TOOLS FOR PRACTICE #365 | May 13, 2024

TOOLS FOR PRACTICE

PEER PATIENTS EXPERIENCE EVIDENCE RESEARCH

Shrooms for Glooms: Evidence for psilocybin for depression

CLINICAL QUESTION

What are the benefits and harms of psilocybin for treatment-resistant/recurrent depression?

BOTTOM LINE

Psilocybin, given in treatment facilities with >10 hours psychological support, improves short-term (≤6 weeks) depression scores, helping 20-30% more patients attain response over control. Effects biased by unblinding, short-term trials and mostly inactive comparators. Psychological distress during treatment is common (75-90%) and requires monitoring/supports.

EVIDENCE

- Statistically significant unless indicated.
- 12 Systematic reviews of randomized controlled trials (RCTs) had serious limitations:
    - Meta-analyzed different conditions/treatments,[1-3] included people without depression,[4,5] descriptive reviews only,[6-10] missed key studies,[11] or dose-response effects.[12]
- Higher-quality RCTs with comparators:[13-16] Most patients had long-term/treatment-resistant/recurrent depression[14-16] and current antidepressants stopped.[13-16] Response generally ≥50% depression score reduction.

- RCT versus placebo:[13]
    - 52 patients. Psilocybin ~16mg/70kg versus placebo, one dose. At two weeks:
        - Montgomery-Asberg Depression Rating Scale (MADRS, 0-60, higher=worse) baseline=24: Psilocybin reduced 13 versus 3.5.
            - Minimal important difference[17]=3-6.
        - Response: Psilocybin 58% versus 15%, number needed to treat (NNT)=3.
- RCTs versus very-low-dose or inactive comparator:[14,15]
    - 233 patients. Psilocybin 25mg, 10mg or 1mg, one dose.[14] At three weeks:
        - MADRS baseline=32: 25mg reduced 12 versus 1mg reduced 5.
        - Response: 37% (25mg) versus 18% (1mg), NNT=6.
        - No statistical difference at 12 weeks, or 10mg versus 1mg anytime.
    - 104 patients. Psilocybin 25mg versus niacin 100mg, one dose.[15] At six weeks:
        - MADRS baseline=35: Psilocybin reduced 19 versus 7.
        - Response: 42% psilocybin versus 11%, NNT=4.
- RCT versus escitalopram[16]
    - 59 patients. Psilocybin 25mg every 3 weeks x2 doses versus escitalopram daily. At six weeks:
        - Remission: Psilocybin 57% versus escitalopram 28%, NNT=4.
        - Other depression outcomes not different.
- Adverse Events:[13-16] Headache and nausea 4-42% more common than control on day 1.
    - Distress common during treatment:[18] Examples "I felt like crying" (92%), sadness (79%), or emotional/physical suffering (77%).
    - 10-15mmHg systolic blood pressure rise x3-hours.[13]
- Limitations: Blinding 93-97% ineffective.[19]

CONTEXT

- Resource intense: Two counsellors for preparation (2-8 hours), during treatment (6-11 hours), and follow-up (2-4 hours).[13-16,18]
- Presently, guidelines recommend psilocybin in research[20,21] or special access-settings only.[20]
    - Longer-term effectiveness (>6 weeks) and serious harms unclear.
- Psilocybin micro-dosing RCTs: patients didn't have depression/anxiety.[22,23]

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Authors do not have any conflicts of interest to declare.

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