Are Cannabinoids Effective in Treating Non-Malignant Chronic Pain in Adult Patients

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Table of Contents

Abstract

A large component of anesthetic practice incorporates pain management, and a growing contingency of patients whom anesthesia providers encounter each day have chronic pain. Multimodal pain regiments and their use in the management of chronic pain in adults have increased as a result. One alternative that has shown potential for pain management is cannabinoids, which work through the endocannabinoid system (ECS). With the legalization of medicinal marijuana in Florida, an increased knowledge base is needed to better drive care. A literature search of CINAHL, PubMed, Cochrane Databases, MEDLINE, and Google Scholar was done to discover the current knowledge of cannabinoids in treating chronic, non-malignant pain. There have been mixed results as to the efficacy of cannabinoids in this population, but they are well tolerated with rare serious adverse effects. A 30-minute presentation was created to better familiarize the master's level Nurse Anesthesia Program's students enrolled at AdventHealth University (AHU) with the current findings. A ten-question evaluation was conducted before and after the PowerPoint presentation. The results were analyzed using a paired sample t-test with a predetermined significance level of $p<.05$ using Statistical Package for the Social Sciences (SPSS). The pre-test mean was 26.19% and post-test was 55.24%. With a p-value < 0.001, statistical significance was achieved, demonstrating the efficacy of the educational module in expanding the knowledge base of current AHU student nurse anesthetists regarding the use of cannabinoids in the treatment of chronic, non-malignant pain.

Keywords: Cannabinoids, Chronic Pain

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Introduction

Pain is a part of everyone's life and a vital function of a healthy body to help protect itself from harm. In the last three months, 55.7% of the population have experienced pain with 40-43% developing recurrent or chronic pain (Institute of Medicine, 2011; Nahin, 2012). Chronic pain is defined by the Centers of Disease Control and Prevention (CDC) (Dowell, Haegerich, & Chou, 2016) as "pain that typically lasts >3 months or past the time of normal tissue healing" (p. 1). For 12.5-17.6% of the population, pain becomes so severe it can become debilitating (Dowell, Haegerich, & Chou, 2016; Institute of Medicine, 2011; Nahin, 2012). Increased pain correlates with poor health status, increased healthcare use, and disability (Gaskin & Richard, 2012; Nahin, 2012). Its economic impact has been estimated to cost $560 and $635 billion to the United States each year (Gaskin & Richard, 2012; Institute of Medicine, 2011). According to the Institute of Medicine (2011), the prevalence of chronic pain is expected to continue to grow in part due to the aging population and increased prevalence of obesity. This is particularly relevant for the state of Florida. Over a quarter of the state population is considered obese and Florida has the highest percent of its population, 20%, over the age of 65 (Centers for Disease Control and Prevention, n.d.; United States Census Bureau, n.d.).

Chronic pain is generally divided into malignant and non-malignant pain due to unique characteristics of the disease process, ethical considerations, goals of treatment, different risk-benefit considerations, and increased medical supervision of those with cancer (Dowell, Haegerich, & Chou, 2016; Fordyce, 2001; Jara, et al., 2018; Paice, et al., 2016). In the CDC's guideline for prescribing opioids for chronic pain, they make this distinction and exclude patients

with cancer from their recommendations (Dowell, Haegerich, & Chou, 2016). As a result, this paper will focus on non-malignant chronic pain.

Treatment for more severe, chronic pain frequently consists of opioid prescriptions (Ballantyne, 2017; Dowell, Haegerich, & Chou, 2016; Institute of Medicine, 2011). Short-term use can be effective in managing pain, but prolonged use requires increased dosing-associated tolerance and untoward side effects. According to Ballantyne (2017), there is overwhelming evidence that higher dosages cause dangerous side effects including abuse and overdosing-related deaths, decreased sex drive, fall-related morbidity, and social and cognitive impairment. Furthermore, the overuse and misuse of prescription pain medications has been labeled an epidemic both nationally and at the state level, including Florida (Compton, Boyle, & Wargo, 2015; Edlund, et al., 2014; Substance Abuse and Mental Health Services Administration, 2017). These concerns have pushed legislators to act both nationally and in Florida to curb the epidemic (Capozzi, Stapleton, & Beall, 2017; Patrick, Fry, Jones, & Buntin, 2016; Raji, Kuo, Adhikari, Baillargeon, & Goodwin, 2018; Voelker, 2016). Complementary and alternative medicines including medicinal marijuana and cannabinoids continue to be researched to either supplement or complement opioids (Hurd, 2017; Levin, 2017; Moran, 2016; Olfson, Wall, & Blanco, 2018; Penney, Ritenbaugh, DeBar, Elder, & Deyo, 2016). Additionally, Florida has legalized medicinal marijuana and it is now available as a prescription to help manage chronic pain (Fla. Stat. § 381.986, 2018). It is becoming essential for certified registered nurse anesthetists to be aware of the effectiveness and safety of cannabinoids in the treatment of non-malignant chronic pain as the likelihood of encountering patients who inquire about cannabinoids may increase.

This project aimed to address two questions. The first question arose from the current clinical concern: in adults with non-malignant chronic pain (P), is the use of cannabinoids (I)

safe and effective in decreasing pain (O)? The second question focuses on our proposed intervention: in students enrolled in the AdventHealth's masters level certified Nurse Anesthetist Program (NAP) (P), does a 30-minute (T) PowerPoint presentation on the safety and effectiveness of cannabinoids in treating chronic non-malignant pain (I) increase their knowledge base (O)?

Review of Literature

The Endocannabinoid System

The endocannabinoid system (ECS) consists of receptors and ligands found at multiple areas throughout the pain pathways. The two most studied endogenous ligands in the ECS are anandamide and 2-arachidonoyl glycerol and when they stimulate the two primary G protein-coupled receptors, cannabinoid type 1 (CB1) and 2 (CB2), they produce a negative feedback loop that can inhibit pain signaling (Burston & Woodhams, 2014; Kaur, Ambwani, & Singh, 2016; Russo, et al., 2016). CB1 receptors are predominately found in the central nervous system including pain pathways in the spinal cord. CB2 receptors are primarily found in peripheral immune cells, but can also be found in peripheral sensory nerves, the spinal cord, and even higher cerebral regions (Aizpurua-Olaizola, et al., 2017; Jarvis, Rassmussen, & Winters, 2017; Burston & Woodhams, 2014).

The most widely known source of exogenous ligands affecting the ECS is the marijuana plant. Containing almost 500 different compounds, over 100 are comprised of cannabinoid ligands, the most prominent being Δ9-tetrahydrocannabinol (Δ9-THC), cannabinol, and cannabidiol (CBD) (De Meijer, 2004; Russo E. B., 2016). There are two synthetic compounds derived from the plant that are available by prescription: Marinol, containing dronabinol, and Cesamet, containing a racemic mixture of THC known as nabilone (AbbVie Inc., 2017; Meda

Pharmaceuticals Inc., 2018). Sativex is an oral spray made of nabiximols THC and CBD extracted from the cannabis plant (GW Pharmaceuticals, 2016). Indications for prescription include chemotherapy-induced nausea and vomiting and anorexia associated with AIDS for Marinol, chemotherapy-induced nausea and vomiting for Cesamet, and as an adjunct in the treatment of spasticity in multiple sclerosis (MS) for Sativex (AbbVie Inc., 2017; Aizpurua-Olaizola, et al., 2017; GW Pharmaceuticals, 2016; Jarvis, Rassmussen, & Winters, 2017; Meda Pharmaceuticals Inc., 2018; Russo E. B., 2016). Cannabinoids have a synergistic effect with each other and this may be why Sativex, the only drug containing more than one cannabinoid, has been the drug most closely associated with a potential for analgesia effects in non-malignant chronic pain (Aizpurua-Olaizola, et al., 2017; Gallily, Yekhtin, & Hanuš, 2015; Hayakawa, et al., 2008).

Efficacy

The use of cannabinoids, for the treatment of non-malignant chronic pain in adults, was shown to be effective short-term, under five hours, and is dose-dependent (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Wilsey B. , et al., 2016; Wilsey B. , et al., 2013). Although moderate doses, between 3.53-4%, were not more effective than lower doses, 1-1.29%, higher doses of 7% were found to significantly decrease pain relative to lower doses (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015). Results for clinical relevance, as determined by the proportion of patients who achieve a 30% decrease in pain, were mixed. When limited to chronic diabetic neuropathy, even with high doses it was not significant, but for neuropathies in general, both low and moderate doses were clinically relevant (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Wilsey B. , et al., 2016; Wilsey B. , et al., 2013).

Over longer periods of time, at least two weeks, there was some evidence showing statistically significant improvements in pain scores when compared to placebo (Hoggart, et al., 2015; Langford, et al., 2013; Turcotte, et al., 2015). However, data also showed that it may not be (Lynch, Cesar-Rittenberg, & Hohmann, 2014; Schimrigk, et al., 2017; Serpell, et al., 2014; De Vries, van Rijckevorsel, Vissers, Wilder-Smith, & van Goor, 2017). All data showed a decrease in pain scores, but the placebo effect negated statistical significance. When scores were evaluated during withdrawal and time to failure was used to evaluate the strength of the placebo effect, this resulted in significance decreases in pain (Langford, et al., 2013). When comparing responders at the 30% level, Sativex for allodynia was the only scenario to show significant results if taken for at least 10 weeks (Hoggart, et al., 2015; Langford, et al., 2013; Serpell, et al., 2014). It should be noted that for all patients, concomitant medications were allowed, but stabilized prior to enrollments. However, there were times that breakthrough pain medication such as acetaminophen and tramadol were allowed as well (Schimrigk, et al., 2017; Serpell, et al., 2014).

One study set itself apart from others by invoking pain in MS patients without a placebo. The study compared the use of Sativex in 20 patients with MS, 10 with pain and 10 without. Both groups took Sativex and were subjected to various methods of pain stimuli, using both numeric and visual pain scales. MS patients with pain experienced reduced pain transmission and a possible a restoration of cortical pain-gated modulation after one month of Sativex (Russo, et al., 2016).

The main limitation came using a relatively weaker pain adjuvant, cannabinoids, as an intervention while ethically being unable to stop stronger pain-relieving concommitants. This problem was compounded with a significant placebo effect. Conclusions regarding the efficacy of cannabinoids for management of non-malignant chronic pain may not lie solely in its

nociceptive properties. The decision to prescribe cannabinoids for adults with non-malignant chronic pain must compare risks against the totality of benefits, versus looking at pain alone. Additional secondary outcome measures such as improved sleep, reported quality of life, and spasticity appear to have mixed results for this population as well, but is beyond the scope of this paper (Hoggart, et al., 2015; Langford, et al., 2013; Lynch, Cesar-Rittenberg, & Hohmann, 2014; Schimrigk, et al., 2017; Serpell, et al., 2014; Turcotte, et al., 2015; De Vries, van Rijckevorsel, Vissers, Wilder-Smith, & van Goor, 2017).

In addition to the possible benefits of cannabinoids regarding pain, there are reservations as to side effects. These include drowsiness, amnesia, dysphoria, anxiety, psychomotor retardation, cognitive impairment, dependency, and adverse effects on the cardiovascular, pulmonary, reproductive, and immune systems (Fitzcharles, et al., 2016; Häuser, Petzke, & Fitzcharles, 2018; Hill, 2015; Hwang & Clarke, 2016; Lynch & Ware, 2015).

Safety

Adverse effects of cannabinoids are common, ranging from 59-100% for those taking them for non-malignant chronic pain with the most common being dizziness, nausea, dry mouth, fatigue, dysgeusia, and somnolence (Hoggart, et al., 2015; Langford, et al., 2013; Lynch, Cesar-Rittenberg, & Hohmann, 2014; Schimrigk, et al., 2017; Serpell, et al., 2014; Turcotte, et al., 2015; Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Wilsey B. , et al., 2013; De Vries, van Rijckevorsel, Vissers, Wilder-Smith, & van Goor, 2017). Short-term use of 1.29-3.53% vaporized cannabis, within five hours, found attention, learning, and memory function to be significantly impaired versus placebo (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Wilsey B. , et al., 2013). Subjects also had more somnolence and euphoria on higher doses ranging from 4-7% (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015). Although these

effects were statistically significant compared to placebo, general conclusions were that these cognitive declines would not significantly impact daily living (Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Wilsey B. , et al., 2013).

When taken longer than two weeks, the THC/CBD combination drug Sativex caused the following ranges of side effects: dizziness 19-39%, dysgeusia 9-38%, nausea 9-31%, fatigue 7-44%, dry mouth 7-11%, and somnolence 7-10% (Hoggart, et al., 2015; Langford, et al., 2013; Lynch, Cesar-Rittenberg, & Hohmann, 2014; Serpell, et al., 2014). THC alone had variable results with dizziness ranging from 17-80%, dysgeusia 4-43%, dry mouth 7-50%, and nausea 6-30% (Schimrigk, et al., 2017; Turcotte, et al., 2015; De Vries, van Rijckevorsel, Vissers, Wilder-Smith, & van Goor, 2017).

Serious adverse effects were rare, only exhibited in two studies using Sativex (Hoggart, et al., 2015; Langford, et al., 2013). In the first study, two out of 339 subjects had suicidal ideations, but one of them was in the placebo control group (Langford, et al., 2013). In the other study, three patients had serious adverse effects: amnesia, paranoia, and a suicide attempt (Hoggart, et al., 2015). Authors of both studies commented that the percentage of subjects with suicidal thoughts or actions was not out of proportion for the general population who experience chronic pain and is in agreement with the Institute of Medicine's (2011) findings. Withdrawal was also rare, only occurring in one case with only mild symptoms noted (Schimrigk, et al., 2017).

Contribution and Dissemination

In AHU's 28-month master's level NAP, the use of cannabinoids in the management of non-malignant chronic pain is not discussed to a great degree. This would typically be addressed in a post-graduate fellowship for pain management. However, with an increased likelihood of

encountering patients that may be taking cannabinoids or have questions about them in the future, exposure to this topic will better prepare the students to guide patient care. Our contribution to the program is a resource for current and future nurse anesthesia cohorts to provide insight into the use of cannabinoids for non-malignant chronic pain management. The fulfillment of this scholarly project allowed the dissemination of current literature to the graduating class of 2019 via a PowerPoint education module, Appendix C, and poster presentation, Appendix D. This provided familiarity on an additional option for non-malignant chronic pain management that is available to the graduate through the library repository.

Project Aim

The project aimed to expand the knowledge base of the current student registered nurse anesthetists enrolled in the master's level NAP to the most recent studies regarding the use of cannabinoids in the treatment of non-malignant chronic pain. It supplemented AHU's NAP with information obtained through the review of current literature. A PowerPoint presentation, Appendix C covering the material found in the literature review was created to use as an intervention for education. The PowerPoint presentation had learning objectives comprised of key concepts regarding the subject matter.

Methods

After review of the current literature, we sought approval from the Institutional Review Board, Grant Management Committee, and Scientific Review Committee. The prepared 30-minute PowerPoint was presented to AHU's NAP graduating class of 2019. Before participation in the study, all subjects were required to review and sign a consent to participate, see Appendix A. The selection criteria were as follows: any students enrolled in the NAP, and a member of the graduating class of 2019. The exclusion criteria stood as follows: anyone absent from the

program on the day of the presentation regardless of reason, anyone who was late to the presentation, or anyone who was unwilling to sign consent. A pre-test was provided to all subjects who signed a consent to participate, see Appendix B. The 30-minute PowerPoint module was presented with a question and answer session following the presentation. After the completion of the presentation, a post-test, identical to the pre-test, was administered. The test answers were anonymous with only a corresponding number to link pre- and post-test results.

Timeline

The project commenced in May 2018 during the fifth trimester of AHU's master's level NAP with a literature review. The proposal continued through June 2018. The first stage of data dissemination, the PowerPoint presentation, along with pre- and post-test data collection occurred during the Fall 2018 MSNA 504 Clinical Conference course. Data analysis was finalized in February 2019. The project concluded with the final stage of data dissemination via poster presentation, see Appendix D, in March and again in April 2019, meeting the requirements of the MSNA 690 Final Student Project course.

Data Collection Plan

Data collection was an identical pre- and post-test based on the information presented in the PowerPoint, given prior to the presentation and then again after the intervention. The pre-intervention test provided a baseline evaluation of the sample group's knowledge of the topic, and the post-intervention test was used to evaluate for any significant change in knowledge. A 10-question test was formulated specific to the learning objectives in the presentation with the goal of showing a statistical increase in post-intervention scores. The outcome was based on a change in the number of correct answers on the questionnaire after the intervention. All test results were collected and entered into an Excel worksheet to be accessible only to project team

members and Dr. Roy Lukman for means of statistical analysis. All data were stored electronically on the project team members' laptops as well as one online backup. Following the conclusion of the project, the information was deleted from both online and local storage. All data collected on paper was shredded following the conclusion of the project.

Evaluation Plan

The pre- and post-test results were collated and entered in an excel spreadsheet before submitting them to Dr. Lukman for review and analysis using SPSS software. The data was analyzed using a paired-sample t-test with a $p<0.05$ to determine statistical significance.

Results

A total of 21 students were present to participate in the pre-test, presentation, and post-test and all were included in the data analysis. Table 1 shows that mean scores improved from 26% on the pre-test to 55% on the post-test.

Table 1

Data Summary of Pre-test and Post-test Results

Test	Mean	N	Std. Deviation	Std. Error Mean
Pre-test	0.2619	21	0.12032	0.02626
Post-test	0.5524	21	0.21591	0.04712

Finally, a two-tailed paired-sample t-test were performed, displayed in Table 2, showing statistical significance at <0.001. There was a significant difference in the pre-test scores (M=.2619, SD=0.12032) and the post-test scores (M=.5524, SD=0.21591): $t(20)=-5.35$, $p=.000$.

Table 2

Statistical Analysis

Pre-test – Post-test	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% CI of Difference				
				Lower	Upper			
	-0.29048	0.24881	0.05429	-0.40373	-0.17722	-5.350	20	0.000

Limitations

The literature review was limited to randomized controlled trials within the last five years only. The maximum sample size of this scholarly project was limited to 21 and was a convenience sample. It was a homogenous sample, consisting solely of members of a single cohort from the same institution and field of study. Results cannot be generalized to all SRNAs. The educational intervention was executed within one class period, so retention was not evaluated. A better approach would include additional questionnaires weeks to months after the presentation to evaluate long-term retention and allow for comments and experiences after the intervention.

Conclusions

The review of literature showed that in cases where cannabinoids were used for under two weeks, higher doses were more effective. When used more than two weeks, clinical relevance and statistical significance were only supported with the use of Sativex in the treatment of allodynia. The placebo effect negated statistical significance in most studies, with only one distinguishing the placebo effect through the addition of a time to failure/withdrawal phase, resulting in statistical significance as a result. Improved data may be possible if additional studies also used this method. With regard to safety, the use of cannabinoids was generally found to be safe. Participants exhibited side effects to various degrees, but common side effects were not considered to significantly affect activities of daily living. Serious side effects were rare and

statistically as prevalent to populations dealing with similar comorbidities linked to chronic pain, such as depression.

There is little evidence to support the use of cannabinoids in the perioperative setting and limited evidence to support its use for chronic pain. However, our project results suggest that evidence-based presentations are effective in improving SRNA's knowledge base. As hypothesized, our results reflected a significant increase in the mean number of correct answers in the post-test following our presentation, $p<0.001$. We conclude that our dissemination of information in the form of the 30-minute PowerPoint presentation was effective, and because of the significant improvement of mean scores, repeating the prediction for a larger sample size would be appropriate.

An additional benefit to our project was the collaboration that was necessary to finish the various project deadlines. The project necessitated the communication and collaboration between multiple parties which expanded when the approval process met unexpected challenges. Communication between project members was also a critical piece that enabled growth and may benefit our patients in the future.

References

AbbVie Inc. (2017, October). *Marinol (dronabinol) capsules*. Retrieved June 13, 2018, from http://marinol.com/

Aizpurua-Olaizola, O., Elezgarai, I., Rico-Barrio, I., Zarandona, I., Etxebarria, N., & Usobiaga, A. (2017). Targeting the endocannabinoid system: Future therapeutic strategies. *Drug Discovery Today, 22*(1), 105-110. doi:10.1016/j.drudis.2016.08.005

Ballantyne, J. C. (2017). Opioids for the treatment of chronic pain: Mistakes made, lessons learned, and future directions. *Anesthesia and analgesia*, *125*(5), 1769-1778. doi:10.1213/ANE.0000000000002500

Burston, J. J., & Woodhams, S. G. (2014). Endocannabinoid system and pain: An introduction. *The Proceedings of the Nutrition Society, 73*(1), 106. doi:10.1017/S0029665113003650

Capozzi, J., Stapleton, C., & Beall, P. (2017, May 3). 'Finally,' Scott declares opioid epidemic a public health emergency. *TCA Regional News*.

Centers for Disease Control and Prevention. (n.d.). *Nutrition, Physical Activity, and Obesity: Data, Trends and Maps*. Retrieved June 13, 2018, from National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity: https://www.cdc.gov/nccdphp/dnpao/data-trends-maps/index.html

Compton, W. M., Boyle, M., & Wargo, E. (2015). Prescription opioid abuse: Problems and responses. *Preventive medicine, 80*, 5.

De Meijer, E. (2004). The breeding of cannabis cultivars for pharmaceutical end uses. In E. M. Williamson, G. W. Guy, B. A. Whittle, & P. Robson (Eds.), *Medicinal Uses of Cannabis and Cannabinoids* (pp. 55-70). London: Pharmaceutical Press. doi:10.1002/hup.631

De Vries, M., van Rijckevorsel, D. C., Vissers, K. C., Wilder-Smith, O. H., & van Goor, H. (2017). Tetrahydrocannabinol does not reduce pain in patients with chronic abdominal pain in a phase 2 placebo-controlled study. *Clinical Gastroenterology and Hepatology*, 1079-1086. doi:10.1016/j.cgh.2016.09.147

Dowell, D., Haegerich, T. M., & Chou, R. (2016). *CDC guideline for prescribing opioids for chronic pain — United States, 2016.* Centers for Disease Control and Prevention. doi:10.15585/mmwr.rr6501e1

Edlund, M. J., Martin, B. C., Russo, J. E., DeVries, A., Braden, J. B., & Sullivan, M. D. (2014). The Role of Opioid Prescription in Incident Opioid Abuse and Dependence Among Individuals With Chronic Noncancer Pain: The Role of Opioid Prescription. *The Clinical Journal of Pain, 30*(7), 557-564. doi:10.1097/AJP.0000000000000021

Fitzcharles, M. A., Ste-Marie, P. A., Häuser, W., Clauw, D. J., Jamal, S., Karsh, J., . . . Walsh, Z. (2016). Efficacy, tolerability, and safety of cannabinoid treatments in the rheumatic diseases: A systematic review of randomized controlled trials. *Arthritis Care and Research, 68*(5), 681-688. doi:10.1002/acr.22727

Fla. Stat. § 381.986. (2018).

Fordyce, W. (2001). Pain in cancer and chronic non-cancer conditions: similarities and differences. *Acta Anaesthesiologica Scandinavica, 45*(9), 1086-1089. doi:10.1034/j.1399-6576.2001.450906.x

Gallily, R., Yekhtin, Z., & Hanuš, L. O. (2015). Overcoming the bell-shaped dose-response of cannabidiol by using cannabis extract enriched in cannabidiol. *Pharmacology & Pharmacy, 6*(2), 75-85. doi:10.4236/pp.2015.62010

Gaskin, D. J., & Richard, P. (2012). The economic costs of pain in the United States. *American Pain Society, 13*(8), 715-724. doi:10.1016/j.jpain.2012.03.009

GW Pharmaceuticals. (2016). *Sativex (delta-9-tetrahydrocannabinol and cannabidiol).* Retrieved June 13, 2018, from https://www.gwpharm.com/products-pipeline/sativex-delta-9-tetrahydrocannabinol-and-cannabidiol

Häuser, W., Petzke, F., & Fitzcharles, M. A. (2018). Efficacy, tolerability and safety of cannabis-based medicines for chronic pain management – an overview of systematic reviews. *European Journal of Pain, 22*(3), 455-470. doi:10.1002/ejp.1118

Hayakawa, K., Mishima, K., Hazekawa, M., Sano, K., Irie, K., Orito, K., . . . Fujiwara, M. (2008). Cannabidiol potentiates pharmacological effects of Δ9 -tetrahydrocannabinol via CB1 receptor-dependent mechanism. *Brain Research, 1188*, 157-164. doi:10.1016/j.brainres.2007.09.090

Hill, K. P. (2015). Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: A clinical review. *Journal of American Medical Association, 313*(24), 2474-2483. doi:10.1001/jama.2015.6199

Hoggart, B., Ratcliffe, S., Ehler, E., Simpson, K. H., Hovorka, J., Lejcko, J., . . . Serpell, M. (2015). A multicentre, open-label, follow-on study to assess the long-term maintenance of effect, tolerance and safety of THC/CBD oromucosal spray in the management of neuropathic pain. *Journal of Neurology, 262*(1), 27-40. doi:10.1007/s00415-014-7502-9

Hurd, Y. L. (2017). Cannabidiol: Swinging the marijuana pendulum from ‘Weed’ to medication to treat the opioid epidemic. *Trends in Neurosciences, 40*(3), 124-127. doi:10.1016/j.tins.2016.12.006

Hwang, J. K., & Clarke, H. (2016). Cannabis and pain: A review. *Journal of Pain Management, 9*(4), 395. Retrieved from https://www.novapublishers.com

Institute of Medicine. (2011). *Relieving Pain in America: A Blueprint for Transforming.* Washington, DC: The National Academies. doi:10.17226/13172

Jara, C., del Barco, S., Grávalos, C., Hoyos, S., Hernández, B., Muñoz, M., . . . de las Peñas, R. (2018). SEOM clinical guideline for treatment of cancer pain (2017). *Clinical and Translational Oncology, 20*(1), 97-107. doi:10.1007/s12094-017-1791-2

Jarvis, S., Rassmussen, S., & Winters, B. (2017). Role of the endocannabinoid system and medical cannabis. *The Journal for Nurse Practitioners, 13*(8), 525-531. doi:10.1016/j.nurpra.2017.05.014

Kaur, R., Ambwani, S. R., & Singh, S. (2016). Endocannabinoid system: A multi-facet therapeutic target. *Current Clinical Pharmacology, 11*(2), 110-117. doi:10.2174/1574884711666160418105339

Langford, R. M., Mares, J., Novotna, A., Vachova, M., Novakova, I., Notcutt, W., & Ratcliffe, S. (2013). A double-blind, randomized, placebo-controlled, parallel-group study of THC/CBD oromucosal spray in combination with the existing treatment regimen, in the relief of central neuropathic pain in patients with multiple sclerosis. *Journal of Neurology, 260*(4), 984-987. doi:10.1007/s00415-012-6739-4

Levin, A. (2017). Tackling opioid overdose epidemic demands multiple approaches. *Psychiatrics News, 52*(13), 1. doi:10.1176/appi.pn.2017.7a6

Lynch, M. E., Cesar-Rittenberg, P., & Hohmann, A. G. (2014). A double-blind, placebo-controlled, crossover pilot trial with extension using an oral mucosal cannabinoid extract

for treatment of chemotherapy-induced neuropathic pain. *Journal of Pain and Symptom Management, 47*(1), 166-173. doi:10.1016/j.jpainsymman.2013.02.018

Lynch, M., & Ware, M. (2015). Cannabinoids for the treatment of chronic non-cancer pain: An updated systematic review of randomized controlled trials. *Journal of Neuroimmune Pharmacology, 10*(2), 293-301. doi:10.1007/s11481-015-9600-6

Meda Pharmaceuticals Inc. (2018). *Cesamet (nabilone) capsules, 1mg: A different path*. Retrieved June 13, 2018, from http://www.cesamet.com/

Moran, M. (2016). The new CDC guideline: When to limit opioids and what to use as alternatives for chronic pain. *Neurology Today, 16*(8), 10-11. doi:10.1097/01.NT.0000483052.94102.2f

Nahin, R. L. (2012). Estimates of pain prevalence and severity in adults: United States, 2012. *The Journal of Pain, 16*(8), 769-780. doi:10.1016/j.jpain.2015.05.002

Olfson, M., Wall, M. M., & Blanco, C. (2018). Medical marijuana and the opioid epidemic: Response to theriault and schlesinger. *American Journal of Psychiatry, 175*(3), 284-285. doi:10.1176/appi.ajp.2017.17101149r

Paice, J. A., Portenoy, R., Lacchetti, C., Campbell, T., Cheville, A., Citron, M., . . . Bruera, E. (2016). Management of chronic pain in survivors of adult cancers: American society of clinical oncology clinical practice guideline. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 34*(27), 3325-3345. doi:10.1200/JCO.2016.68.5206

Patrick, S. W., Fry, C. E., Jones, T. F., & Buntin, M. B. (2016). Implementation of prescription drug monitoring programs associated with reductions in opioid-related death rates. *Health Affairs (Project Hope), 35*(7), 1324. doi:10.1377/hlthaff.2015.1496

Penney, L. S., Ritenbaugh, C., DeBar, L. L., Elder, C., & Deyo, R. A. (2016). Provider and patient perspectives on opioids and alternative treatments for managing chronic pain: A qualitative study. *BMC Family Practice, 17*(1), 2161. doi:10.1186/s12875-016-0566-0

Raji, M. A., Kuo, Y., Adhikari, D., Baillargeon, J., & Goodwin, J. S. (2018). Decline in opioid prescribing after federal rescheduling of hydrocodone products. *Pharmacoepidemiology and Drug Safety, 27*(5), 513-519. doi:10.1002/pds.4376

Russo, E. B. (2016). Beyond Cannabis: Plants and the Endocannabinoid System. *Trends in Pharmacological Sciences, 37*(7), 594-605. doi:10.1016/j.tips.2016.04.005

Russo, M., Naro, A., Leo, A., Sessa, E., D'Aleo, G., Bramanti, P., & Calabrò, R. S. (2016). Evaluating Sativex® in neuropathic pain management: A clinical and neurophysiological assessment in multiple sclerosis. *Pain Medicine, 17*(6), 1145-1154. doi:10.1093/pm/pnv080

Schimrigk, S., Marziniak, M., Neubauer, C., Kugler, E. M., Werner, G., & Abramov-Sommariva, D. (2017). Dronabinol is a safe long-term treatment option for neuropathic pain patients. *European Neurology, 78*(5-6), 320-329. doi:10.1159/000481089

Serpell, M., Ratcliffe, S., Hovorka, J., Schofield, M., Taylor, L., Lauder, H., & Ehler, E. (2014). A double-blind, randomized, placebo-controlled, parallel group. *European Journal of Pain, 18*(7), 999-1012. doi:10.1002/j.1532-2149.2013.00445.x

Substance Abuse and Mental Health Services Administration. (2017). *Key substance use and mental health indicators in the United States: Results from the 2016 National Survey on Drug Use and Health.* (HHS Publication No. SMA 17-5044, NSDUH Series H-52). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from https://www.samhsa.gov/data

Turcotte, D., Doupe, M., Torabi, M., Gomori, A., Ethans, K., Esfahani, F., . . . Namaka, M. (2015). Nabilone as an adjunctive to gabapentin for multiple sclerosis-induced neuropathic pain: a randomized controlled trial. *Pain Medicine, 16*(1), 149-159. doi:10.1111/pme.12569

United States Census Bureau. (n.d.). *QuickFacts: Florida*. Retrieved June 13, 2018, from QuickFacts: https://www.census.gov/quickfacts/geo/chart/FL/

Voelker, R. (2016). Insurer curbs opioid prescriptions. *Journal of the American Medical Association, 316*(22), 2349-2349. doi:10.1001/jama.2016.17522

Wallace, M. S., Marcotte, T. D., Umlauf, A., Gouaux, B., & Atkinson, J. H. (2015). Efficacy of inhaled cannabis on painful diabetic neuropathy. *Journal of Pain, 16*(7), 616-627. doi:10.1016/j.jpain.2015.03.008

Wilsey, B., Marcotte, T. D., Deutsch, R., Zhao, H., Prasad, H., & Phan, A. (2016). An exploratory human laboratory experiment evaluating vaporized cannabis in the treatment of neuropathic pain from spinal cord injury and disease. *Journal of Pain, 17*(9), 982-1000. doi:10.1016/j.jpain.2016.05.010

Wilsey, B., Marcotte, T., Deutsch, R., Gouaux, B., Sakai, S., & Donaghe, H. (2013). Low-dose vaporized cannabis significantly improves neuropathic pain. *Journal of Pain, 14*(2), 136-148. doi:10.1016/j.jpain.2012.10.009

Appendix A

AHU NAP Capstone Project Informed Consent

We are MSNA students in the Nurse Anesthesia Program (NAP) at AdventHealth University (AHU). We are doing a Capstone Project called *Are Cannabinoids Effective in Treating Chronic Non-malignant Pain in Adult Patients*. This project is being supervised by department faculty. We would like to invite you to participate in this project. The main purpose of this form is to provide information about the project so you can make a decision about whether you want to participate.

WHAT IS THE PROJECT ABOUT?

The purpose of this project is to expand the knowledge base of our cohort in regards to cannabinoids in the treatment of non-malignant chronic pain in adult patients.

WHAT DOES PARTICIPATION IN THIS PROJECT INVOLVE?

If you decide to participate in this project, you will be asked to complete an anonymous pre-assessment, attend a classroom presentation, and then complete an anonymous post-assessment. The assessment will address your initial knowledge regarding the use of cannabinoids in the treatment of non-malignant chronic pain, then afterwards it will test what you have just heard from the presentation. Your participation by attendance at the presentation and completion of the survey is anticipated to take approximately one hour.

WHY ARE YOU BEING ASKED TO PARTICIPATE?

You have been invited to participate as part of a convenience sample of students currently enrolled in the AHU NAP. Your participation in this study is voluntary. You may choose to not to participate. The decision to participate or not participate in this research study is completely up to you. If you choose not to participate your refusal to participate in this research study will involve no penalty or loss of benefits to you. If you choose to participate, you can change your mind later and withdraw your consent and discontinue participation from this study at any time. If you chose to withdraw from the study, inform the primary investigator of your wishes.

WHAT ARE THE RISKS INVOLVED IN THIS PROJECT?

Although no project is completely risk-free, we don't anticipate that you will be harmed or distressed by participating in this project.

ARE THERE ANY BENEFITS TO PARTICIPATION?

We don't expect any direct benefits to you from participation in this project. The possible indirect benefit of participation in the project is the opportunity to gain additional knowledge about cannabinoid use in treatment of chronic non-malignant pain.

HOW WILL THE INVESTIGATORS PROTECT PARTICIPANTS' CONFIDENTIALITY?

The results of the project will be published, but your name or identity will not be revealed. To maintain confidentiality of assessments, the investigators will conduct this project in such a way to ensure that information is submitted without participants' identification. The information on paper will be securely stored and shredded upon completion of the project. The digital information will be stored locally and online until the conclusion of the project at which point the information will be deleted from all sources. Thus, the investigators will not have access to any participants' identities.

WILL IT COST ANYTHING OR WILL I GET PAID TO PARTICIPATE IN THE PROJECT?

Your participation will cost approximately one hour of your time but will require no monetary cost on your part. You will not be paid to participate.

VOLUNTARY CONSENT

You do not have to participate in this research study and choosing not participate in this study will not involve any penalty or loss of benefit to you. The decision to participate or not participate in this research study is completely up to you. If you choose to participate, you can change your mind later and withdraw your consent and discontinue participation from this study at any time. If you choose to withdraw from the study, inform the primary investigator of your wishes.

By signing this form, you are saying that you have read this form, you understand the risks and benefits of this project, and you know what you are being asked to do. The investigators will be happy to answer any questions you have about the project. If you have any questions or concerns about the project process or the investigators, please contact the Nurse Anesthesia Program at (407) 303-9331.

_____ **Date** _____

Participant Signature/ Participant Name

_____ **Participant Name (PRINTED LEGIBLY)**

Appendix B

Pre/Post-Test

1. Which of the following is not a reason why is it becoming more important for anesthesia providers to have a basic understanding of cannabinoids in the management of non-malignant chronic pain in adults?
   a) The opioid epidemic has lead to increased interest in complimentary or alternative approaches to pain management.
   b) Anesthesia providers are starting to prescribe cannabinoids for peri-operative pain.
   c) Providers may encounter more patients either taking cannabinoids or have questions regarding their use.
   d) Florida has legalized medicinal marijuana and cannabinoids.

2. Which of the following is/are an endogenous source(s) of cannabinoid ligands?
   a) Anandamide (AEA)
   b) Cannabidiol
   c) Dronabinol
   d) Δ9-tetrahydrocannabinol

3. ECS stands for
   a) Extra Cortical System
   b) Endo Cerebral Stimulus
   c) Endocannabinoid System
   d) Extra-Curricular Sativex

4. What type of cannabinoid receptor is found primarily in the peripheral immune cells among other locations?
   a) CB1
   b) CB2
   c) a & b
   d) None of the above

5. Which of the following is not true regarding the efficacy of cannabinoids in the treatment of non-malignant chronic pain in adults?
   a) The type of cannabinoid was not relevant
   b) They were effective in the short-term
   c) Clinical significance (> 30% reduction in pain) was mixed in both short and long-term studies
   d) Higher dosages had greater efficacy

6. According to recent studies, the strength of the placebo effect was greatly portrayed in the following method(s)
   a) Short term studies
   b) Long term studies
   c) No control

d) Withdrawal and Time to failure

7. Cannabinoids are a great substitute for opiates.
   a) True
   b) False

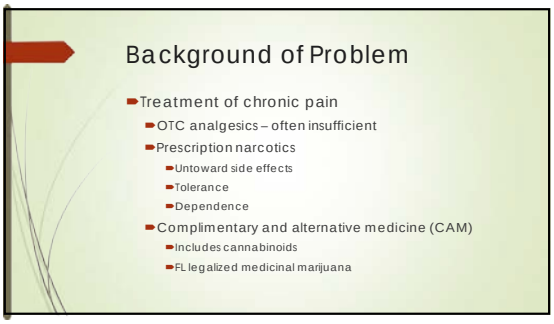
8. Which of the following statements is false regarding short-term side effects associated with cannabinoid use in adults with non-malignant chronic pain?
   a) Attention, learning, and memory function were found to be significantly impaired versus placebo.
   b) Somnolence and euphoria are associated with higher dosages.
   c) Cognitive declines were thought to significantly impact daily living.
   d) All the following statements are true.

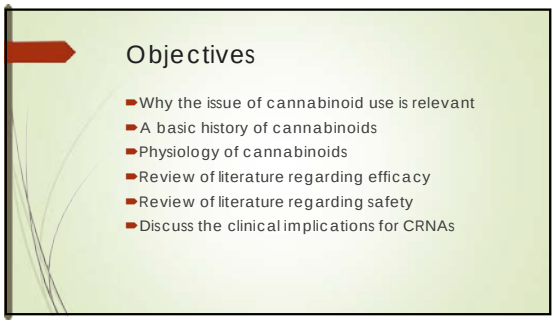
9. Which of the following are common side effects associated with cannabinoid use in adults with non-malignant chronic pain when taken more than two weeks?
   a) Dizziness
   b) Dysgeusia
   c) Nausea
   d) Fatigue
   e) All the above

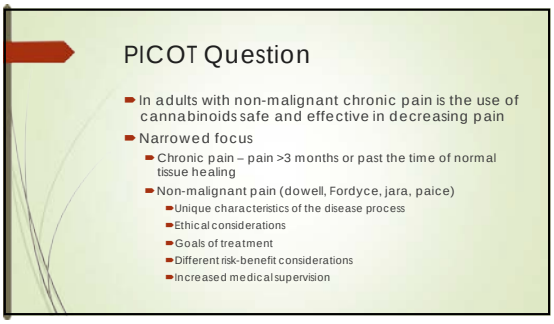
10. Which of the following are common serious adverse effects associated with cannabinoid use in adults with non-malignant chronic pain?
   a) Suicidal ideations
   b) Amnesia
   c) Paranoia
   d) All the above
   e) No serious adverse effects were found to be common

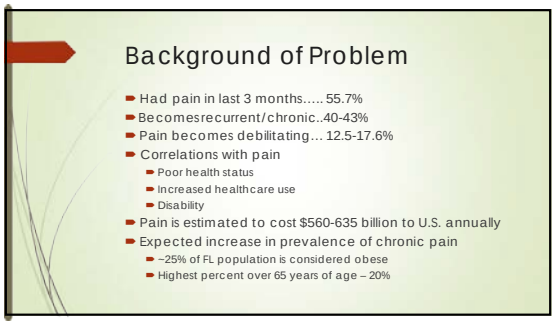
Appendix C

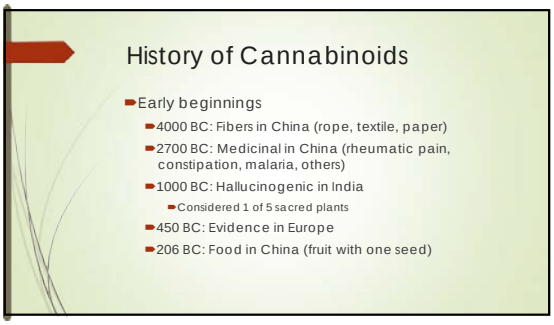
PowerPoint Presentation











History of Cannabinoids

- Western medicine
  - Mid-1800s: Europe
    - Willian B. O'Shaughnessy – therapeutic effects
    - Jacques-Joseph Moreau – psychoactive effects
  - 1860: 1st clinical conference in U.S. at Ohio State University
  - ~1900: pharmaceutical tinctures and extracts
  - Early 1900s: decline in use
  - 1970: Controlled Substance Act made it a controlled substance

ECS – G protein-coupled receptors

- Cannabinoid receptor 1 (CB1)
  - Primarily in CNS and digestive organs
  - Presynaptic nerve cells in spinal cord
  - Negative feedback loop to inhibit pain signaling
- Cannabinoid receptor 2 (CB2)
  - Primarily found in spinal cord and bone marrow
  - Predominant receptor in immune cells
  - No psychoactive effects
  - Thought to stimulate endorphin release

History of Cannabinoids

- Recent history
  - 1964: Δ9-Tetrahydrocannabinol (THC) is isolated
  - 1970s: research peaks and then declines
  - 1990s: receptors/endogenous cannabinoid isolated
  - 1996: California legalizes medicinal marijuana
  - 2012: Colorado/Washington legalize recreational use
  - Currently
    - Recreational use is legal in 9 states
    - Medicinal use is legal in 30 states (FL in 2016)
    - The endocannabinoid system (ECS) research continues to grow

Prescription Cannabinoids

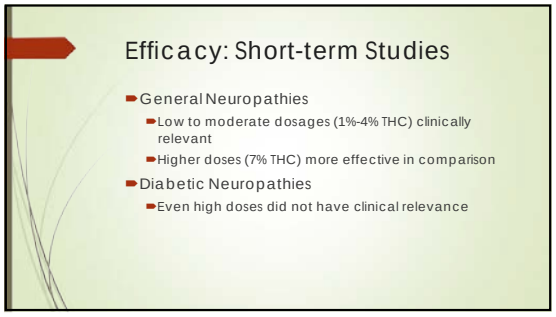
Drug	Brand Name	Route of Admin
Dronabinol (synthetic THC)	Marinol	Capsule
Indications: chemotherapy-induced nausea and vomiting anorexia associated with AIDS		
Nabilone (racemic THC)	Cesamet	Capsule
Indications: chemotherapy-induced nausea and vomiting		
Cannabidiol extract (CBD)	Epidiolex	Oral solution
Indications: 2 forms of epilepsy in children two and older		
THC/CBD combination	Sativex	Sublingual Spray
Indications: spasticity in multiple sclerosis		
Full-spectrum extract	Idrasil	Tablet
Indications: None; considered a dietary supplement		

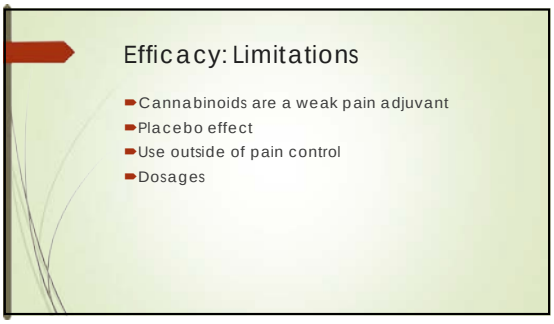
ECS – Endocannabinoids

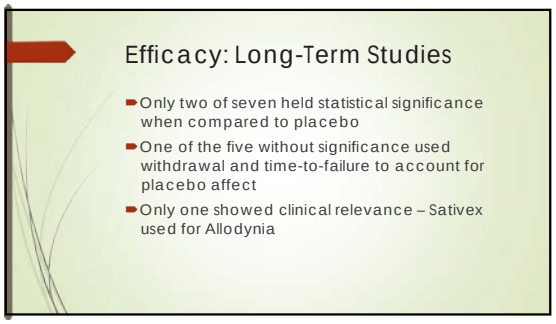
- Five known endogenous ligands
  - Anandamide (AEA)
  - 2-archidonoylglyceral (2-AG)
  - 2-archidonoylglyceral ether (noladin ether)
  - O-archidonoyl ethanolamine(virodhamine)
  - N-arachidonoyl dopamine
- Only known retrograde synaptic neurotransmitters
- Produced on demand rather than being stored
- Stimulated by pain, stress, infection, or inflammation

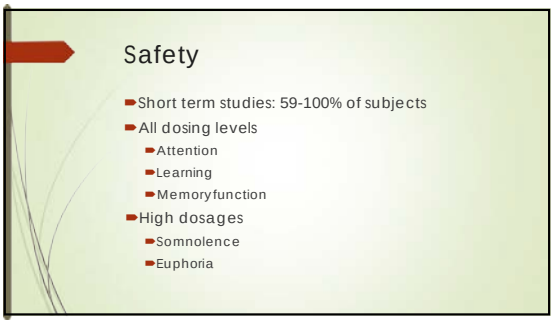
Clinical Premises

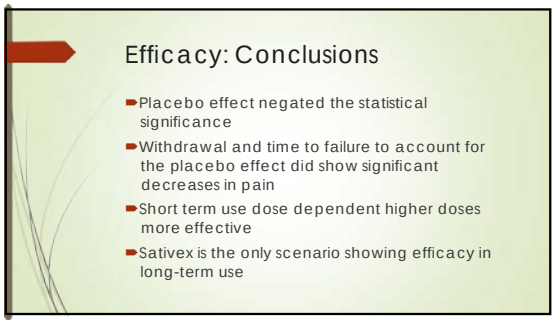
- Clinical Relevance
  - 30% pain reduction
- All studies were looking at cannabinoids as an additional adjuvant never alone.
- Placebo Effect
- Withdrawal and Time to Failure
- Breakthrough pain medicine was available

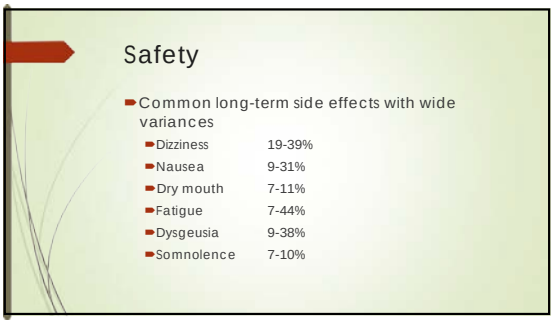

Efficacy: Short-term Studies
General Neuropathies
Low to moderate dosages (1%-4% THC) clinically relevant
Higher doses (7% THC) more effective in comparison
Diabetic Neuropathies
Even high doses did not have clinical relevance


Efficacy: Limitations
Cannabinoids are a weak pain adjuvant
Placebo effect
Use outside of pain control
Dosages


Efficacy: Long-Term Studies
Only two of seven held statistical significance when compared to placebo
One of the five without significance used withdrawal and time-to-failure to account for placebo affect
Only one showed clinical relevance – Sativex used for Allodynia


Safety
Short term studies: 59-100% of subjects
All dosing levels
Attention
Learning
Memoryfunction
High dosages
Somnolence
Euphoria


Efficacy: Conclusions
Placebo effect negated the statistical significance
Withdrawal and time to failure to account for the placebo effect did show significant decreases in pain
Short term use dose dependent higher doses more effective
Sativex is the only scenario showing efficacy in long-term use


Safety
Common long-term side effects with wide variances
Dizziness 19-39%
Nausea 9-31%
Dry mouth 7-11%
Fatigue 7-44%
Dysgeusia 9-38%
Somnolence 7-10%

Safety

- Rare Side Effects
  - Two out of 339 subjects had suicidal ideations, but one of them was in the placebo group
  - Three out of 234 subjects had amnesia, paranoia, and a suicide attempt

Questions?

- Thank You

Safety: Conclusions

- The demographic of patients
- Placebo effect strong regarding side effects
- The dosage results in more side effects
- The common side effects did not significantly impact daily living

References

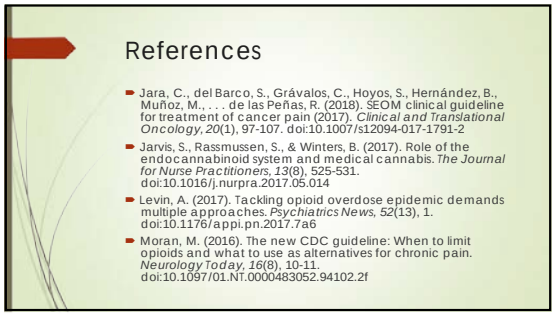
- Ballantyne, J. C. (2017). Opioids for the treatment of chronic pain: Mistakes made, lessons learned, and future directions. *Anesthesia and analgesia, 125*(5), 1769-1778. doi:10.1213/ANE.0000000000002500
- Centers for Disease Control and Prevention. (n.d.). *Nutrition, Physical Activity, and Obesity: Data, Trends and Maps.* Retrieved June 13, 2018, from National Center for Chronic Disease Prevention and Health Promotion, Division of Nutrition, Physical Activity, and Obesity: https://www.cdc.gov/nccdphp/dnpao/data-trends-maps/index.html
- Dowell, D., Haegerich, T. M., & Chou, R. (2016). *CDC guideline for prescribing opioids for chronic pain — United States, 2016.* Centers for Disease Control and Prevention. doi:10.15585/mmwr.rr6501e1

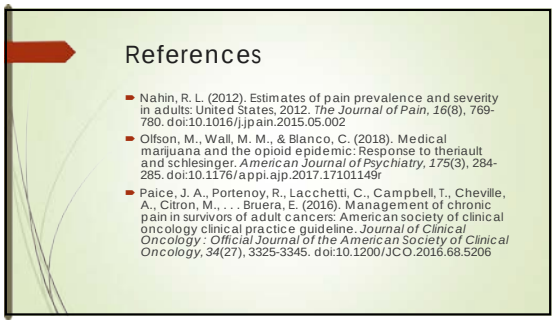
Clinical Implications

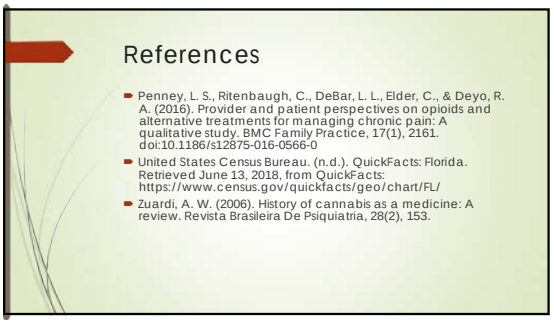
- Very limited evidence for the perioperative setting – non-diabetic neuropathy
- Limited clinical relevance for chronic pain management
- Cannabinoids appear to be safe without significantly impacting daily function
- Non-pain benefits of cannabinoids
- One study on emergence

References

- Fordyce, W. (2001). Pain in cancer and chronic non-cancer conditions: similarities and differences. *Acta Anaesthesiologica Scandinavica, 45*(9), 1086-1089. doi:10.1034/j.1399-6576.2001.450906.x
- Gaskin, D. J., & Richard, P. (2012). The economic costs of pain in the United States. *American Pain Society, 13*(8), 715-724. doi:10.1016/j.jpain.2012.03.009
- Hurd, Y. L. (2017). Cannabidiol: Swinging the marijuana pendulum from 'Weed' to medication to treat the opioid epidemic. *Trends in Neurosciences, 40*(3), 124-127. doi:10.1016/j.tins.2016.12.006
- Institute of Medicine. (2011). *Relieving Pain in America: A Blueprint for Transforming.* Washington, DC: The National Academies. doi:10.17226/13172


References
Jara, C., del Barco, S., Grávalos, C., Hoyos, S., Hernández, B., Muñoz, M., . . . de las Peñas, R. (2018). SEOM clinical guideline for treatment of cancer pain (2017). Clinical and Translational Oncology, 20(1), 97-107. doi:10.1007/s12094-017-1791-2
Jarvis, S., Rassmussen, S., & Winters, B. (2017). Role of the endocannabinoid system and medical cannabis. The Journal for Nurse Practitioners, 13(8), 525-531. doi:10.1016/j.nurpra.2017.05.014
Levin, A. (2017). Tackling opioid overdose epidemic demands multiple approaches. Psychiatrics News, 52(13), 1. doi:10.1176/appi.pn.2017.7a6
Moran, M. (2016). The new CDC guideline: When to limit opioids and what to use as alternatives for chronic pain. Neurology Today, 16(8), 10-11. doi:10.1097/01.NT.0000483052.94102.2f


References
Nahin, R. L. (2012). Estimates of pain prevalence and severity in adults: United States, 2012. The Journal of Pain, 16(8), 769-780. doi:10.1016/j.jpain.2015.05.002
Olfson, M., Wall, M. M., & Blanco, C. (2018). Medical marijuana and the opioid epidemic: Response to theriault and schlesinger. American Journal of Psychiatry, 175(3), 284-285. doi:10.1176/appi.ajp.2017.17101149r
Paice, J. A., Portenoy, R., Lacchetti, C., Campbell, T., Cheville, A., Citron, M., . . . Bruera, E. (2016). Management of chronic pain in survivors of adult cancers: American society of clinical oncology clinical practice guideline. Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology, 34(27), 3325-3345. doi:10.1200/JCO.2016.68.5206


References
Penney, L. S., Ritenbaugh, C., DeBar, L. L., Elder, C., & Deyo, R. A. (2016). Provider and patient perspectives on opioids and alternative treatments for managing chronic pain: A qualitative study. BMC Family Practice, 17(1), 2161. doi:10.1186/s12875-016-0566-0
United States Census Bureau. (n.d.). QuickFacts: Florida. Retrieved June 13, 2018, from QuickFacts: https://www.census.gov/quickfacts/geo/chart/FL/
Zuardi, A. W. (2006). History of cannabis as a medicine: A review. Revista Brasileira De Psiquiatria, 28(2), 153.

Appendix D

Poster

Are Cannabinoids Effective in Treating Non-Malignant Chronic Pain in Adult Patients

Kenneth W. Luk, RN, SRNA and Terry L. Tokash, BSN, SRNA
Project Mentor: Dr. Kayvan Ariani, MD
Project Chair: Dr. Sarah Snell, DNP, CRNA
AdventHealth University

AdventHealth UNIVERSITY

Sigma GLOBAL NURSING EXCELLENCE — Chi Upsilon Chapter

Problem

- Chronic pain is expected to continue to rise in prevalence. Cannabinoids have shown potential in managing this patient population. With the legalization of medicinal marijuana, an educational intervention is indicated to increase the knowledge base of cannabinoids to better drive care.
- This project aims to address two questions:
  1. In adults with non-malignant chronic pain, is the use of cannabinoids safe and effective in decreasing pain?
  2. In students enrolled in the AdventHealth University's masters level certified Nurse Anesthetist Program (NAP), does a 30-minute PowerPoint presentation on the safety and effectiveness of cannabinoids in treating chronic non-malignant pain increase their knowledge base?

Literature Review

- The endocannabinoid system (ECS) produces a negative feedback loop that can inhibit pain signaling.
- The marijuana plant contains Δ9-tetrahydrocannabinol (Δ9-THC), cannabinol, and cannabidiol (CBD). These three ligands form the bulk of research and all prescribed cannabinoids contain at least one.
- **Short-term**
  - Efficacy: clinically effective for general neuropathies
  - Safety: 59-100% experienced symptoms, but did not impact ADLs
- **Long-term**
  - Efficacy: only Sativex for allodynia showed clinical relevance
  - Safety: similar to placebo, with rare serious side effects expected for the population

Exogenous Ligand Medication	Brand Name	Route of Admin
Dronabinol (synthetic THC)	Marinol	Capsule
Indications: chemo-induced nausea & vomiting anorexia associated with AIDS		
Nabilone (racemic THC)	Cesamet	Capsule
Indications: chemo-induced nausea and vomiting		
Cannabidiol extract (CBD)	Epidiolex	Oral solution
Indications: 2 forms of epilepsy in children two and older		
THC/CBD combination	Sativex	Sublingual Spray
Indications: spasticity in multiple sclerosis		
Full-spectrum extract	Idrasil	Tablet
Indications: none; considered a dietary supplement		

Analysis & Conclusions

- Mean scores improved from 26.19% to 55.24%
- A two-tailed paired-sample t-test showed statistical significance at <0.001

Test	Mean	N	Std. Deviation	Std. Error Mean
Pre-test	0.2619	21	0.12032	0.02626
Post-test	0.5524	21	0.21591	0.04712

Pre-test – Post-test	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std. Deviation	Std. Error Mean	95% CI of Difference Lower	Upper			
	-0.29048	0.24881	0.05429	-0.40373	-0.17722	-5.350	20	<0.001

Methods

- Quantitative pre-post test design
- Statistical data collected & analyzed with a paired t-test
- Significance threshold for the paired sample t-test was set using the traditional p <0.05

Findings

- Very limited evidence for the perioperative setting
- Cannabinoids appear to be safe without impacting daily function
- A 30-minute PowerPoint presentation was effective in improving knowledge

References

- Available upon request on a separate paper.

Acknowledgements

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