Natural Medicines for Trauma, Palliative Care, & Hospice Care Patients

Executive Summary

"Natural medicines" containing psychoactive compounds (such as psilocybin, ibogaine, mescaline, and dimethyltryptamine/DMT) have been used widely in both indigenous cultural and spiritual contexts. However, these compounds have not been thoroughly explored in the context of Western medicinal use. Although federal funding to research certain compounds has been restricted, privately-funded clinical studies have shown potential in psychiatric settings, including for depressed and anxious cancer patients, those with substance abuse disorders, and those who suffer from post-traumatic stress disorder. Two bills have been introduced in the 2022 Missouri legislative session (HB 2850 and HB 2429) that would allow terminally-ill or treatment-resistant trauma patients to obtain dimethyltryptamine, ibogaine, mescaline, or psilocybin, or would expand the Missouri Right to Try Act to allow terminally-ill patients to be administered these compounds (as well as methylenedioxymethamphetamine and lysergic acid).

Highlights

- Anywhere from 25-77% of terminally-ill patients experience high rates of anxiety and/or depression, and up to 50% experience delirium.
- Compounds like psilocybin have been shown in small trials to reduce depression, anxiety, and improve mood in 80% of terminal cancer patients.
- Oregon remains the only state to have approved the use of psilocybin for medicinal use.
    - Several states (like CO, WA, NJ, and OR) have decriminalized possession of compounds like psilocybin, while Texas and Connecticut have approved the creation of state health agency working groups to investigate the potential of these compounds.

Limitations

- Given the status of many "natural medicines" as Schedule I substances under the Controlled Substances Act, there is a lack of data on how these compounds can or should be used clinically, and what ailments they may be effective in treating.
- Most clinical-setting research has been done on psilocybin and methylenedioxymethamphetamine, and as such data is still needed on the effect of other medicines of this type.

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Research Background

Terminal Illness and Trauma

Palliative care consists of treatments meant to aid and improve the quality of life of patients with serious chronic conditions (such as post-traumatic stress disorder or PTSD), whereas *hospice care* patients are those who have received a terminal illness diagnosis and require medical assistance to ease their end-of-life progression and improve the quality of remaining life.[1] Terminally-ill patients can experience anxiety and depression (between 25-77%) and high rates of delirium (between 5-50% as nursing home-bound patients age).[2] As recently as 2018, an estimated 1.55 million Americans received hospice care, and 55% of Missourians who died while on Medicare were enrolled in hospice care near the end of life.[3]

Traditional treatments for depression, such as selective serotonin reuptake inhibitors, are used for reducing stress, aggression, impulse, and anxiety in a way that may cause "blunting of emotions" and increased resilience. Psychotherapeutic drugs have been suggested as an alternate treatment that may change the ability for one to release certain emotions, provide heightened awareness of the environment, and expand the processing of thoughts.[4] Many "natural medicine" psychotherapeutics such as psilocybin, ibogaine, mescaline, and dimethyltryptamine (DMT) target a brain receptor known as 5-HT, and can elicit various behavioral and cognitive experiences such as changes in mood, associative learning, and coping strategies for trauma.[5]

Studies of Psychotherapeutic Treatments on Patients

Medicines with psychoactive substances have been used for thousands of years for both spiritual and medicinal purposes,[6] but many have been placed on Schedule I of the Controlled Substances Act in the U.S. for their proliferation in recreational settings or high risk for abuse.

These compounds have been investigated to varying degrees for their potential to treat ailments like depression, PTSD, anxiety disorders, substance abuse disorder, and alcohol use disorder; there are indications that some compounds may have positive, sustained effects after a single administration.[7] Several compounds have also shown safety and efficacy when combined with psychedelic-assisted psychotherapy models that address psychiatric crises.[8,9]

Psilocybin

Psilocybin may have therapeutic potential in treating addiction and anxiety.[10] One randomized double-blind clinical trial found that in a group of 56 patients with life-threatening cancer diagnoses, 80% of patients who had been administered psilocybin for 5 weeks showed sustained decreases in depression and anxiety about death and self-reported improvements in mood, quality of life, life meaning, optimism, life satisfaction, relationships, and spirituality at a 6-month follow up session.[11] Another study of 24 major depressive disorder patients found 54% of psilocybin-administered patients experienced rapid decreases in major depressive symptoms after a 4-week post-session assessment.[12] Further, one study on psilocybin found that the drug

had no higher abuse potential than drugs on the federal Schedule IV list of drugs (which includes Xanax and Valium).[13] Other studies on reducing obsessive-compulsive disorder symptoms, and cocaine or alcohol abuse are currently underway.[14]

Mescaline

Mescaline may have treatment potential in addiction, and in a study of 452 patients with depression, anxiety, PTSD, and substance abuse disorders, 68% of individuals self-reported improvements in their psychiatric symptoms with mescaline use.[10,15] Further, studies have determined that mescaline has virtually no propensity for addiction or dependence.[16]

Ibogaine

Ibogaine is the most likely of the natural medicines considered here to warrant further study of safety and toxicity concerns, as cardiac arrhythmias and cardiac arrests leading to fatalities have been reported. However, preclinical models of addiction indicate that ibogaine's therapeutic uses may include reducing opioid-withdrawals and cravings, as well as reduced alcohol, cocaine, and nicotine use.[17]

Dimethyltryptamine (DMT)

DMT may have clinical potential in treating addiction, depression, and anxiety, and very small non-randomized trials have suggested changes in sadness, pessimism, suicidal thoughts, and concentration.[9,10]

Limitations in Research Findings

Importantly, use of these compounds is not without established risk; reports exist of individuals who experience "flashbacks" as well as psychosis when known to have a family history of such issues. However, given that these reports often originate from the years where polysubstance use in illicit settings was common, determinations of how these substances interact in a controlled clinical environment remains to be established.[10]

Restrictions on federal research funding have also meant that access and research on the effects and therapeutic potential of natural medicines are limited, given the inability to determine precise doses, regimens, and on what ailments these compounds may have a therapeutic effect (e.g., evidence for efficacy treating PTSD is sparse).[18,19] The vast majority of existing research has investigated the effects of psilocybin and methylenedioxymethamphetamine (MDMA), and trials often have high bars to participation.[7] To date, only a single psychotherapeutic, Spravato®, has been FDA-approved for the treatment of refractory and adult major depressive disorder, with associated quarterly costs in the tens of thousands of dollars given the lengthy observational period during dosing and psychiatric follow-up.[7]

Legislative Policies Regarding Patient Use

In the 2022 legislative session, HB 2850 would allow terminally-ill or treatment-resistant trauma patients or their caregivers to legally acquire compounds such as DMT, ibogaine, mescaline, or

psilocybin with a physician prescription. The administration must occur at a health-related facility (such as a hospice or residential care) or at the patient's home, and does not need to be covered by a health insurer. Also filed this session, HB 2429 would expand the Missouri Right to Try Act to allow terminally-ill patients to be administered these compounds (as well as MDMA, and lysergic acid or LSD) under doctor recommendation should these compounds qualify as an investigational drug for clinical trial. While the bill states limitations of ten grams possession of the compounds if used for therapy, there are no recommendations on duration of use or whether at-home use requires supervision.

Several states (like CO, WA, NJ, and OR) have decriminalized possession of compounds like psilocybin. Texas (HB 1802) and Connecticut (SB 1083) are the only states to currently call for state agencies to develop a working group for the investigational use of drugs like MDMA or psilocybin as therapies. Oregon is also the only state to approve the use of psilocybin for medicinal purposes through licensing and regulation from the Health Authority's Public Health Division, and is set to begin licensure procedures in 2023.[20] While mescaline and DMT have no approved medical use, use in herbal forms (such as peyote or ayahuasca) for cultural or religious purposes have been allowed under the federal Religious Freedom Restoration Act of 1993.

At the federal level, the Right to Try Act of 2017 allows patients who have been diagnosed with life-threatening conditions and have tried all approved treatment options to access certain unapproved treatments that have at least gone through a Phase I clinical trial with the approval of the physician and the manufacturer under FDA guidance.[21] However, a 2022 study found that no government-funded clinical trials approved by the National Institutes of Health have been conducted for the study of any of the compounds listed in HB 2850 or HB 2429. Given the listing of these compounds under federal Schedule I classification, and that studies have mostly been funded only in small trials by private funds, conclusions about large-scale efficacy are unknown.[22]

Certain compounds, such as cannabis and kratom, are on the federal Schedule I list, however they have been approved for medicinal use, decriminalized, or fully authorized for personal use in various jurisdictions. For more information, please see the Science Notes: Cannabis Legalization, Kratom Consumer Protection Act.

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