoid arthritis are encouraging, with overall improvements in pain on movement and at rest, improvement in the quality of sleep and improvement in the overall condition of the patients' arthritis. Whilst the differences are small and variable across the patient group, they represent benefits of clinical relevance and indicate the need for more detailed investigation through larger trials to see exactly where CBM could be best used with minimum side effects."

If further trials are run, researchers will probably extend the dosing period over the full 24-hour period. Dr Robson said: "The beneficial effects in this study occurred in the context of a dosing regime restricted to evening dosing in order to minimise any possible intoxication-type reactions. However, 24-hour dosing with Sativex, using a self-titration regime, in trials for multiple sclerosis resulted in only minimal intoxication scores."

He continued: "The element that can cause the 'high' in cannabis - THC - also has valuable pharmacological activity. It is thought to be an essential therapeutic component and therefore it can't be removed from the medicine. However, the method of giving the doses, via the mouth spray, and the principle of self-titration, where each patient gradually determined their own optimal dose level up to a maximum of six doses a day, minimised the risk of intoxication."

Dr Robson said that fears that the CBM could be abused by patients hoping to get a "high" were probably unfounded. "It seems that in practice this is a very rare event. More than 1,000-patient years of treatment with Sativex in clinical trials have been accumulated and to date there has not been a

single documented case of abuse. The fact is that the motivation of medicinal users of cannabis-based medicine is entirely different from recreational users: the former simply want symptom relief and the ability to go about their normal lives, and for them intoxication would be a distinct disadvantage; for the latter, smoking marijuana is infinitely more intoxicating than Sativex and is still easily available."

[1] Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. Rheumatology Advance Access published on November 9, 2005.
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[2] Rheumatoid arthritis affects three times as many women as men. Prevalence in the UK is approximately 0.5% in men and 1.8% in women, increasing after the age of 64 to 2% in men and 5% in women. There are many more people with less severe forms of RA that do not meet the diagnostic criteria for definite or classical disease.

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