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A silver lining in the dark clouds: Medical Marijuana, in the Neurological disorders and its future in Pakistan.

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ABSTRACT

Marijuana has been included in the list of illicit drugs for a long time despite its use as a remedy for several medical problems. However this use has been on the basis of the individual experiences with no concrete scientific evidence. Its positive effects have been mostly overshadowed by its recreational use worldwide. It has recently become the topic of hot debate due to several studies showing its role in various medical and especially neurological disorders. These new findings have created a controversy and world is still divided on its legalization for medicinal purpose. Several countries and states have legalized it recently, but many experts have raised concerns about its misuse and long term legal, ethical, financial and health implication, that need to be answered yet. Pakistan is considered as one of the largest cannabis producing country and with increasing evidence for potential medicinal benefits; we need to develop a consensus on this topic, considering health, legal and ethical perspectives linked to its medical uses in our society.

KEY WORDS: Marijuana, Epilepsy, legal, cannabiniods.

ABBREVIATIONS:(THC)Tetrahydrocannabinol .FDA(Federal Drugs Agency)

ALS(Amyotrophic Lateral Sclerosis)

INTRODUCTION:

To date, about 86 Cannabinoid compounds have been identified in nature and some other are synthesized chemically. They have been mostly used for recreational purposes with major psychoactive ingredient being delta-g-tetrahydrocannabinol (THC) and some of these compounds like dronabinol and nabilone have been used as prescription drugs¹.

Cannabis has been used for various therapeutic purposes for thousand of the years. Initially it was grown as an agricultural crop called Hemp, in China which then traveled through Asia into Middle East and Africa where it was used for pain and other various conditions like gout, malaria, Rheumatism, and poor memory for a long time alongside its use for recreational purposes as well².

In 1970, it was categorized as Schedule 1 drug and was listed as having no accepted medical use and further research was restricted until recently where it was found to be of several uses and less side effects than previously documented². These findings have lead to its legalization for medical purposes in April 2015 in about 23 states of USA. Several other

countries including Holland, Germany, Spain France, Colombia, Czech Republic, Canada have legalized its use for medicinal purpose. According to a study, in USA about 17% of past-year marijuana users reported its use for medical purposes recently³.

USES OF CANNABINOIDS IN VARIOUS NEUROLOGICAL DISORDERS:

Currently, pill form of “dronabinol” and “nabilone” has received FDA approval only for nausea caused by chemotherapy and to increase the appetite of people with AIDS⁴. Various studies have shown its beneficial effects in several neurological disorders recently. For some indications, significant data has been found to recommend its use where traditional therapies were not found to be effective while for several other disorders its use is still on the experimental basis and we still have insufficient evidence to use it.

1. INDICATIONS WITH GOOD EVIDENCE:

Epilepsy: Dronabinol and Nabilone have been

found beneficial in various childhood onset epilepsies including Dravet and Lennox-Gastaut syndromes that are resistant to the traditional therapies. Their addition may reduce median monthly seizure frequency by about 36.5%⁵. They were also found useful in the management of super refractory status epilepticus⁶. But we still need evidence to recommend it as alternative to traditional antiepileptics in more common epilepsies and as a first line agent in drug resistant epilepsies.

Multiple Sclerosis: Cannabinoids (nabilone and nabiximols) have been found useful for various symptoms of multiple sclerosis like pain, spasticity and urinary dysfunction⁷. Although these indication have not got FDA approval, health agencies like American Academy of Neurology (AAN) recommend that it can be considered in suitable patients as alternative to typical therapies⁸.

Neuropathic and other type of pain: These may provide effective analgesia in conditions that are refractory to other treatments including refractory neuropathic pain cause by diabetes mellitus, central neuropathic pain, pain in cancer patients, and in HIV-positive patients. According to a study about 90% of patients reported an improvement in nerve pain after cannabis use⁹. Several guidelines recommend its use when traditional therapies are not helpful.

Depression and anxiety: Data about anxiety suggested a greater benefit of cannabinoids (dronabinol, nabilone, and nabiximols) than placebo and can be consider for suitable patients¹⁰. However no difference between cannabinoids and placebo in outcomes of depression was seen and some reported a negative effect at high doses.

Tics and Tourette syndrome: There is insufficient evidence to support or refute the clinical use of cannabis for tics. However, it could be an option in resistant cases as positive effects of THC were seen in few studies¹¹.

2. INDICATIONS WITH BENEFITS BUT INSUFFICIENT EVIDENCE:

Dementia: Recently few studies have found that tetrahydrocannabinol and other compounds may reduce B-Amyloid in the brain¹². A recent study has concluded that cannabis extract containing THC can relieve various cognitive and psychiatric symptoms of Alzheimer's disease and found them to be safe and promising treatment option¹³. However more data is required for its use in dementia clinically.

Parkinson's disease: It has been studied in the context of improving motor features, functional

outcomes and in dopa related dyskinesias with mixed results¹¹. Evidence is needed for its recommendation for these and target symptoms (e.g. dystonia, psychosis, sleep) related to Parkinson's disease.

Huntington's disease: Although limited data is available to recommend its use in Huntington's disease but various case series and small studies showed significant improvements in chorea and the neuropsychiatric symptoms in patients with Huntington's disease. Further large scale studies may be needed to find its usefulness for these indications¹¹.

Dystonia: Data for its use in dystonia is limited to few small randomized placebo-controlled clinical trials with mixed results. Further large studies are needed to clear its role¹¹.

(Amyotrophic Lateral sclerosis (ALS): Some studies showed that they might be helpful in some aspects in ALS patients like delaying the onset of ALS and slowing the progression. These might also help to manage pain, appetite loss, depression, sleep problems, spasticity and drooling¹⁴. However more evidence is needed for recommendation of its use in ALS.

Migraine: They have been found to inhibit pain response in migraine patients, but clinical trials are needed to recommend its use for this indication¹⁵.

Prion disease: On the experimental basis they have shown to reduce the risk of prion disease and protect from prion toxicity but still need to be tested clinically¹⁶.

Stroke: They seem to reduce the infarct size and improve functional, histological and neurobehavioral recovery but no large scale data is available for its recommendation¹⁷.

Sleep disorders: There was some evidence that cannabinoids may improve sleep in some patients. Cannabinoids were associated with a greater average improvement in sleep quality and sleep disturbance than the placebo¹⁸. Further large scale studies are needed to find its benefit for this purpose.

Other uses: Some studies have shown its anti tumor activity, as it showed to inhibit growth of the cancer cells. Its benefits have also been observed in Spinal cord injury and Fibromyalgia as well¹⁹.

Despite significant positive data, several factors pose a challenge to its use as a medicine. These include Medical, ethical and legal and economical factors. Medically it is found to be much safer to traditional pharmacological agents and addictive potential of cannabis is quite low. The risk of dependence on cannabis is reported to be 9% in long-term users, significantly less than the addiction rates of heroin, cocaine, alcohol, and prescribed anxiolytics²⁰. Its side effect profile includes euphoria, disorientation, drowsiness, dizziness, motor in coordination, and poor concentration.

The peripheral adverse effects include tachycardia, hypotension, conjunctival injection, bronchodilation, muscle relaxation, and decreased gastrointestinal motility. Long term effects include risk of psychiatric disorders, apathy and cognitive impairment and hazards related to pregnancy²¹. So its use should be based on the benefit outweigh the risk assessed by an expert.

Ethically in various cultures a negative image is linked to its use and possession. Good awareness campaign may help patients, their families and societies to make a decision based on evidence and knowledge. Ultimately, the medical cannabis debate is not about making it widely available for a broad range of health conditions but about giving a small number of patients an option where they may have none.

Legally in Pakistan under The Anti-Narcotic policy 2010²², person may get punishment up to 6 months on possessing the cannabis, but still it is the most commonly used drug with prevalence of recreational use being 3.6 % in our population²³. Due to increasing argumentation for its use for medicinal purpose, like the other many developed countries law amendments will be needed for relaxation regarding its use for medicinal purpose in Pakistan.

Various necessary measures should be taken for its controlled use that may include:

- (1) Only be prescribed by experts.
- (2) Specific registered points with monitoring units to monitor the dose or amount each time.
- (3) Regular follow ups by experts to monitor side effects and check the possibility of misuse.
- (4) When to stop or taper the use in case of negative effects.

Law amendments will be important as there is risk that if its judicious use is not legalized then patients may start acquiring it from illegal ways, which might lead to the poor quality and uncontrolled use opening ways for more hazards than bringing the good.

CONCLUSION:

Cannabinoids have been found useful in many neurological and medical disorders. To keep its use judicious and controlled, a frame work by the health authorities in collaboration with law agencies should be made so that it might be available when other hopes are lost and its use is justifiable and only under a strict protocol. The three forces scientific knowledge, social and political acceptance and legislation may help to reach a consensus about its medicinal use.

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