Cochrane for Clinicians

Putting Evidence Into Practice

Systemic Pharmacologic Treatments for Plaque Psoriasis

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Clinical Question

What are the most effective treatments for moderate to severe plaque psoriasis?

Evidence-Based Answer

Infliximab, bimekizumab (Bimzelx), ixekizumab (Taltz), and risankizumab (Skyrizi) are the most effective medications for achieving a 90% reduction in symptoms among patients with moderate to severe plaque psoriasis.[1] (Strength of Recommendation: A, consistent, good-quality patient-oriented evidence.)

Practice Pointers

Psoriasis is a chronic, immune-mediated inflammatory disorder involving the skin and other organ systems. It affects an estimated 3.2% of people older than 20 years in the United States.[2] Psoriasis can present significant challenges due to its variable clinical manifestations, potential for comorbidities, and the evolving landscape of treatment options.[3]

This Cochrane review included 179 randomized controlled trials with a total of 62,339 participants and evaluated 20 unique treatments.[1] The patient population included adults older than 18 years with moderate to severe plaque psoriasis. The Psoriasis Area and Severity Index (PASI) score was used to assess psoriasis severity (range = 0 to 72, with a score of 5 to 10 indicating moderate disease and a score greater than 10 indicating severe disease). The PASI instrument is completed by examiners, and the score considers the extent and severity of skin involvement, including factors such as redness, scaling, and thickness of psoriatic lesions in four body regions (i.e., head, upper extremities, trunk, and lower extremities). PASI 90 describes when a patient has symptoms of psoriasis that have improved by 90% or more compared with their initial baseline PASI score and is, therefore, a measure of treatment effectiveness. Of the studies included in this review, 56% were placebo-controlled, and at least 77% were industry-sponsored.

The participants' average PASI score at baseline was 20.4 (range = 9.5 to 39). A network meta-analysis demonstrated that, compared with placebo, all interventions at the class level (e.g., nonbiologic systemic agents, small molecules, biologic treatments) helped more patients reach PASI 90. Compared with those using the nonbiologic systemic agents, more patients using the biologic treatments (i.e., anti-IL17, anti-IL12/23, anti-IL23, and anti–tumor necrosis factor alpha) reached PASI 90. Anti-IL17 treatments (i.e., brodalumab [Siliq], bimekizumab, ixekizumab, and secukinumab [Cosentyx]) helped more patients reach PASI 90 than other interventions. Compared with placebo, the most effective drugs for reaching PASI 90 were infliximab (risk ratio [RR] = 49.16; 95% CI, 20.49 to 117.95), bimekizumab (RR = 27.86; 95% CI, 23.56 to 32.94), ixekizumab (RR = 27.35; 95% CI, 23.15 to 32.29), and risankizumab (RR = 26.16; 95% CI, 22.03 to 31.07). When compared with each other, these medications had similar clinical effectiveness. Serious adverse events analysis was based on a very low number of events with low to moderate evidence; however, none of the interventions increased the risk of serious adverse events compared with placebo.

Limitations of this review were that the trials assessed benefit during the induction treatment phase (from eight to 24 weeks), and the studies may have been of insufficient duration to detect rare or long-term adverse effects. It was also noted that there was variation in how well the studies took measures to blind investigators and participants; one-third of the trials in the review were at high or unclear risk of performance bias.

This Cochrane review supports the use of infliximab, bimekizumab, ixekizumab, and

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risankizumab to treat moderate to severe plaque psoriasis. These findings align with current recommendations from the American Academy of Dermatology, the National Psoriasis Foundation, and the National Institute for Health and Care Excellence.[4,5] Further study is needed to better evaluate long-term adverse effects and safety data of the systemic treatments for psoriasis and to allow subgroup analysis on patient groups such as those who had been treated previously and those with obesity, serious comorbidities, different durations of illness, and the presence of complications such as arthritis. Further assessment is also needed to determine the value of nonbiologic systemic treatments.

The practice recommendations in this activity are available at https://www.cochrane.org/CD011535.

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Cannabis Use for Cancer-Related Pain

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Clinical Question

Does cannabis improve cancer-related pain control in adults compared with placebo or other standard analgesics?

Evidence-Based Answer

For adults with cancer-related pain, the use of cannabis or synthetic cannabis products improves scores on the Patient Global Impression of Change (PGI-C) scale and mean pain intensity scores compared with placebo but does not reduce pain scores, sleep disruption, or the use of opioids. Nabiximols therapy can lead to more central nervous system adverse effects compared with placebo.[1] (Strength of Recommendation: B, inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

Many distressing symptoms are associated with cancer, but pain is one of the most feared symptoms related to cancer in the general population.[2] It is noteworthy that one-third of patients with cancer experience moderate to severe pain.[3] The World Health Organization (WHO) guideline recommends opioid analgesics as the first-line treatment for moderate to severe cancer pain; however, up to 15% of patients may not respond to opioids.[4,5] New analgesics are needed for cancer pain. Tetrahydrocannabinol (THC) and cannabidiol (CBD) have been considered as potentially effective analgesics for cancer pain. CBD is an allosteric modulator of cannabinoid 1 receptors (analgesic, antispasmodic, and anti-inflammatory properties), and THC is a partial agonist of cannabinoid 1 and 2 receptors (analgesic, anti-inflammatory, anxiolytic, and antipsychotic properties). The authors of the Cochrane review sought to evaluate the benefits and risks of cannabis for cancer pain in adults.

The Cochrane review comprised 14 randomized, double-blind, controlled studies that included 1,823 adults with cancer-related pain (cancer pain, cancer therapy-related pain, or both) and compared cannabis with placebo or any other standard analgesics.[1] Among the 14 studies, six were conducted in North America. Five studies examined nabiximols (oromucosal THC and CBD; not available in the United States) for opioid-refractory cancer-related pain, and seven studies assessed synthetic oral THC analogues for cancer-related pain. Nabiximols (2.7-mg THC and 2.5-mg CBD) was administered in 1 to 16 actuations per day, and single doses of synthetic THC analogues ranged from 4 to 20 mg. Study duration varied from less than one day (a single dose) to eight weeks and included between 10 and 399 participants. Eight studies excluded patients with serious chronic conditions (e.g., hepatic impairment, ischemic heart disease, epilepsy), and five studies excluded patients with serious psychiatric disorders (e.g., substance use disorder). The study outcomes were an improvement on the PGI-C scale (a 7-point scale to assess self-reported overall health status improvement, ranging from 1 [very much worse] to 7 [very much improved]), pain relief of 50% or greater, mean pain intensity, sleep disruption, opioid maintenance and breakthrough dosages, withdrawals due to adverse events, central nervous system adverse events, or any serious adverse events.

In adults with opioid-refractory cancer-related pain, more participants in the nabiximols group than in the placebo group reported being very much improved or much improved on the PGI-C scale (number needed to treat = 16; 95% CI, 8 to 100; three trials; 996 participants; moderate-certainty evidence); but, nabiximols did not reduce pain, sleep disruption, or opioid maintenance and breakthrough dosages. More participants in the nabiximols group developed central nervous system adverse events compared with the placebo group (number needed to harm = 9; 95% CI, 6 to 25; four trials; 1,331 participants; moderate-certainty evidence), although withdrawal rates and any serious adverse

events did not differ between groups. A single dose of synthetic THC analogue reduced mean pain intensity for adults with cancer-related pain compared with placebo (mean difference = −0.98; 95% CI, −1.36 to −0.60; three trials; 301 participants) but did not reduce mean pain intensity scores compared with codeine. More participants in the THC analogue group experienced central nervous system and psychiatric adverse effects compared with the placebo and codeine groups (low-certainty evidence).

Due to small sample sizes and variability of treatment duration and doses across studies, current evidence regarding the effect of cannabis on cancer-related pain is limited. Because nearly one-half of the studies received pharmaceutical company funding and most excluded patients with common chronic conditions, the findings of this review should be interpreted with caution. In the United States, nabiximols is currently unavailable, but cannabis is widely accessible. Family physicians should be prepared to discuss the potential risks and benefits of cannabis for patients with cancer-related pain.

The practice recommendations in this activity are available at https://www.cochrane.org/CD014915.

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