Medical Cannabis 2018

The International Annual Congress on

Controversies on Cannabis-Based Medicines

25-26 June 2018 | Vienna, Austria

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ABSTRACT BOOK

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Poster Board #60

Endocannabinoids and Insomnia

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Background

The sleep-waking cycle is a complex trait modulated by several brain structures and neurotransmitters. In the last 2 decades mounting evidence has involved endocannabinoids in the regulation of this cycle. It has also been shown that treatment of insomnia with cannabinoids has been useful for some patients.
Objective

To further explore the role of the endocannabinoid system in the regulation of sleep in a rodent model.

Method

In this study, Wistar male mother-care deprived (MCD) and non-mother-care deprived (NMCD) rats were utilized. MCD rats were deprived for 3h daily from the postnatal day (PND)2 through PND16. When they become adult (PND90) the spontaneous or endocannabinoid-induced sleep-waking cycle was evaluated by means of polysomnography. Oleamide was systemically administered while 2-AG was infused into the lateral hypothalamus.

Results

MCD rats exhibit short total time of spontaneous Non-Rapid-Eye-Movement (NREM) and REM sleep as compared to NMCD. Both endocannabinoids increased sleep, particularly REM sleep. Endocannabinoid-treated MCD rats exhibit a sleep-waking cycle comparable to vehicle-treated NMCD rats. Western blot analysis indicated that MCD express less CB1 receptor in the frontal cortex and hippocampus while higher in the nucleus accumbens than NMCD rats.

Conclusion

We believe MCD interferes with endocannabinoid system maturity thereby inducing an insomnia-like pattern. In addition, endocannabinoid treatment restores the sleep normal pattern. These findings further support the notion that endocannabinoids participate in the regulation of sleep and stress out their potential utility to treat some types of insomnia.

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Poster Board #61

The Improvement of Memory Deficits in a Familiar Mouse Model of Alzheimer's Disease due to Prolonged Treatment with Tetrahydrocannabinol

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Introduction

The endocannabinoid system is viewed as part of the neuroprotective endogenous mechanism of the central nervous system and the activation of cannabinoid receptors could be seen as a promising therapeutic strategy and also as a target for the treatment in Alzheimer's Disease.
The aim of the study was to analyze the therapeutic potential of Tetrahydrocannabinol (THC) in a typical AD's mouse model: 5XFAD. This model is useful to study the effects produced by high levels of human amyloid in the brain and by the appearance of amyloid deposits in the brain parenchyma in form of neurotic plaques. (Oakley et al.,2006).

Material and Methods

Five months old 5XFAD-mice (female) were treated daily with an intraperitoneal injection of THC (20mg/kg) or a Vehicle (5% ethanol, 5% Tween80 in 0,9% sodium chloride solution) and were compared with sex and age-matched WT mice .
Behavorial tests including Elevated-Plus-Maze, Crossmaze and Morris Water Maze were performed to exhibit cognitive and anxiety impairments.
Plaqueload quantification will be performed via DAB-staining.

Results and Discussion

THC alleviate spatial memory deficits in the MWM. Furthermore an improved performance in the Crossmaze is exhibited after THC treatment. THC causes anxiety alterations in the 5XFAD-mice.
The effects prolonged THC treatment on Aβ-induced neurotoxicity, neuroinflammation and Beta-Amyloid plaque deposition will be presented.
In conclusion, the present study shows that prolonged THC treatment can be therapeutic beneficial for several altered parameters in AD including anxiety and memory.

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Poster Board #62

Positive Effects of Cannabinoid-based WIN 55,212-2 Therapy in a Mouse Model of Sporadic Alzheimer`s Disease

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Background

Targeting the endocannabinoid system could be an approach for new treatments of Alzheimer`s Disease (AD). Endocannabinoid signaling has been demonstrated to be involved in memory formation, motor control, inflammation & oxidative stress. Several *in vitro* studies showed that cannabinoids reduce Aβ-induced neurotoxicity as well as cell death & facilitate neurogenesis. Recently, it could be demonstrated that cannabinoids stimulate the removal of intraneuronal Aβ *in vitro*. WIN 55,212-2 (WIN) is a synthetic cannabinoid binding more efficient to CB_1 and CB_2 receptors than Tetrahydrocannabinol (THC).

Objective

The aim of the study was to investigate the multi-faceted therapeutic potential of WIN *in vivo* using Tg4-42 mice. These mice expressing N-truncated Aß 4-42 develop severe hippocampal neuron loss & memory deficits (Bouter et al. 2013).

Material & Methods

A group of five months old male & female Tg4-42 mice (therapeutic group) and a group of three months old Tg4-42 (preventive group) were treated daily with WIN (0,2mg/kg) for six weeks. Sex and age-matched control Tg4-42 mice treated with the vehicle solution (5% ethanol, 5% Tween80 in 0,9% sodium chloride solution) were used for control group. Behavior tests were performed at the age of six months assessing memory, motor functions & anxiety (Rota Rod, Elevated-Plus-Maze, Dark/Light & Morris Water Maze). Design-based Stereology will be used to analyze neuron loss and neurogenesis in Tg4-42 mice.

Results

Therapeutically and especially preventively treated mice show significantly better spatial memory in Water Maze Test. The effects of the neurogenesis in the dentate gyrus of the hippocampus of Tg4-42 mice and WT mice will be presented.

Conclusion

Our findings reinforce a preventive cannabis-based medicine as a potential therapy against Alzheimer's Disease.

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Poster Board #63

Pharmacology of GABAA Receptor Subtypes: Phytocannabinoids Act on GABAA Receptors

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Phytocannabinoids had been identified as promising cannabis derived pharmacologically active compounds. Their actions are not limited to molecular targets of the endocannabinoid system as CB1, CB2 and GPR55 receptors. Instead, TRP channels were found to be main targets of CBD, the non-psychoactive phytocannabinoid with an astonishing pharmacological profile. Increasing evidence of modulatory effects on Cys-loop receptors as GlyR, 5HT3A and n7-AChR had been shown. GABAA receptors, members of Cys-loop receptors display complex structural and pharmacological properties and are distributed in different compositions in many cell types but mainly in neurons. 19 different subunits form pentameric chloride ion channels and most of them were activated by GABA. Their main function is inhibition due to hyperpolarization by synaptic and extrasynaptic receptors. Many endogenous and exogenous compounds influence the function of GABAA receptors. We demonstrate direct positive allosteric modulation of CBD and THC in distinct subtypes of GABAA receptors. We identified a novel action of CBD and not THC as potent positive allosteric modulator (PAM) of α4β3δ receptors. Moreover, delta containing receptors displayed strong response to phytocannabinoids compared to gamma containing receptors. Actions of CBD on delta containing receptors suggest pharmacological relevance, based on the enhancement of tonic inhibition in neurons.

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Poster Board #64

Anticancer Effects of Phytocannabinoids Used With Chemotherapy in Leukaemia Cells Can Be Improved By Altering the Sequence of Their Administration

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Objective

Phytocannabinoids possess anticancer activity when used alone, and a number have also been shown to combine favourably with each other *in vitro* in leukaemia cells to generate improved activity.

Methods

We have investigated the effect of pairing cannabinoids and assessed their anticancer activity in cell line models. Those most effective were then used with the common anti-leukaemia drugs cytarabine and vincristine, and the effects of this combination therapy on cell death studied *in vitro*.

Results

We show a number of cannabinoids could be paired together to generate an effect superior to that achieved if the components were used individually. For example, in HL60 cells, the IC50s at 48 h for cannabidiol (CBD) and tetrahydrocannabinol (THC) when used alone were 8 and 13 µM respectively; however, if used together, it was 4 µM. Median-effect analysis confirmed the benefit of using cannabinoids in pairs, with calculated combination indices being <1 in a number of cases. The most efficacious cannabinoid-pairs subsequently synergised further when combined with the chemotherapy agents, and were also able to sensitise leukaemia cells to their cytotoxic effects. The sequence of administration of these drugs was important though; using cannabinoids after chemotherapy resulted in greater induction of apoptosis, whilst this was the opposite when the schedule of administration was reversed.

Conclusions

Our results suggest that when certain cannabinoids are paired together, the resulting product can be combined synergistically with common anti-leukaemia drugs allowing the dose of the cytotoxic agents to be dramatically reduced yet still remain efficacious. Nevertheless, the sequence of drug administration is crucial to the success of these triple combinations and should be considered when planning such treatments.

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Poster Board #65

The Endocannabinoid System in Muscular Dystrophy – a Possible Therapeutic Target?

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Background

Muscular dystrophy (MD) is an X-linked neuromuscular disease manifesting as skeletal-muscle atrophy and cardiomyopathy. Existing therapy has limited effect and many patients die of heart failure by the second decade of life. Therefore, discovering new therapies for MD cardiomyopathy (MDC) is a clinical imperative. Despite the knowledge that endocannabinoid system (ECS) modulation impacts cardiomyopathy of various aetiology *e.g.* diabetic and doxorubicin (Pacher P *et al Nat Rev Cardiol*. 2018; 15(3):151-166) the role of the ECS in MDC remains unexplored.

Objectives

We aimed to determine ECS tone in cardiomyocytes derived from MD patient-specific induced pluripotent stem cells (iPS-CM) and to assess therapeutic targeting of cannabinoid receptor types 1 and 2 (CBR1/2).

Methods

Validated iPS cell lines (Gowran A *et al Stem Cell Res*. 2018;28:21-24; Spaltro G *et al Stem Cell Res*. 2017;25:128-131) were derived from MD patients (*n*=6) and healthy subjects (*n*=4). iPS were differentiated into cardiomyocytes (iPS-CM) by using a small molecule-based protocol (Lian X *et al Nat Protoc*. 2013;8(1):162–175). Healthy control and MD patients' iPS-CM were screened for ECS tone and cardiomyopathy hallmarks e.g. CBR1/2 gene expression and cTnI release respectively. In some experiments iPS-CM were treated with the CBR1 antagonist AM251 or the CBR2 agonist JWH133 before determining cardiomyopathy markers.

Results

MD patients' iPS-CM displayed altered ECS tone and cell death. iPS-CM cell-death was ameliorated by CBR1 and CBR2 modulation (Figure 1).

Conclusion

Collectively these results show that altered ECS tone is associated with MD cardiac pathology and targeting CBRs is a promising therapeutic approach.

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Poster Board #66

Chronic Tetrahydrocannabinol-Treatment Lowers Inflammation and Improves Behavior Deficits in a Sporadic Alzheimer Model

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Background and Objective

The endocannabinoid system (ECS) is connected to several processes of the human body and has among others neuroprotective and anti-inflammatory functions. Therefore influencing the ECS with THC could be beneficial for the treatment of Alzheimer's-Disease (AD). In our current project transgenic Alzheimer-mice (Tg4-42) were used to study the potential positive effects of THC in vivo.

Material and Methods

Tg4-42 were injected daily with 20mg/kg THC for 6 weeks, starting with 5 month (n=12 per group). Tg4-42 mice express intraneuronal N-truncated Abeta and represent the sporadic form of AD. To analyze the effects of THC motoric as well as memory tests were performed. The Rotarod-test was used to evaluate motoric learning. The Morris-Water-Maze was used to study spatial learning and memory.
Furthermore DAB-stainings with anti-IBA1-antibody as neuroinflammatory marker and anti-Doublecortin-antibody as neurogenesis marker were performed. In addition the effects of THC on the neuron loss in CA1-region and dentate gyrus of the hippocampus were analyzed using stereology.

Results and Conclusion

The Rotarod-test showed a significant improvement in motoric learning of THC-treated Tg4-42 compared to the placebo-treated mice. Furthermore THC-treated Tg4-42 showed an improved short- and long-term memory in the Morris-Water-Maze. THC also lowered the number of microglia in Tg4-42.
In summary our results show that chronic THC treatment lowers inflammation and improves behavior deficits in AD mice. Our findings suggest that THC may has therapeutic potential as a treatment for AD patients.

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Poster Board #67

Epigenetic Effects of Cannabidiol in Pilocarpine-Induced Epilepsy

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Background

Epilepsy is a disorder characterized by recurrent spontaneous seizures. Treatment with cannabinoids for resistant epilepsy is a promising therapy. The main non-psychotropic component of marijuana, cannabidiol (CBD), has anticonvulsant properties. However, the mechanism of its anticonvulsant effect is unknown. We hypothesize that epigenetic modifications underlie CBD effects. In particular, we are interested in the histone demethylase enzyme LSD1 (KDM1A) and its neuronal-exclusive isoform neuroLSD1, since it was shown that mice lacking neuroLSD1 are resistant to epilepsy. LSD1 and neuroLSD1 form transcriptional complexes with the corepressor CoREST and the histone deacetylases HDAC1/2 (LCH complexes) to demethylase lysine targets on histone H3.

Objective

To relate epigenetic and neurochemical modifications induced by CBD with its anticonvulsant properties.

Methods

We used an epilepsy model in mice induced with 300 mg/kg of pilocarpine, a muscarinic cholinergic agonist that causes seizures in the temporal lobe of the brain. To avoid systemic reaction to pilocarpine, mice were previously (30 min) injected with scopolamine (1mg/kg). CBD was injected 20 min after pilocarpine injection. All experiments were carried out 24 h after pilocarpine injection.

Results

Immunofluorescent and western blot assays show that the enzymes LSD1 and HDAC1/2 increased in the hippocampus after 24 h of seizure. A significant increase of CoREST2 and a decrease of CoREST1 in the hippocampus were induced by pilocarpine. These modifications in the LCH complex were accompanied by significant changes of K4 and K9 methylation in histone H3. CBD treatment did not reverse the epigenetic modifications either LCH changes induced by pilocarpine. Conversely, CBD induced a similar increase of CoREST2 and seizures were potentiated.

Conclusions

Administering CBD after pilocarpine can potentiate the epigenetic modifications occurring in the hippocampus and the seizures.

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Poster Board #68

Impact of Different Procedures of Galenic Formulations of *Cannabis* on Cannabinoids Contents

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Background

In Italy the "Stabilimento Chimico Farmaceutico Militare" of Florence has sold since 2016 a type of medical *Cannabis* called FM2. The galenic formulations with this raw material allowed by the current law are the tea and the oil.

Objective

A multidisciplinary network established within the University of Turin aimed to optimize the galenic formulations of FM2 oil and tea and to evaluate the impact on the cannabinoids extraction efficiency by changing some variables in order to obtain standardized formulation with high cannabinoid content.

Methods

We developed different procedures to prepare tea and oil using FM2, by changing kinetics and temperatures of *Cannabis* inflorescence extractions. The evaluation of cannabinoids concentration and stability was conducted using a fast ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) assay, by measuring the content of THC, CBD and their acidic precursor. Chromatographic separation was performed on an Acquity UPLC HSS T3 column (Waters) maintained at 30 °C through the column oven.

Results

Our results (on more than 200 samples) obtained using the developed method of FM2 oil extraction showed a significantly higher efficiency compared with the water one ($p<0,01$), moreover the decarboxylation of cannabinoids was almost exhaustive. We also demonstrated that by changing some variables in the procedures like time, temperature and raw material/solvent ratio the cannabinoids concentration increased up to 10 times compared to the standard literature formulation.

Conclusion

Our results convincingly demonstrate that the development of a strictly standardized preparation protocol is necessary to assure the availability of a homogeneous product. We concluded also that, since the tea has not a high cannabinoids content, it's not the best solution for long and high dosage therapies. Nevertheless, our study may contribute to guarantee quality and therapeutic continuity in treated patients, facilitating the hospital and community pharmacists in the procedures to prepare the galenics prescribed by MDs.

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Poster Board #69

The Effect of Rimonabant on Adipokines and Proinflammatory Cytokines Concentration in Adipose and Hepatic Tissue in Mice with NAFLD

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Background

Nonalcoholic fatty liver disease (NAFLD) is associated with obesity, insulin resistance, hyperglycaemia, increased production of proinflammatory cytokines and altered adipokine secretion. In high-fat diet (HFD) induced NAFLD, there is an increase in the endocannabinoid system (ECS) activity, inducing fatty acid synthesis, which significantly contributes to steatosis development.

Objective

The aim of our study was to investigate the effects of CB1 receptor blockade on adipokines and proinflammatory cytokines content in adipose and hepatic tissue in mice with NAFLD.

Methods

Male mice C57BL/6 were divided into: control group fed with control diet 20 weeks (C; n=6); group fed with HFD 20 weeks (HF; n=6); group fed with control diet and treated with rimonabant after 18 weeks (R; n=9); group fed with HFD and treated with rimonabant after 18 weeks (HFR; n=10). Rimonabant (10 mg/kg) was administered daily to HFR and R group by oral gavage.

Results

Rimonabant significantly decreased leptin, resistin, apelin, visfatin, IL-6 and IFN-γ concentration in subcutaneous and visceral adipose tissue in HFR group compared to HF group ($p<0.01$). In the liver rimonabant reduced IL-6 and IFN-γ concentration in HFR group compared to HF group ($p<0.01$). Rimonabant significantly decreased plasma glucose and insulin concentration, as well as HOMA index in HFR group compared to HF group ($p<0.01$). Conclusion: It can be concluded the potential usefulness of CB1 blockade in the treatment of HFD-induced NAFLD, due to modulation of adipokines profile and proinflammatory cytokines in both adipose tissues and liver, as well as glucose metabolism.

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Poster Board #70

The Phytocannabinoid Cannabidiol Inhibits Migration and Reactive Oxygen Species Generation in Human Polymorphonuclear Leukocytes

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Background

Polymorphonuclear leukocytes (PMN) represent a valid druggable target for inflammatory disorders. Cannabidiol (CBD) is the major nonaddictive component of cannabis, and circumstantial evidence suggests that it may affect the immune response. However, its effects on immune cells are yet to be unravelled.

Objective

To evaluate the effects of CBD on human PMN functions including cell migration and reactive oxygen species (ROS) generation.

Methods

Human PMN were isolated from buffy coats. Migration was investigated by the Boyden chamber assay by adding CBD in the upper chamber to PMN alone and in the presence of IL-8 (10 ng/mL) in the lower chamber. PMN migration was quantified by light microscopy measuring the distance (in µm) from the surface of the filter to the leading front of cells. Intracellular ROS production was evaluated by spectrofluorimetry in PMN in resting conditions and after stimulation with fMLP (0.1 µM). ROS levels were measured as fluorescence intensity and expressed in arbitrary units (AU).

Results

IL-8 increased PMN migration [(mean±SEM) 33.29±1.41 µm vs. 12.50±0.61 µm in resting cells, n = 7, P<0.001], and this effect was concentration-dependently reverted by CBD 10^{-8}-10^{-5} M, down to 15.21±0.60 µm with CBD 10^{-5} M (n=7, P<0.001 vs. IL-8 alone). ROS production was increased by fMLP from 32.99±2.88 AU to 212.8±39.43 AU (n = 8, P<0.001). In contrast, 1 h preincubation with CBD attenuated fMLP-induced ROS production in a concentration-dependent way with the maximum effect at 10^{-5} M (61.26±5.50 AU, n = 8, P<0.01 vs fMLP alone). Interestingly, CBD 10^{-5} M increased ROS production in resting PMN up to 150.8±35.69 AU (n = 8, P<0.01 vs resting cells alone).

Conclusion

CBD reduces migration and ROS generation in human PMN, suggesting its usefulness in treating or preventing inflammatory disorders. The stimulatory effect of CBD on ROS production by resting cells warrants further evaluation.

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Poster Board #71

Potential Use of Cannabis in Overactive Bladder Syndrome

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Introduction

Currently, the use of *Cannabis sp.* for medical purpose has increased, but its effects on urinary tract have not been completely elucidated. The objective of this study was to evaluate the effect of *Cannabis sp.* preparations on bladder mioactivity in rat.

Methods

The study was approved by the ethics committee of the University of Antofagasta. Bladder rings were obtained from Sprague Dawley rats. The relaxant effect was evaluated in rat bladder rings pre-contracted with 1 µM of carbachol maintained in organ bath system. The tension was measured using isometric transducer connected to PowerLab system. Oxybutynin was used as positive control.

Results

The 100 µg/mL of macerated, aqueous, resin, essential oil or rosin preparation of *Cannabis sp* caused detrusor relaxation of 26±8%, 32±1%, 45±1% 47±1%, and 86±2%, respectively. A 10 nM of Oxybutynin caused 46±1% of relaxation.

Conclusions

Cannabis preparations caused a relaxation on rat bladder. The relaxant effect was dependent of *Cannabis* preparations. *Cannabis* preparations could have medical application for the treatment of detrusor overractivity.

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Poster Board #72

Suspected Adverse Reactions to *Cannabis* for Medical Use in Italy

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Background

In Italy *Cannabis* can be prescribed and reimbursed within the National Health System according to Regional laws for selected indications. Since 2016 the Military Pharmaceutical Chemical Works in Florence has been authorised by the Ministry of Health to produce *Cannabis* under controlled and standardised conditions.

Objective

To describe suspected adverse reactions (ARs) associated with *Cannabis* for medical use.

Methods

Spontaneous reports of suspected ARs to natural health products (including galenic preparations containing herbals) are collected in Italy within the Italian Surveillance System of suspected adverse reactions to Natural Health Products coordinated by the National Institute of Health, in collaboration with the Italian Medicines Agency and the Ministry of Health.

Results

At December 2017 fifty-seven suspected adverse reactions to *Cannabis* for medical use were reported. Median age of patients was 60 years (range 22-84), women represented 77% of reports. In nine reports reactions required hospitalisation. *Cannabis* was mainly used for neuropathic pain; in other cases *Cannabis* was assumed as palliative care, for lack of appetite, cancer pain and headache. In 65% of cases concomitant use of drugs was reported.

The reactions reported were: psychiatric disorders (dysphoria, panic attack, visual hallucinations, stupor, *drowsiness*, major depression, …); dermatological symptoms (itchiness, redness and swallowing of eyelids and face); laryngospasm and lack of efficacy. Causality assessment was performed for all reactions and the association between *Cannabis* use and the reaction was almost always probable (in only two cases it was defined as possible). *Cannabis* was assumed almost in all cases by decoction, in 9 cases oil extract was assumed.

Conclusion

Cannabis for medicinal use is usually well tolerated. The adverse effects collected were similar to that observed in clinical trials. However, it is important to continuously monitor safety *of Cannabis* medical use in the population.

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Poster Board #73

Prescription of *Cannabis* for Medical Use in Italy

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Background

Medical use of *Cannabis* is authorised in Italy and reimbursed within the National Health System for selected conditions, among these: chronic and cancer pain, spasticity, Tourette's syndrome. Italian production of *Cannabis* was authorised since 2016 and the Military Pharmaceutical Chemical Works (Florence) grows and process *Cannabis* under controlled and standardised conditions.

Objective

To describe prescriptions of *Cannabis* for medical use in Italy.

Methods.

An hoc monitoring system was set up to collect prescriptions issued in Italy. Prescription web-based forms are filled in by physicians. Data collected included: anonymous identifier of the patient, age and sex, daily dose, type of *Cannabis* (imported or national production), and motivation for use. Identification of patients is not allowed according to Italian legislation.

Results

At December 2017, 8.275 prescriptions, related to 4.457 patients, were registered. On average, each patient received almost 2 prescriptions. As for type of Cannabis, 376 prescription of the national product (FM2: 5-8% THC e 6-12%CBD) were collected. Mean age of patients was 58 years, women represented 63%. *Cannabis* was mainly prescribed for chronic pain; spasticity in multiple sclerosis and in other conditions. *Cannabis* was prescribed by general practitioners in 20%, and by specialists such as: anaesthesiologists, rheumatologists and neurologists, in the other 80%. *Cannabis* was assumed almost in all cases by decoction. Dosage was very variable; for example a median daily dose of 114 mg (10°-90° percentile: 15-1000 mg) was prescribed for chronic pain. Almost in all prescriptions Cannabis was used as add-on to other therapies.

Conclusion

Few studies have been published on medical use of *Cannabis*. Since the prescription monitoring system is still in a preliminary phase, our data do not represent the prevalence of use in the Italian population. However, this is the first Italian nationwide surveillance of *Cannabis* use for medical purposes.

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Poster Board #74

Prevalence and Characterization of Cannabis-Use in Epidermolysis Bullosa: a Cross-Sectional Survey with 44 Patients in The Netherlands

Nicholas Schräder

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Anecdotal evidence has shown that patients with EB have been using cannabis as a method of symptom alleviation, with specific regard to pain and pruritus, two of the most debilitating problems in EB. Cannabinoid receptors can be localized in the brain and the immune system amongst others with a substantiated role in similar dermatologic and painful conditions. As effective symptom control in EB directly improves clinical outcomes, combined with the fact that patients experience insufficient treatment, the need to look for alternative therapies that provide a higher level of relief accompanied by tolerable side effects is justified.

This study aimed to gain insight into the prevalence of cannabis-use and patient-perceived effectiveness in Dutch patients with EB.

This study comprised a cross-sectional survey addressing patients with EB registered at the University Medical Center of Groningen in the Netherlands. Patients fulfilling the inclusion criteria were sent three surveys assessing their: current states of pain, pruritus and use of- cannabis in relation to their symptomatic management of pain and pruritus.

Forty-four patients responded to the survey (response rate: 33%) of which 7 (16%) currently use or have used cannabis. Within this group, 4 of 5 reported a successful alleviation of pain, and 2 of 3 reported a successful alleviation of pruritus owing to the therapeutic use of cannabis. Patients reported tolerable minor side effects including nausea, a slower reaction time and an increased appetite.

The use of cannabis for epidermolysis bullosa (EB) symptoms is substantial. Patients have reported pain and itch alleviation as well as a generally positive attitude toward the side effects of cannabis-use. This study is an important indicator for future investigations in EB regarding novel methods of symptom alleviation, encouraging research and development of cannabis based medicines in relation to pain and pruritus for EB. Determining the safety and effectiveness of numerous administration forms and cannabinoid compositions should be a priority.

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Poster Board #75

A Case Report of the Resolution of Hidrandenitis Suppurativa Using Oral Cannibinoid Oil

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We discuss the case of a 56 year old gentleman who presented with Hidrandenitis Suppurativa (HS) with Seronegative Rheumatoid Arthritis treated with Methotrexate and low dose oral Prednisolone. On presentation his HS lesions were present in his left axillia and groin and required recurrent surgical resections which proved unsuccessful and resulted in complications. Despite using Metronidazole, steroid creams and non-steroidal anti-inflammatories (NSAIDs) his condition failed to improve and three years later was prescribed anti-TNF treatment (Humira) without success. He then commenced oral Cannabinoid oil in 2017 which resulted in improvement within 8 weeks and the HS completely resolved.

HS is a recurrent and suppurative disease with an insidious onset (Shanmugam *et al*. 2017). Obesity, smoking and inflammatory bowel disease are all known risk factors. HS is characterized by abscesses, fistulae, sinus tracts and scarring with a prevalence of 0.3% to 4% of the population (Shuia *et al*. 2010).

Medical treatment is often ineffective and, in severe disease, surgery remains the main therapy. While surgical interventions can be helpful in reducing disease burden, there remains a high recurrence rate. Patients experience a significant reduction in quality of life and the need for new treatment modalities is urgent (Haslund *et al*. 2009). Medical treatment is based on the use of antibiotics, retinoids, and anti-inflammatory drugs. Anti-TNFα drugs have been used and has the highest level of scientific support (Martorell et al. 2016).

The discovery of the human endocannabinoid system and its dominant presence throughout the integumentary system provides a valid and logical scientific platform to consider the use of cannabinoids for wound treatment (Maida and Corban 2017). Whilst there is limited discussion regarding this in the scientific literature, our case report demonstrates the potential benefit of oral cannabinoid oil in treating HS.

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Poster Board #76

Prescribing Medicinal Cannabis in Australia for Cancer Patients: a New Era in Medicine with All its Complexities

Judith Lacey

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Introduction

Australia has recently introduced the limited prescribing of cannabis for symptom management in cancer patients with "refractory" symptoms. This presentation will look at the Australian model and the strategy used to develop a program to prescribe for selected patients, the limitations and strengths.

Objectives

To highlight the key strategies in developing prescribing medicinal cannabis for cancer related symptoms in Australia. Looking at clinical trials in the cancer population, the development of partnerships, the role of observational/n=1 studies in this setting.

Methods

Case studies, guidance document development, current clinical trials presented from the perspective of a palliative and supportive care specialist involved in studies, prescribing and policy development. Taking a look at prescribing skills required and strategies to improve evidence

Results

Australian prescribing of cannabis for symptom management in cancer patients is evolving rapidly. One proposed strategy is the N=1 model whilst the gold standard remains the Randomised Control Trial. The skills of palliative care and supportive care training and experience in balancing benefit and side effect of medications to improve quality of life can be applied in this new field coupled with knowledge of the products available, their potential role as a therapeutic agent, potential adverse side effects and interactions will presented.

Conclusions

Medicinal Cannabis plays a growing role with ongoing exploration of i it`s potential in Supportive Cancer Care for the patient with refractory symptoms

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Poster Board #77

The Case for Community-Based Specialized Medical Cannabis Clinics

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Background

Canada's *Access to Cannabis for Medical Purposes Regulations* (ACMPR), provide a unique opportunity for healthcare practitioners (HCPs) and clinical researchers to conduct impactful pharmacovigilance research and to develop clinical knowledge within a well-controlled regulatory framework. A wide variety of strictly regulated medical cannabis products are available; however, significant gaps remain in the published medical literature, education and resources for HCPs. As a result, the vast majority of HCPs cite lack of knowledge to prescribe medical cannabis and 80-85% of Canadian authorizations are completed at specialized cannabis clinics where education, training and support are available in a collaborative model. These sites can be controversial due to variation in provided services and potential for conflicts of interest, but these risks can be mitigated by following a best practice model.

Objective

To describe a model of patient assessment, data collection, follow-up and monitoring of medical cannabis treatment in a community-based setting.

Methods

Santé Cannabis, a leading specialized medical cannabis clinic with various locations in the province of Quebec, Canada, has an established clinical model (Figure 1) and has collected a database of efficacy and side effect reporting from approximately 3000 medical cannabis patients (demographics in Table 2, safety data in Table 3).

Optimal clinical data obtained from patient and caregiver include the following quantitative and qualitative measurements:

- Complete medical history
- Pain, symptom burden and quality of life validated measurement tools (i.e. Brief Pain Inventory - Short Form, Edmonton Symptom Assessment Scale, EQ-5D-5L)
- Cannabis formulations prescribed, dosage, frequency and route of administration
- Adverse event reporting and severity classification guidelines

Conclusion

Specialized medical cannabis clinics provide opportunity for valuable data collection, specific training and development of clinical practices in a collaborative and interdisciplinary setting. The established community-based model at Santé Cannabis can be adapted to new care settings and to emerging regulatory environments.

Figure 1:

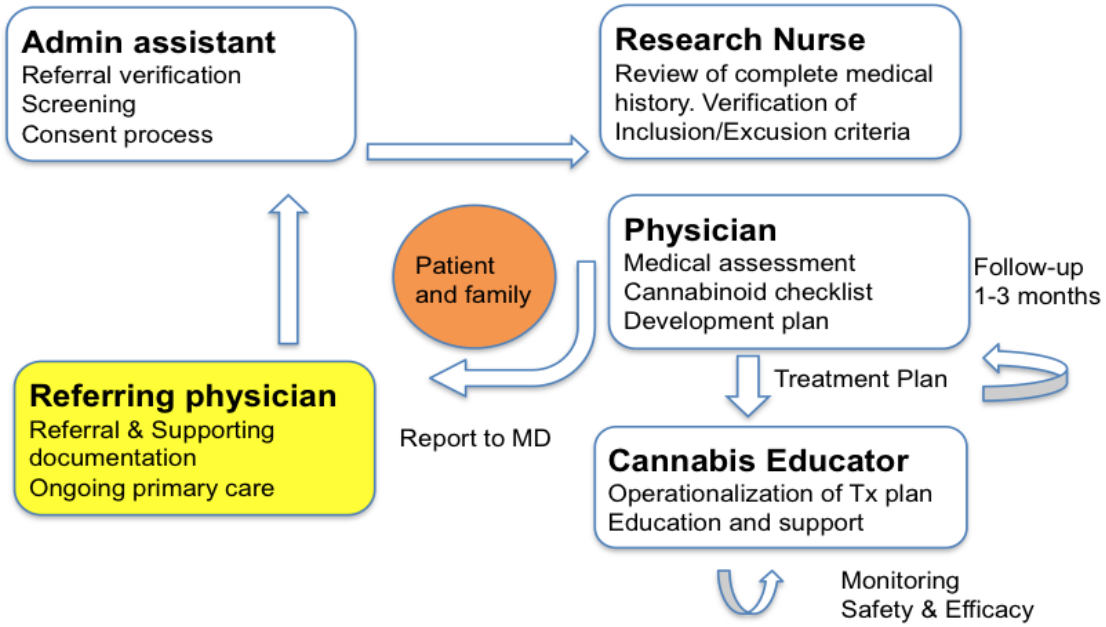

Table 1:

TOTAL PATIENTS		
	Assessed for medical cannabis treatment	3415
	Followed for at least 3 months	2952
Gender		
	Male	53.4%
	Female	46.6%
Age		
	> 80 Years	4.4%
	70-80 Years	8.0%
	60-70 Years	19.1%
	50-60 Years	25.4%
	40-50 Years	18.8%
	30-40 Years	14.4%
	20-30 Years	8.7%
	< 20 years	1.2%
Primary Diagnosis		
	Chronic non-cancer pain	49.1%
	Cancer	11.7%
	Arthritis	11.5%
	Anxiety, depression, other mental health conditions	9.4%
	Epilepsy	5.2%
	Inflammatory bowel disease	4.8%
	Multiple Sclerosis	2.1%
	Spinal cord injury or neurological disease	3.2%
	Other	3.0%

Table 2:

Number of patients reporting at least one side effect		935
Severity of side effect reported		
	Mild	864
	Moderate	67
	Severe	4
	Serious	0
THC:CBD ratio of suspected product		
	THC rich	51%
	THC:CBD	40%
	CBD-rich	9%
Route of administration of suspected product		
	Oral administration	68%
	Inhalation	30%
	Other	2%

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Poster Board #78

Integrating Medical Cannabis within Supportive Cancer Care:

A University Hospital-Based Model

Maria-Fernanda Arboleda[1], Saro Aprikian[1], Gligorka Raskovic[2], Rosa Christodoulopoulos[2], Doneal Thomas[2], Virginie Bacis[1], Nathalie Aubin[1], Antonio Vigano[1]

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Background

Integration of medical cannabis (MC) into supportive cancer care (SCC) has been hindered by conflicting regulations, lingering stigma and significant research gaps. In Canada, access to MC has become a common request by patients and caregivers in oncology and SCC clinics. Nevertheless, no specific MC model of care in the hospital setting has been implemented for oncology patients.

Objective

To report initial data regarding the outcomes and feasibility of a hospital-based MC model for SCC.

Methods

A seven-month initiative was designed and implemented at the McGill University Health Center to incorporate MC as a complementary treatment for cancer patients. An interdisciplinary team was established to systematically assess patients, prescribe and monitor cannabis treatment. Outcome measures included: 1) Resource utilization to support operations of the clinic and 2) Improvement in symptom control as measured by the Brief Pain Inventory-Short Form, revised Edmonton Symptom Assessment Scale and EQ-5D-5L (quality of life questionnaire).

Results

Twenty-five patients were enrolled since January 2018 (mean age 60.3 years, SD ±13.5; 44% male). Gastrointestinal (24%), breast (20%), and lung (12%) cancers were the most frequent diagnoses. Cannabis products rich in Cannabidiol (CBD) (54.5%) and oral administration (i.e. cannabis oil) (80%) were most frequently prescribed (Table 1). On a visual analogue scale of 0-100 the average health state reported by patients was 52.1 (SD ±20). On average, three patients were seen per half-day clinic and resources required were: 6.2 hours (nurse), 2.5 hours (project coordinator), 2.8 hours (palliative care physician) (Figure 1). The mean time spent by each patient at the clinic was approximately 1 hour. At 1-month follow-up (n=8), 50% of patients showed improvements for pain and tiredness, 75% for drowsiness and 62.5% for well-being (Table 2).

Conclusion

Our preliminary data suggest that a hospital-based MC service appears to be effective when specialized health professionals are involved in the care of SCC patients.

Table 1. Demographics and Clinical Characteristics at baseline (N=25)

Characteristics	
Age	
Mean (SD)	60.3 (13.5)
Median (IQR)	64 (52-69)
Range	28-83
	Number (%)
Sex	
Female	14 (56)
Male	11 (44)
Occupation status	
Employed	2 (8)
Unemployed	3 (12)
Medical leave	5 (20)
Retired	15 (60)
Cancer type	
Gastrointestinal/Pancreas	6 (24)
Breast	5 (20)
Lung	3 (12)
Gynecological	3 (12)
Sarcoma	2 (8)
Prostate	2 (8)
Other	4 (16)
Primary symptom	
Pain	17 (68)
Fatigue	4 (16)
Vomiting	2 (8)
Anorexia	1 (4)
Shortness of breath	1 (4)
Previous Cannabis use	
No	9 (36)
Yes	16 (64)
Type of Products	
THC-rich	5 (22.7)
CBD-rich	12 (54.5)
THC:CBD 1:1	5 (22.7)
Route of Administration	
Oral	20 (80)
Inhaled	5 (20)

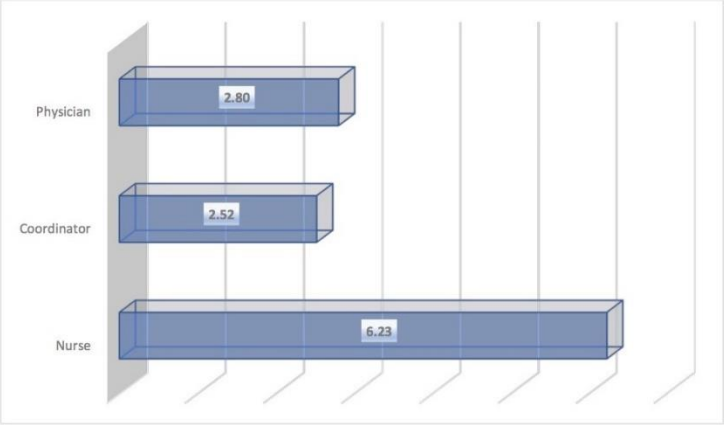

Figure 1. Average Time Spent by Staff Members per Half-Day Clinic (in Hours)

Table 2. Change in patient's score on the revised Edmonton Symptom Assessment Scale items (N=8)

	Number (%)		
ESAS	Improvement	No Change	Worst
Pain	4 (50)	2 (25)	2 (25)
Tiredness	4 (50)	2 (25)	2 (25)
Drowsiness	6 (75)	1 (12.5)	1 (12.5)
Nausea	3 (37.5)	5 (62.50	
Lack of appetite	2 (25)	3 (37.5)	3 (37.5)
Shortness of breath	4 (57.1)		3 (42.9)
Depression	3 (37.5)	4 (50)	1 (12.5)
Anxiety	2 (25)	5 (62.5)	1 (12.5)
Wellbeing	5 (62.5)	1 (12.5)	2 (25)
Other problem			1 (100)

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Poster Board #79

Effects of Vaporised Cannabis, with and without CBD, on Driving Performance and Cognition

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Background

Tetrahydrocannabinol (THC) impairs driving performance and cognition in a dose-dependent manner. However, medicinal cannabis patients may prefer cannabis containing cannabidiol (CBD), which has been shown to modulate the pharmacological action and dampen the psychotomimetic properties of THC. Here we tested whether CBD-containing cannabis is less impairing than cannabis containing THC alone.

Objective

To test the effects of vaporised cannabis (Chemovar I = 11% THC, <1% CBD; Chemovar II = 11% THC,11% CBD) versus placebo cannabis on simulated driving performance and cognition.

Methods

Fourteen participants completed the study. Over three sessions, separated by at least 1 week, participants self-administered 125mg of Chemovar 1, Chemovar 2 and Placebo in a random and balanced order using a *Mighty Medic* vaporiser. Driving performance was assessed throughout a 30-minute scenario in a high-fidelity simulator environment. Cognitive function was assessed using a battery of computerised tests. Driving performance and cognition were assessed at acute and sub-acute intoxication phases (+0.5h, +3.5h). Plasma and saliva samples were taken before and after drug administration (-0.5h, +0.2h, +1h, +2h, +3h, +4h). Subjective drug effects and self-reported driving ability were also assessed.

Preliminary Results

During a car-following task, driving performance was significantly impaired in both cannabis conditions versus placebo as indicated by an increase in standard deviation of lateral position (SDLP). There was no difference between the THC and THC/CBD conditions. When averaged across the entire drive, SDLP was unaffected by cannabis. During the acute intoxication phase, cognitive test performance was significantly impaired by cannabis. Plasma and saliva are currently being analysed.

Conclusion:

THC-induced driving impairment appears pronounced under challenging conditions but is not evident during monotonous driving. Lateral vehicular control appears to be a highly automatic process that may only be inhibited by THC under demanding driving conditions. Overall results suggest that CBD does not mitigate THC-induced impairment, although further detailed analyses are currently underway.

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Poster Board #80

Prolonged Cannabidiol Treatment in Cannabis Users Improves Psychological Symptoms and Cognitive Function and Increases Hippocampal Subfield Volumes

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Background

Chronic cannabis use is associated with impaired cognition, elevated psychological symptoms and reduced hippocampal volumes. Adverse outcomes are associated with prolonged exposure to Δ^9-tetrahydrocannabinol (THC), whereas evidence suggests that cannabidiol (CBD) may ameliorate some of these effects. This has never been tested in a prolonged administration trial.

Objective

We report the first study of prolonged CBD administration to a community sample of regular cannabis users in a pragmatic trial investigating potential restorative effects of CBD on brain structure, psychological symptoms and cognition.

Methods

Twenty cannabis users (16 male, median age 25) underwent a ~10-week open label trial of 200mg daily oral CBD treatment, whilst continuing to use cannabis. The majority were daily cannabis users with several years use (median 5 years regular). Participants underwent psychological and cognitive assessments and magnetic resonance imaging (MRI) scans at baseline and post-treatment and were monitored weekly throughout the trial.

Results

CBD was well tolerated with no side effects. Participants retrospectively reported reduced euphoria when smoking cannabis. Participants reported significantly fewer depressive and psychotic-like symptoms at post-treatment relative to baseline and exhibited improvements in attentional switching, verbal learning and memory (all $p<0.05$), with greater benefits in dependent users. No change was observed in left or right hippocampus as a whole. However, left subicular complex (parasubiculum, presubiculum, subiculum)

volume significantly increased from baseline to post-treatment (p=0.017), as did CA1 in heavy users. Associations with increased plasma CBD concentrations were observed.

Conclusion

Prolonged CBD treatment appears to have promising therapeutic effects for improving psychological symptoms and cognition in regular cannabis users and restoring hippocampal subfield volumes. Our findings require replication given the lack of a placebo control in this pragmatic trial, but suggest that CBD may be a useful adjunct treatment for cannabis dependence, and therapeutic for a range of clinical disorders characterised by hippocampal pathology.

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Poster Board #81

Do Underlying Neural Correlates of PTSD Symptomatology Dispose Individuals Towards Temporary Cannabinoid Therapeutics?

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Background

To date there has been sparse neurological research evaluating the use of medical cannabis in those with PTSD making it devious for practitioners to recommend cannabinoids to their patients. While patients claim that cannabis helps alleviate PTSD associated symptoms, large scale reviews on the therapeutic effects of cannabinoids show insufficient empirical evidence to support those claims. Some studies even suggest that cannabinoid use in PTSD patients could deter therapeutic effects, worsen certain symptoms, and cause additional problems.

Objective

The objective of this review is to support a framework where PTSD patients have dispositions towards temporary cannabinoid treatments. This paper aims to provide a refined understanding of the relationship between cannabis use and PTSD symptom modification to guide future research and offer an important footnote for those considering cannabinoid treatments for PTSD.

Methods

We review current literature on the neurology of PTSD and pharmacology of cannabinoids, focusing on regions of interest in the brain that have large cannabinoid receptor densities and correspond to underlying PTSD symptomology. Additionally, we highlight different cannabinoid's pharmacological effects on PTSD symptom reduction and promotion.

Conclusion

Cannabinoids permit the reduction of PTSD symptoms, but not enduringly. Cannabinoid therapeutics provide temporary alleviation of symptoms due to a biological disposition of the endocannabinoid system in those with PTSD coupled with the dose-dependent biphasic effects of cannabinoids. With the temporal-window of effectiveness being unknown cannabinoids can potentially lead to the exacerbation of PTSD problems. In sum, while the use of cannabinoids for PTSD symptom alleviation is possible more research is needed to fully discover the lasting effects cannabinoid use has in PTSD patients.

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Poster Board #82

Sleep Architecture, Insomnia and Non-Restorative Sleep (NRS): a Case Study and Proposed Rational for Treatment with Medical Cannabis

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Background

For centuries cannabis was used for sedation and pain management in the treatment of insomnia. Studies suggest cannabis can be used as a safe and effective treatment for insomnia and NRS. When treating insomnia and NRS, a comprehensive approach must be adopted which takes into account all aspects of sleep/wake health, as there is a bi-directional relationship between daytime processes and sleep quality. Polysomnographic sleep studies are essential in providing objective data of the effects of cannabis on sleep architecture and, in combination with self-report questionnaires, provide a more comprehensive assessment of the potential roles for medical cannabis in optimizing sleep/wake health and function.

Objective

To study the potential role for medical cannabis treatment in insomnia and NRS, as well as optimizing sleep/wake health.

Methods

This case study was conducted in a sleep medicine clinic and assessed the effects of medical cannabis on objective sleep measures using PSG sleep study recordings and on overall improvement in daytime symptoms associated with insomnia and NRS. The patient protocol was to medicate with high CBD: low THC cannabis oil during the day, taking 0.25ml in the morning and afternoon, and low CBD: high THC cannabis oil, taking 0.25ml 1 h before bedtime. This treatment was under the supervision of a sleep medicine specialist, who assessed PSG recordings before the initiation of medical cannabis treatment and 3 months after its initiation. Patient outcome measures included daily sleep diaries, self-report measures of Insomnia Severity Index and Daytime Fatigue Severity Scale.

Results

Objective PSG sleep study results revealed clinically significant improvements in sleep onset latency, wake time after sleep onset, sleep efficiency, and decrease sleep fragmentation and sleep instability (ie. autonomic instability). Subjective data revealed a decrease in insomnia severity, and an overall increase in daytime energy and function after 3 months treatment with medical cannabis.

Conclusion

Medical cannabis is a viable option for treating insomnia and NRS. Anti-inflamatory and autonomic effects have the potential to improve sleep/wake health.