Are cannabinoids safe and effective for treatment of patients with rheumatoid arthritis?

Bottom line

Sativex® (an oral-mucosal cannabinoid spray containing tetrahydrocannabinol and cannabidiol), as an adjuvant treatment, improves morning pain with movement and at rest, and sleep quality, with minimal adverse events, for patients with rheumatoid arthritis (RA) refractory to standard therapy. Morning stiffness was not significantly improved. (SOR: **B**, based on a single small RCT.) Sativex is not yet available in the United States.

Evidence summary

A multicenter, randomized, double-blind, parallel-group comparison trial (total n=58; treatment group=31; control group=27) compared Sativex with placebo for ancillary treatment of RA over a total of 5 weeks, including an initial 2-week titration period. A key inclusion criterion was prior failure to achieve adequate pain control using standard treatment for RA (nonsteroidal anti-inflammatory drugs, prednisolone, and/or disease-modifying antirheumatic drugs). Patients with a history of substance abuse; psychiatric conditions; cardiac, hepatic, or renal disorders; or a diagnosis of epilepsy were excluded.[1]

The primary outcome measure was pain on movement (measured each morning with numerical rating scale of 0–10). Secondary measures (mostly measured on scales of 0–10, with 10 being the most severe pain) included such outcomes as pain at rest, morning stiffness, and sleep quality.[1]

Patients began with a dose of 1 actuation (containing 2.7 mg tetrahydrocannabinol and 2.5 mg cannabidiol in the treatment group) 30 minutes before bedtime. Bedtime dosing was used to reduce symptoms of intoxication. Both Sativex and placebo were titrated by 1 actuation every 2 days up to a maximum daily dose of 6 actuations. Patients continued their standard therapy throughout the trial.[1]

Statistical significance was achieved for the primary outcome, decreased pain on movement (mean difference –0.95; 95% CI, –1.83 to –0.02; *P*=.044).[1] Two secondary measures also improved significantly: pain at rest (mean difference –1.04; 95% CI, –1.90 to –0.18; *P*=.018) and sleep quality (mean difference –1.17; 95% CI, –2.20 to –0.14; *P*=.027). Changes in morning stiffness did not reach statistical significance.

Most adverse events were reported as mild to moderate. Constipation and malaise were occasionally severe, but occurred more often in subjects using placebo (6 of 27 patients) than in those using Sativex (2 of 31 patients; no *P* value reported for comparison). Mild transient dizziness was reported by 8 of 27 patients in the Sativex group and 1 of 31 patients in the placebo group (no *P* value reported). One subject withdrew from the Sativex group because of a need for surgery (not related to the protocol), whereas 3 in the placebo group dropped out because of adverse events.[1]

Product information

Sativex is not currently available in the United States.[2] GW Pharmaceuticals and their American licensing partner, Otsuka Pharmaceutical Company Ltd, have recently completed Phase IIb trials of Sativex in patients with cancer pain and have applied to the FDA to start Phase III for that indication.

Sativex has been approved for use with cancer pain and multiple sclerosis spasticity in Canada and is currently undergoing regulatory examination for these indications in the United Kingdom and Spain.

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REFERENCES

1. Blake DR, Robson P, Ho M, Jubb RW, McCabe CS. Preliminary assessment of the efficacy, tolerability and safety of a cannabis-based medicine (Sativex) in the treatment of pain caused by rheumatoid arthritis. *Rheumatology (Oxford)*. 2006; 45(1):50–52. **[LOE 1b]**
2. Positive data in Sativex Phase IIb trial support advancing into Phase III development in cancer pain [press release]. Warsaw, Poland: Biotechnology Europe; March 27, 2010. http://www.biotechnology-europe.com/news. Accessed April 12, 2010.