PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #464
PSILOCYBIN USE IN PALLIATIVE CARE
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Background: Since the United Nations 1971 Convention on Psychotropic Substances, psilocybin, and other psychedelics (lysergic acid diethylamide (LSD), mescaline, etc.) have been schedule one controlled substances (1). In the United States, this means psychedelics are felt to have no accepted clinical use even when administered under medical supervision. Hence, most clinicians in the United States cannot prescribe psychedelics outside of a clinical trial. This is despite small, controlled trial data demonstrating the potential to alleviate depression, anxiety, and existential distress when administered under the supervision of a therapist (2,3). Despite this, a growing number of regions and countries have recently decriminalized the use of psilocybin. Canada allowed health care professionals to request the use of psilocybin for patients with serious illness (4). In the United States, Oregon and Colorado along with multiple other cities (e.g., Detroit, San Francisco) decriminalized its use (5). Generalist clinicians therefore should have familiarity about the published evidence and pharmacology of psychedelics (specifically psilocybin) to treat psychiatric symptoms common to patients with life-limiting illness (6).

Potential use in palliative medicine: Refractory existential distress (see *Fast Facts* #319 and 320), anxiety, and depression affect many patients facing a short prognosis due to a serious illness (7). Unfortunately, traditional psychotherapy-oriented approaches have shown limited efficacy for these symptoms and/or may not always be feasible in this patient population (8). A series of controlled studies have suggested that one administration of psilocybin significantly reduced anxiety and depression associated with a life-threatening cancer when utilized under the direct supervision of a trained therapist and followed up with a few psychotherapy sessions (9,10). Furthermore, greater than 80% of participants described a significant increase in life satisfaction 6 months after the session; many even rated the experience as one of the most important in their lives. For treatment-resistant depression, psilocybin has shown improvement in depressive symptoms in a randomized controlled trial (3,11). Psilocybin has also shown promise in tobacco and alcohol use disorder and post-traumatic stress disorder (PTSD) (12). Clinicians administering psilocybin should have specific training on how to administer, monitor, and assist patients during a controlled psychedelic-assisted therapy session. Many programs now exist in the United States to acquire this training (13).

Pharmacology of psilocybin: Psilocybin is an alkaloid found in multiple species of fungi within the genus *Psilocybe.* When ingested, it is converted into the active metabolite, psilocin, which is a potent serotonin 5HT-2A cell surface receptor agonist. At usual therapeutic doses (0.3-0.4 mg/kg), psilocybin induces an altered state of consciousness characterized by changes in mood, perception, and thought. Feelings of transcendence, euphoria, mysticism, or even an epiphany have been reported. Onset of action is 30-60 minutes; peak effect 90-120 minutes; the duration of effect is 4-6 hours. Animal models and human trials suggest a low potential for dependence or abuse (14,15).

Methods of therapeutic use: Response may vary based on individual pharmacodynamics, as well as the *set* and *setting* of the experience. *Set* refers to the individual's intention, mindset, and mood; s*etting* refers to the physical, auditory, and emotional tenor of the environment (16). Optimizing these two parameters during the experience is a key part of psychedelic-assisted therapy. As such, it should be utilized under the supervision of a therapist or guide; not, recreationally or at the sole discretion of the patient.

Side effects: Relative contraindications to psilocybin include use of serotonergic medications; significant cardiac abnormalities (uncontrolled hypertension, arrhythmias); and a personal or family history of schizophrenia, bipolar disease, or other psychotic illness (17). Acute cardiovascular effects in healthy volunteers are minimal with transient elevations in heart rate, systolic, and diastolic blood pressure (18). Headache, nausea, and fatigue are common side effects lasting hours to days post ingestion.

Risks: Although the frequency of "bad trips" in which users become violent, irrational, or suicidal have been exaggerated, challenging experiences have been reported, especially near peak effect. These range in severity from a mild sense of depersonalization to overwhelming experiences of a complete loss

of self-identity (ego dissolution). Revisiting challenging memories, negative experiences, or trauma has been reported too. Pooled studies suggest these episodes are usually self-limited when therapists are supervising the experience (18). Psilocybin is not associated with organ toxicity, significant drug interactions, long-term increase in illicit drug use, nor psilocybin abuse/dependence (19,20).

The cost of psilocybin assisted therapy is variable and not currently covered by insurers. Given the resources involved, patients may pay more than $1000 out of pocket for a single session (21).

Other psychedelics: LSD has been studied for anxiety associated with life-threatening disease with similar results to psilocybin (22,23). DMT (N,N-Dimethyltryptamine), a plant alkaloid in ayahuasca; and mescaline, a plant alkaloid in the peyote and San Pedro cacti, have been used therapeutically under the guidance of shamans for generations. In non-controlled trials, they have shown promise in reducing depressive symptoms (24). Ketamine and MDMA-assisted psychotherapy have shown efficacy for PTSD and resistant depression among otherwise healthy volunteers (25).

Summary: Early data suggest psilocybin is a promising modality for end-of-life anxiety, depression, and existential distress when utilized under the guidance of a guide or therapist. However, its use is limited currently outside of a clinical trial. Clinicians who care for patients with serious illness should inquire about its non-prescribed use.

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