American Cannabis Nurses Association

Position Statement on Concurrent Cannabis and Opiate Use

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Introduction The American Cannabis Nurses Association supports the monitored and controlled use of cannabis in conjunction with opiate administration for patients (either human or animal) who are suffering from severe pain, intractable pain, severe neuropathy or pain associated with terminal illness. Additionally, any patient on long-term opiate therapy should be evaluated for cannabis therapy to *lessen* the risk of adverse events associated with opiates. This position is justified by the evidence base of use patterns, the in-vitro research demonstrating the interaction of endocannabinoid receptors with opiate receptors, the potential severity of adverse events associated with long-term opiate use and the ethical responsibility of health care practitioners to advocate on behalf of their patients.

Pain and Conventional Treatments Pain is the neurological process that provides internal communication via nerve cells indicating an injury or disease. Pain is a cardinal symptom of many disease processes especially if it is associated with tissue or organ nerve damage.

Pain impulses are carried through nerve fibers which are present in all tissues and organs, and exist in huge numbers in the central nervous system. The CNS is composed of the spinal chord and the brain. The peripheral nervous system (PNS) contains nerves located in the arms, legs, skin and other parts of the body outside the brain and spinal chord. Neurotransmitters like serotonin, dopamine, adrenalin and glutamate, are released by receptors in the cell, in response to specific nerve impulses which trigger their activity. The anatomy of a nerve cell is arranged in order to carry sensory impulses from one cell to another and into the brain and motor impulses from the brain back to a specific area.

There are many different qualities and types of pain. Pain may also be non-physical in nature, arising from psychological trauma or mental illness. Phantom limb pain, for instance, is the perception of pain in an appendage (arm or leg) which has been amputated. Intractable pain is excruciating pain which is unresponsive to medical or pharmacologic interventions.

Analgesics are a class of drugs which (are intended to) block or reduce the movement of pain signals to the brain, reducing the perception of pain. There are many different types of analgesics- including opiates- which treat many different types and intensities of pain.

Prescribers attempt to match the analgesic to the pain in the lowest effective dose. As the severity of the pain increases, so does the potency of the drug prescribed. Severe pain, by definition, is pain which defies easy control. The pain cycle often results in escalating doses of one pharmaceutical, until it fails to adequately control the pain or the side effects become excessive. This is followed by a different and more potent analgesic. The side effects and toxicities increase in proportion.

Patient's suffering from severe pain- like migraines, neuropathy or cancer, present a huge challenge to prescribers because the pain continues often for the patient's entire life and involve potentially lethal doses of analgesics over a long time period. Large doses of opiates additionally render many patients unable to effectively function, further reducing quality of life.

Morphine is considered the standard for the most severe pain. It comes in many forms and dosages and combinations with other agents which are meant to synergistically work with the morphine at lower doses. Morphine activates specific receptors which release endorphins. It has very potent central nervous system activity, blocking pain signals in the brain. It can also depress the vital functions of the CNS, like breathing. High doses of morphine can also impair liver function and sensory function and result in constipation. From 1999 to 2010, the number of U.S. drug poisoning deaths involving any opioid analgesic (e.g., oxycodone, methadone, or hydrocodone) more than quadrupled, from 4,030 to 16,651 per year, accounting for 43% of the 38,329 drug poisoning deaths and 39% of the 42,917 total poisoning deaths in 2010. *(1)*

Analgesic Properties of Cannabis Cannabis is effective as an analgesic due to its potent CB_1 receptor binding activity in both peripheral and central nervous system nerve pathways. When inhaled, it rapidly crosses the blood brain barrier. Researchers have demonstrated that cannabinoids reduce hyperalgesia- or increased sensitivity to pain- through activation of CB_1 receptors at the site of injury. (2) Endocannabinoid receptor activity represents a parallel, separate, but interconnected pain modulation system with the opioid receptor system in the CNS. (3,4,5) The foundation of the endocannabinoid system is the activity of CB_1 and CB_2 receptors which cause the release (or inhibit) a complex cascade of endocrine, hormonal or cellular chemicals from the brain or tissues themselves. This is the "homeostatic regulatory function" of the endocannabinoid system which help patients "relax, eat, sleep, forget and protect" (6). CB_1 receptors are mainly located in the brain and CB_2 receptors are located throughout the body in enormous numbers, especially immune system tissues. Cannabinoid receptors may be activated either by the internal endocannabinoid signaling process with anandamide or 2-AG (arachidonyl glycerol)- which all mammals synthesize- or activated through the administration of exogenous cannabinoids found in the cannabis plant. In essence, the cannabis plant has co-evolved over millions of years with humans to produce homeostatic regulatory chemicals nearly identical to those humans and animals produce themselves.

The neurochemical receptor binding actions of cannabinoids have been described in detail through animal modeling experiments. Cannabinoids interact with serotonergic, dopaminergic, glutaminergic, opioid neurotransmitters , and inflammatory processes. Δ-9-THC reduces serotonin release from the platelets of humans suffering migraine thus inhibiting the pain signals triggered by serotonin.

Clinical considerations with cannabis and opioid co-administration Any patient suffering from serious pain conditions should be evaluated for cannabis use. Many analgesics are combined with synergistic compounds in order to decrease the total dose of the most powerful one- usually morphine or codeine. Cannabis is no exception. A clinician whose patient is requesting or using cannabis should consider the patient's total pain management program especially the total dosage of opiates, muscle relaxants (flexeril) or benzodiazepines in long-term pain management and the adverse experiences, if any, resulting from high doses. (Documentation of changes in prescription amounts over time after initiating cannabis treatment is easily accomplished. Examination of previous prescription records presents an opportunity to retrospectively determine the therapeutic value of cannabis *if the clinician knows when the patient began using it.)* Patient's commonly report a decrease of opiate use from 1/3 to ½ as well as increased functional ability. Some patients eliminate the use of opiates nearly completely. There is no documented data indicating that concurrent use of opiates and cannabis increases adverse outcomes.

Adverse events and contraindications from cannabis/cannabinoids do occur. Most significantly, worsening or precipitation of psychosis. Anxiety or panic reactions may sometimes occur to naive users or patients ingesting substantial doses by mouth. There is no known lethal overdose recorded. Additionally, cannabis (like opiates) may mask underlying diseases. It may also adversely influence the metabolism of other drugs the patient may be using. Cannabis has a long history of use as a harm-reduction substitute for addiction to other substances. Co-occurring substance abuse may or may not be a contraindication to the use of cannabis. A detailed understanding of pharmacological, medical and social circumstances will provide guidance to clinicians. *Cannabis Hyperemesis Syndrome* has been documented in a small number of long-term cannabis users. Users report colicky abdominal pain, recurring nausea and vomiting, with symptom resolution upon abstinence. The etiology of this disorder is unknown and the occurrence is rare.

Clinician guidelines should include evaluating the risks and benefits of all treatments relative to one another (as well as presence *and severity* of co morbid substance abuse). Clinician guidelines *should not* include coercive drug tests based solely on a patient's report of cannabis use. The standardized use of detailed "pain contracts" with mandatory- or unannounced- drug

screens should be reserved for only those patients who have significant compliance issues which have been demonstrated over time. The general use of coercive pain contracts undermines the patient's trust in the physician and fosters miscommunication and deception. "Agreements" (as opposed to contracts) with patient's to monitor and document analgesic use over time with the addition of cannabis allows a working relationship with the prescriber which fosters trust.

In the event that a patient's drug screen indicates the presence of cannabinoid metabolites, an enlightened health care provider will engage in a detailed discussion with the patient in order to determine the underlying reason for the use of cannabis and if it is improving the quality of life of the person. A patient's report that he/she "feels better" after they use cannabis should not be detrimental, since the homeostatic regulatory functions of cannabis generally improve comfort.

The refusal of a clinician to discuss with or seriously evaluate the use of cannabis specifically in relation to that person's underlying medical diagnoses violates the clinicians' practice guidelines which include detailed evaluation of the patient's condition through an educated understanding of the complexity of their circumstances *and* knowledge of different treatments.

Cannabis has been used as an analgesic for 5000 years. (7) As restrictive laws give way to sensible regulation, its use as a medicine will increase, because patients are unable or unwilling to tolerate potent pharmaceuticals, or cannot afford them. All clinicians should be undertaking an education in endocannabinoid therapeutics in order to gain the understanding of this complex system. Clinicians should also understand route-dependant metabolism, federal and state legal barriers, strain evaluation processes, safe handling considerations, research advancements, novel cannabinoid drug development and dosing options- like vaporizers.

The American Medical Association's Code of Medical Ethics, Opinion 1.02 - The Relation of Law and Ethics (8) reads, in part:

> *"Ethical values and legal principles are usually closely related, but ethical obligations typically exceed legal duties. In some cases, the law mandates unethical conduct." "In exceptional circumstances of unjust laws, ethical responsibilities should supersede legal obligations."*

The federal ban of the use of medical cannabis by patients may be interpreted as an ethical dilemma for physicians, compounded by the DEA prescriptive authority which may be revoked, rendering the clinician incapable of practice. Physicians and Nurse Practitioners must weigh these factors. The unwillingness of federal legislators and regulators on all levels to change the scheduling of cannabis represents an unconscionable and inhumane obstacle to cannabis patients, researchers *and* clinicians. Ethical principles of medical practice require clinicians to

work actively to eliminate these injustices and advocate for an intelligent federal policy which does not victimize suffering people and waste tax revenues in the process.

Endocannabinoid therapeutics represents a subspecialty of medicine. The guidelines of clinical practice require “evidence- based” practice resting on the principles of science and ethics. Endocannabinoid therapeutics has evolved to the point where it meets these requirements of practice.

Sources

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