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Palliative Care in Amyotrophic Lateral Sclerosis... (Hardcover)  
by David Oliver, Gian Domenico Borasio

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Book sections

Front Cover

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Table of Contents

First Pages

Index

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## Cannabis

Intriguingly, the endocannabinoid system is implicated in the pathophysiology of ALS in animal studies, either directly as part of the underlying disease mechanism or indirectly inasmuch as this system plays a role in the homeostatic functioning of the neuromuscular system. Cannabinoids slow disease progression in mouse models of ALS, perhaps as an anti-oxidant, among other mechanisms involving endocannabinoid receptor activation.<sup>13-15</sup> Awareness of this literature increases the interest of patients in cannabis use, beyond the potential symptomatic benefits.

Cannabis has been reported by ALS patients to manage disease symptoms.<sup>16-18</sup> In a survey of 131 patients with ALS, those who were able to obtain cannabis found it moderately effective at reducing symptoms of pain, spasticity, drooling, appetite loss, and depression.<sup>16</sup> The main barrier to its use was availability, for either legal or financial reasons or lack of safe access.<sup>16</sup>

Pain increases in frequency and severity as disease progresses in ALS, and can have a pronounced influence on the quality of life and suffering.<sup>11,12,19</sup> Despite this, a Cochrane Review found no controlled trials specifically looking at the use of cannabis for pain relief in ALS.<sup>19</sup>

Cannabinoids are centrally and peripherally acting analgesics with a different mechanism of action from opioids, although the analgesic effect produced by cannabinoids and opioids may involve similar pathways at the brainstem level.<sup>20-22</sup> Multiple, well-controlled clinical studies have demonstrated the analgesic efficacy of cannabis in the treatment of pain.<sup>18,20</sup> Cannabis does not cause suppression of the respiratory drive.<sup>20</sup> A recent systematic review and meta-analysis of double-blind randomized controlled trials that compared any cannabis preparation with placebo among subjects with chronic pain showed a total of 18 completed trials.<sup>20</sup> The review concluded that cannabis is moderately effective for treatment of chronic pain.<sup>20</sup> Combining cannabis with narcotics may also be beneficial, since, as noted above, the opioid receptor system is distinct from the cannabinoid system.<sup>21</sup> The anti-emetic effect of cannabis diminishes the nausea associated with opioid medications.<sup>21</sup>

Spasticity, a cause of pain and dysfunction in ALS, is induced at the level of both the motor cortex and spinal cord through the loss of motor neuron inhibition.<sup>22-24</sup> Cannabis has an inhibitory effect via augmentation of gamma-aminobutyric acid (GABA) pathways in the CNS.<sup>24</sup> This produces inhibition of motor neurons at spinal levels in mice and clinical studies, mostly in MS patients, suggest that cannabinoid therapy reduces spasticity symptoms.<sup>22-24</sup>

Cannabis effectively dries the oral cavity and upper airway, potentially reducing the risk of aspiration pneumonia and increasing patient comfort. Other unproven but potential benefits include improved appetite, mood, and sleep.<sup>18,25</sup> Dosing is by titration to effect and dependent on route of delivery.<sup>26</sup> However, smoking cannabis is never recommended.

### **Entheogens (classic hallucinogens)**

The use of classical hallucinogenic compounds is experiencing a renaissance in medicine and psychiatry whether as adjuncts to psychotherapy or to induce spiritual experiences.<sup>27</sup> Trials of these compounds in the treatment of existential or death anxiety have focused on patients living with cancer. Articles, such as one in the *New York Times* in April 2012 entitled 'How psychedelic drugs can help patients face death,'<sup>28</sup> have been profiled by ALS patients in online forums addressing anxiety regarding death and dying.

The psychological rationale for this therapeutic approach in terminal illness may lie in the purported capacity of entheogens to facilitate powerful states of spiritual transcendence that exert in the patient a profound therapeutic impact with often dramatic improvements in psychological well-being.<sup>29</sup>

Enthnobotanical researchers coined the term entheogen (from the Greek, meaning 'generate god within'),<sup>30</sup> to generically describe substances, typically plants, that contain psychoactive substances that alter a person's perception of reality, used to bring a patient closer to God or the realm of the transcendent.<sup>29</sup> Entheogens have been used by in many cultures for millennia but primarily sacramentally to enhance a religious/spiritual ritual.<sup>29</sup> Many patients feel ill-prepared for death and that there is insufficient knowledge to help them make choices that will cover their medical needs (pain, sleep, etc.) yet honour and maintain their autonomy and dignity.<sup>31,32</sup>

Psilocybin is the most studied entheogen from a palliative/end-of-life perspective. It is the active compound found in mushrooms belonging to the genus *Psilocybe*, which contain the psychoactive tryptamines psilocybin and psilocin.<sup>33,34</sup> Other species also contain the weaker psychoactive alkaloid compounds baeocystin and norbaeocystin, which may potentiate the effects of psilocybin. Psilocybin has been used for centuries for religious purposes.<sup>34</sup> Its

inclusion as a Schedule 1 drug by the US Drug Enforcement Administration (DEA) has limited research on it.

Psilocybin administered under supportive conditions produced a dose-related mystical experience in 72% of subjects, although 39% also reported feelings of anxiety and fear. 'Set and setting', or the emotional state of the user and the type of environment they are in, largely determine whether the experience is positive.<sup>34</sup> Follow-up over 14-months found nearly 90% of the

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subjects considered it to be the most personally meaningful and spiritually significant event of their lives to date.<sup>34</sup> Supratherapeutic doses of dextromethorphan induced effects similar to psilocybin but with more acute cognitive impairment.<sup>35</sup>

The contribution of psilocybin or other entheogens to treatment of end-of-life distress in people with ALS remains to be determined. Palliative medicine is concerned with spiritual and psychological care, but the administration of medical therapies for psychospiritual purposes faces barriers in both law and medicine.

### **Ayurvedic medicine**

Ayurvedic medicine (Ayurveda) preceded and evolved independently of Western medicine.<sup>36</sup> The Sanskrit word *Ayurveda* means 'the scripture for longevity'.<sup>37</sup> Developed in India approximately 3000 BCE the sacred texts were passed on through generations of oral tradition,<sup>36</sup> and Ayurveda continues to be practised in India and other South Asian countries. It seeks to treat and integrate body, mind, and spirit using a comprehensive, holistic approach that emphasizes diet, herbal remedies, meditation, breathing, and physical medicine (exercise, physical therapy, yoga, etc.).

Ayurvedic medicine (Ayurveda) defines health as a state where the mind and