Research Article

Use of Cannabinoid is Effective in Multiple Sclerosis Symptoms

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Abstract

Multiple sclerosis (MS) can be widely identified as a neurological disability which affects a wider population of young adults. in the UK. One of the major areas of treatment and control of the disease is in the area of symptom control. Although conventional drug-based interventions show some efficacy in alleviating symptoms; the benefits are marginal and often leads to long term adverse effects. On the other hand, there is a tremendous prospect of cannabis-based interventions which has been under extensive research and experimentation since centuries. In the recent past, the effects of non-psychoactive components of cannabis such as cannabinoids have been shown through animal samples as well as randomised controlled trials to have some efficacy in pain reduction and alleviating symptoms of muscular spasticity.

Based on a systematic review methodology, online databases are searched in this review for identifying and selecting recent research using established inclusion criteria and exclusion criteria. The purpose of this paper to develop a review of the efficacy of cannabinoids in the treatment and control of MS.

Findings indicate that the efficacy of cannabinoids and cannabis-based interventions in the treatment and control of MS was repeatedly highlighted in alleviating symptoms of pain and spasticity. In selected research findings, anti-inflammatory and anti-apoptotic properties of the compound were detected showing potential for addressing neuro-degeneration in MS. However, a wide range of other potential effects such as cognitive repair, mobility and treatment of other symptoms were found to be questionable due to the lack of clinical evidence.

Keywords: Cannabinoid; Multiple Sclerosis; Pain; Spasticity; Neurodegenartion; Side Effects

Introduction

The cannabinoid is a chemical component of cannabis plant having effects on the body included in the central-nervous-system and the immune system. There are numerous effects of cannabinoid-based medical interventions such as it helps to reduce anxiety, reduce inflammation and relieve pain, control nausea and vomiting caused by cancer chemotherapy, kill cancer cells and slow tumour growth, relax tight muscles in people with multiple sclerosis or stimulate appetite and improve weight gain in patients with cancer and AIDS [1,2]. As it has been noticed that it also helps in chronic pain and muscles spasms, it is used to reduce nausea during chemotherapy, improve appetite in HIV/AIDS, improving sleep as well as in Tourette syndrome [3]. There are, however, prominent side effects such as dizziness, feeling tired, vomiting, and hallucinations [4,5].

Multiple sclerosis (MS) is a chronic disease that can affect the brain, spinal cord, and the optic nerves in eyes impairing vision, balance, muscle control, and other basic body functions. As it da-mages the brain, the brain is impaired to send signals to the body resulting in mobility and other sensory impairments. Million people are affected by multiple sclerosis and the proven efficacy of cannabinoids has emerged as a major reason in approval of medical cannabinoids for the symptoms for multiple sclerosis [6,7]. Based on such emerging research evidence, this paper attempts to develop a systematic review of the most current research in this context to evaluate the effectiveness of cannabinoid-based interventions in the treatment and control of MS.

Methods

In this study, a methodology of searching for relevant studies in databases such as Google Scholar, Elsevier and PubMed was adopted while the PRISMA model was used for the selection of the studies for review based on inclusion and exclusion criteria as mentioned below. Studies that were published before the year 2000 were excluded considering that increased research attention to this hypothesis has only been exhibited in the last two decades. Using the below-established inclusion and exclusion criteria, a sample of

8 research papers was developed which were reviewed to achieve the purpose of this study.

Inclusion criteria

- Studies that were available in the English language were included.
- Studies for which full text could be availed without purchase were included.

Exclusion criteria

- Studies published on or before the year 2005 were excluded.
- Studies for which abstract was not available were excluded
- Duplicates were excluded
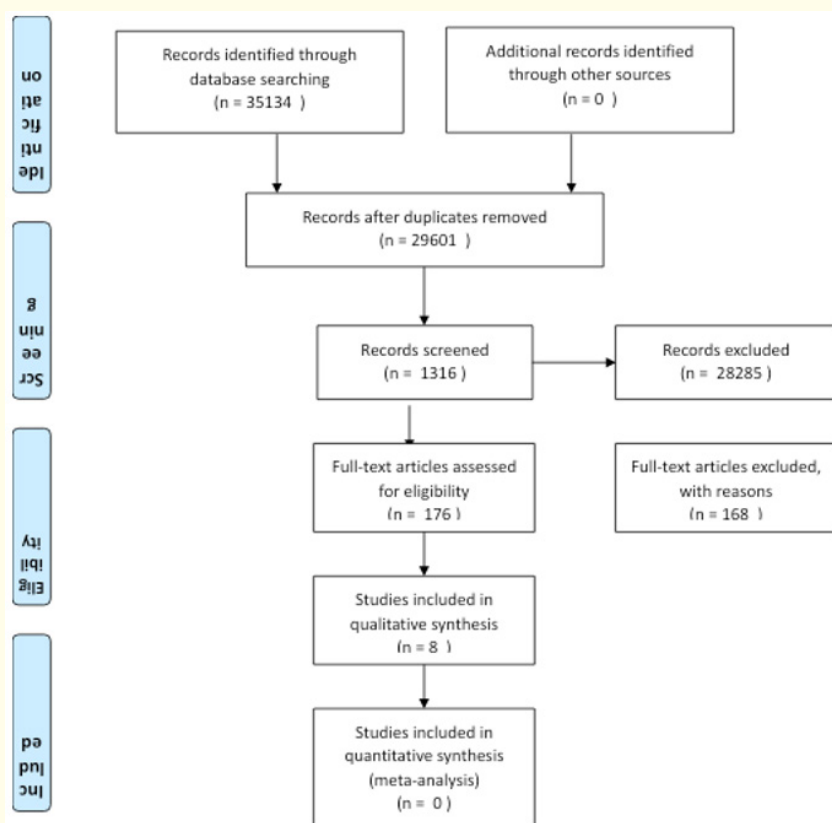- Randomised controlled trials and placebo-controlled trials were excluded.

Figure 1

Results

Zajicek and Apostu [8] analysed the role of cannabinoids in MS treatment and indicated symptomatic improvement in symptoms such as spasms and stiffness, neuropathic pain, sleep and bladder disturbance although clinical trials in patients suffering from symptoms of tremors and nystagmus did not provide any beneficial results. From a review of existing clinical studies, the authors concluded that cannabinoid-based interventions could lead to minimising of oligodendrocyte apoptosis in MS patients. It can also further ameliorate the inflammatory response and enhance the process of re-myelination in such patients.

Patti., *et al.* [9] on the basis of data collected from 1615 patients recruited from 30 MS centres related to their use of tetrahydro-cannabinol (THC) and Cannabidiol (CBD) oromucosal spray (Sativex) in the management of MS related spasticity found that in the MS patients, the effectiveness of Sativex was higher than common anti-spastic prescription drugs. 70.5% of the patients reached the initial response (IR) threshold and 28.2% had already reached the clinical response rate (CRR) threshold at the end of one-month trial period. Based on the variation of the number of puffs at different trial stages, the findings indicated that the effectiveness could be maintained with lower doses than identified in clinical trials. Furthermore, the study findings indicated that progressive MS resistant to treatment using anti-spastic drugs could be treated effectively using THC and CBD based oromucosal spray.

Rice and Cameron [10] in their review paper established that cannabinoid based products have been helpful for relieving spasti-

city and pain associated with MS while being the only known Complementary and Alternative Medicine (CAM) supported by research evidence. From evidence cited from randomised control trials of the use of cannabinoids as CAM in the treatment of MS, the review reported that patients administered cannabis products such as Dronabinol and Cannador exhibited enhancements in their profile of spasticity, spasms and sleep compared to placebo results. The authors deduced that that the use of cannabis interventions such as nabiximols, oral cannabis extracts and synthetic tetrahydrocannabinol were possibly effective at reducing spasticity related to MS.

Fitzpatrick and Downer [11] on the context of the review of Toll like receptors (TLRs) as a cannabinoid target in MS indicated that the mechanism existing between TLR signalling and MS pathogenesis is highly complex and still the specific cellular and molecular mechanisms were unexplored. Cannabis based interventions such as the use of Sativex has shown effective propensity in the management of pain and spasticity in MS patients. Toll like receptors (TLRs) are essentially sensory elements of pathogen associated molecules that leads to innate immune intracellular signalling responses for the initiation of innate immune reactions. Evidence suggested that innate immune cells like dendritic cells (DC), microglia and astrocyte activation has a major role in MS pathogenesis and influence T cell activation while also acting as generators of pro-inflammatory cytokines.

Giacoppo., *et al*. [12] in their aim of evaluating the effects of intraperitoneal administration of cannabidiol (CBD) in multiple sclerosis experimental models identified that purified form of cannabidiol, the main non psychotropic component in cannabis exhibited anti apoptotic power against neurodegeneration in multiple sclerosis conditions. Immunohistochemical and western blot results of fundamental apoptotic markers identified that cannabidiol based interventions were capable in avoiding Fas pathway activation, phosphor- ERK p42/44 and cleaved caspase-3 initiating other alterations in mitochondrial permeability due to Bax/Bcl-2 imbalance. The study findings indicated that in addition to the well-known anti-inflammatory features of cannabidiol, the anti-apoptotic characteristics of the compound can be developed for interventions using cannabidiol against neuro degenerative diseases.

Baker., *et al*. [13] explained that cannabinoids may affect the glial response within the damaged central nervous system leading to slow, neurodegenerative process and thus improved prognosis and better quality of life. Therefore, it exhibited the propensity of enhancing cannabis-related drugs for symptom control in MS subjects. Cannabinoids may have some limited potential for modulating neuro-immune responses based on the immune oppressive mode of action of cannabis. Therefore, cannabinoids may shape the inflammatory response such that it(delete) again positively affecting neurodegenerative components of neurological disease.

Papathanasopoulos., *et al*. [14], recognised neuroprotective roles of cannabis-based interventions in the CNS citing experimental data claiming the release of endocannabinoids in various types of toxic insults including exciting toxicity and stress, traumatic injury and ischemia to initiate a repair process. Based on such principle and results of mice samples, the study concluded that cannabinoid-based interventions can be effective in developing a defence system for the brain. Chronic cannabis users have been shown in research to exhibit symptoms of side effects on neurocognitive processes leading to cognitive impairment. One of the most apparent symptoms of MS is cognitive impairment. On the other hand, clinical trials on animal models have suggested that the efficacy of cannabis-based interventions for alleviating symptoms of muscle spasticity and pain are evident as a therapeutic role of the drug. Neuropsychological effects of cannabinoid-based interventions could not be positively recognised from the paper, whereas other clinical trials indicated a reduction in the performance [15]. Thus, the authors concluded that a balanced assessment of the risk and benefit ratio of cannabinoid-based interventions in the treatment of MS.

Chong., *et al*. [16] recognised MS as the most common cause of neurological disability affecting the young as well as adults in the UK and cannabis' propensity to alleviate symptoms and reduce chronic effects established that in MS patients. Cannabis usage can lead to symptom relief evidenced from the clinical observation of MS patients at two hospitals at London and Kent, 30% of the patients indicated the use of cannabis to alleviate symptoms which comprised of pain and muscle spasm constituting more than 80% of their symptoms. On the other hand, side effects were widely prevalent including the feeling of euphoria and sedation, lethargy and increased appetite. The apparent impact of cannabis interventions in MS patients related to mobility issues indicated that the effects were more prevalent and apparent among patients who were chair bound or needed aid in walking compared to those who did not need any aid in walking and moving. Thus the study found that the effects of cannabis were more beneficial in the management of pain

especially neuropathic pain which is not relieved by minor opiates. Furthermore, the study also indicated that some of the patients were ready to try cannabis for the management of the symptoms only when it is provided in a prescribed manner.
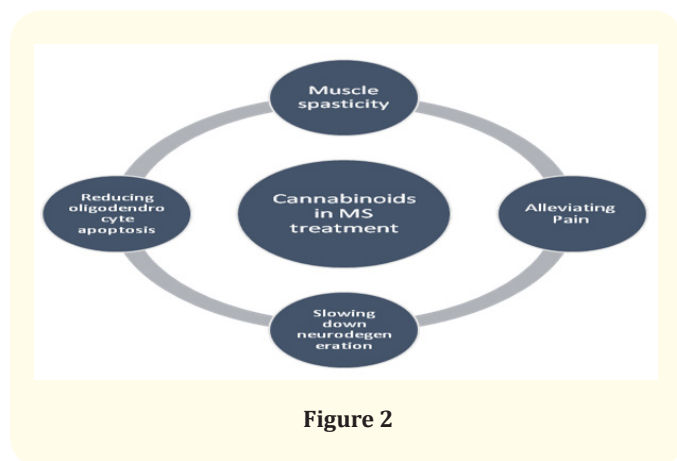

Figure 2

Discussion

Cannabis-based interventions, particularly the compound of cannabinoid can be recognised from the review of the selected studies to exhibit specific benefits in symptom alleviation of MS patients. However, similar results of studies were only exhibited in minimising of the muscle spasms and pain. From the research evidence gathered from the results, the use of the oromucosal spray Sativex tested for MS patients indicated higher effectiveness compared to prescription anti-spastic drugs in the management of pain and spasticity [9,11]. The later study revealed that the complex mechanism existing between TLR signalling and MS pathogenesis was a causal factor leading to the anti-inflammatory characteristics of cannabinoids. Furthermore, Giacoppo., *et al*. [12] indicated that besides the anti-inflammatory properties, cannabinoid based interventions also exhibited the anti-apoptotic properties based on the Bax/Bcl-2 imbalance leading to the propensity of the intervention to be used in neurodegenerative processes as well. Although all of the research that was reviewed indicated that higher propensity of cannabinoids and cannabis-based interventions to impact other symptoms such as neuropathic pain, cognitive improvement and even sleep and bowel disturbances, the effectiveness of cannabinoids and cannabis-based interventions are still questionable either due to the lack of clinical results or trials performed that showed solid evidence. For instance, in Zajicek and Apostu [8] research, although propensity of the drug was

found to lead to reduction in pain and muscle stiffness and spasm, their effects in tremors and nystagmus did not show any beneficial results. It is evident that although beneficial effects in these areas are somewhat observable from a patient perspective, almost all of the studies reviewed raised a question demanding further substantial clinical evidence to prescribe cannabis-based interventions in MS patients. One of the studies by Chong., *et al*. [16] indicated that patients that were immobile or required aids in walking exhibited a better response to cannabis-based interventions. However, the paper also indicated that those patients who have never tried cannabis-based interventions were only ready to undertake such interventions only when provided as prescribed medication. On the other hand, such studies also indicated the possible side effects some of which are psychoactively attributed to the components of THC. Although neuroprotective roles were evidence in a study by Papathanasopoulos., *et al*. [14], their efficacy in cognitive impairment did not show any valid results. However, chronic users have been recognised to develop dependency and exhibit psychoactive side effects.

Conclusion

Numerous treatment interventions for MS are currently available starting from oral gents to parenteral drugs and they have the ability to reduce the rate of disability accumulation among the patients. The new McDonald's diagnostic criteria which was evaluated indicating a beneficial result in case of MS. Furthermore, it can be stated that mainly there are three categories of treatment regimens can be followed for MS such as treatment of the exacerbations, reducing the disease progression with disease-modifying therapies (DMTs), and symptomatic therapies and following these treatment can be helpful for the significant reduction of the quality of life of the patients suffering from the disease.

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