

Case Report

Rehabilitating Effect of Marijuana on Post-Covid-19 Pain Syndrome

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Abstract

Post-COVID-19 syndrome is a condition that develops after the infected patient has recovered as evidenced by laboratory tests. It is characterized by persistence of physical symptoms and subjective sensations considered to be late effects of the virus on body functions. There are currently no therapeutic means to attenuate these symptoms without inducing adverse effects. A communication of the successful use of medical marijuana in a patient with post-COVID-19 syndrome is herein released.

Keywords: Arthralgia; Cannabis; Fatigue; Myalgia; Post-COVID-19 syndrome

1. Case Description

A 60-year-old female presented to a community pain clinic complaining of persistent, unrelieved muscle and joint tenderness and pain, generalized fatigue, depression, and further worsening of these symptoms after minimal physical activities. She had a history of remised Hashimoto thyroiditis, smoking, L₅-S₁ disc lesion due to a traumatic fall, and minor mixed anxiety and depression and obsessive-compulsiveness. Prior to confirmation as being SARS-CoV-2 infected, those conditions were satisfactorily controlled with occasional use of over-the-counter compounds or single doses of Non-Steroidal Anti-Inflammatory Drugs (NSAIDS). She seldom used opioids.

Treatment for the SARS-CoV-2 infection consisted of oxygen supplementation, steroids and antithrombotics for several weeks both in the hospital and later at home. Serum antibodies to SARS-CoV-2 were evaluated as requested. The patient experienced intensification of her above-listed symptoms around 2 weeks following recovery from the SARS-CoV-2 infection. They became relentless rather than intermittent as before, and her musculoskeletal pain, polyarthralgia, depression and fatigue were especially disturbing. The former medications now barely controlled the symptoms, and, more importantly, night sleep became non-restorative and nothing seemed to energize her; she spent most of the time in bed. The physical examination evidenced signs and symptoms compatible with the patient's complaints. Interestingly, she described the tender, painful knots produced by pressure exerted on various body areas ("trigger points" related to deep and aching muscle pain, myalgia) and joints (arthralgia). These reactions were essentially absent before her COVID-19 infection. She rated the level of pain as 8-9/10 on a Visual-Analog Scale (VAS), and described her mood as having had deteriorated significantly (Zung depression scale ~70 [1]). She had been prescribed various analgesics throughout the following period, including tricyclic antidepressants (amitriptyline, sertraline), pregabalin, duloxetine, NSAIDs, opioids (oxycodone/paracetamol) and various tranquilizers (alprazolam, mirtazapine); all failed to ameliorate her conditions.

Her request for medical cannabis was approved by the physician and the Israeli Medical Cannabis Agency, which authorizes medical cannabis provision in Israel. The patient stated that she had used several times THC/CBD cannabis at concentrations of 20%/4% introduced to her by a family member who had been prescribed with for his medical

condition, and that this relieved her from most symptoms for several hours. She was then provided with the same composition at a daily maximal dose of 15 mg/kg as sprouts (for inhalation/smoking) divided in tid. Within a week of continuous use, the patient reported significant improvement in her conditions with no adverse events. Her pain VAS level decreased to 3-4, and she was now able to cook and do housework, go for walks, feel less feeble, and importantly, sleep well and wake up refreshed. She was much less depressed (Zung scale 45), and the spontaneous and pressure-generated myalgia and arthralgia had diminished significantly as well. At 3 months since the initiation of treatment with medical cannabis, she maintains a stable and near-normal health status.

2. Discussion

Most patients who had experienced various forms of a COVID-19 would recover completely within weeks. However, some will experience ongoing or newly emerged symptoms 3-4 weeks after the patients have been declared virus free. These symptoms can appear even if the illness had been mild or absent altogether. Symptoms include fatigue, joint pain, memory, concentration or sleep problems, muscle pain or headache, arthralgia, depression and anxiety, dizziness, and more [2, 3]. This post-COVID-19 syndrome (also known as long COVID-19, long-haul COVID-19, post-acute COVID-19, long-term effects of COVID, or chronic COVID), appears to significantly affect the ability to function, and patients can remain incapacitated for many months. The pathophysiological mechanisms that connect between the post-COVID-19 syndrome and the above symptoms is probably the consequence of diffused inflammation and a cytokine response, which result in nociceptive activation and central sensitization. Pennisi et al [4] observed that post-COVID-19 syndrome could also

intensify by repercussions of earlier social isolation, hospitalization-related stress, anxiety, and fear of dying, resulting in depression or post-traumatic stress disorder. Although yet unproven by random controlled trials, over 30% of the elderly, as well as individuals of all ages with medical conditions existing before being diagnosed with COVID-19, were reportedly noted to complain of debilitating conditions for weeks or months after the infection [5]. Apart from respiratory signs and symptoms, cardiac and neurological ones can also linger over time, including fatigue, joint pain, muscle pain and headache, with patients describing worsening of the symptoms after minimal physical or mental activities, and unexplained depressive states and anxiety [2, 3, 6, 7].

Cannabis was shown to relieve intense pain, such as that attributed to arthralgia, myalgia, arthritis and other bone- or ligament-associated suffering, as well as deterioration in mood and emotional state [8], although the mechanism by which the neurophysiological network responds to the compound remains unclear. Evidence of specific relief of myalgia and arthralgia has been provided in several recent studies [9, 10]. The feasibility of medical cannabis to attenuate the post-COVID-19-associated persistent myalgia and arthralgia and to allow patients to return to their usual lifestyles has not been described before. The herein described patient had a history of mild malaise before she was infected, but she was physically active, ran her household efficiently, and was involved with all of her usual family activities. Her post-COVID medical conditions changed radically to the point of rendering her too weak to even minimally manage her usual activities of daily living. Clinically, the cannabis rehabilitated her to a status she described as “getting her life back”. The effects of the drug were stable at 3 months of treatment, there were no

relapses, and she could manage with minimal opioid intake and sustained no adverse effects whatsoever also.

Cannabis even at low doses significantly improves neuropathic pain [11]. This effect stands at the basis of the decision to grant medical cannabis to the patient, even though a medium dose (9.4% tetrahydrocannabinol herbal cannabis tid) sufficiently reduced the intensity of pain, improved sleep and was well tolerated [12]. The reason for prescribing the patient with twice the above dose was triple: 1) the dose and composition were similar to those prescribed to similar non-post-COVID-19 patients that proved effective and devoid of untoward effect in other patients cared in the clinic; 2) uncertainty if the symptoms would react dissimilarly to cannabis as those observable during/after trauma-engendered chronic pain; 3) THC was combined with CBD, which would calm down psychoactive effects that are THC-related. Data are still fuzzy as to why, to what extent and for how long would the immunological hyperactivation generated by COVID-19 virus reign and what cannabis composition would control it best; medical cannabis herein proved to lastingly achieve these goals.

A single dose of cannabis is ineffective in generating sustained neuropharmacological effects over time [13]; treatment becomes efficacious following sustained use. As such, evaluation of therapeutic efficacy should start at day 5-7 [12] into treatment and continue weekly and monthly. This report is of clinical importance since there are no available data on a reliably helpful compound to effectively attenuate Long COVID-19 muscle pain and arthralgia syndromes or depression. As recommended by Hill et al [14], this line of therapy was chosen after first and second line analgesics and tranquillizers, including opioids, did not ameliorate the patient’s conditions but rather produced

adverse effects, such as gastrointestinal discomfort and lack of energy to manage daily activities, as well as tiredness. The well-known adverse effects of opioids, amitriptyline-derivatives and anti-depressants, gabapentinoids or duloxetine, vanished by approximately one week after starting using cannabis and tapering down the former drugs. The patient's performances stabilized, the sense of humor returned to normal, and pain was mitigated to a level similar to her pre-COVID-19-infected state. Importantly, there were no adverse side effects related to cannabis use during the follow-up period. Indeed, cannabis has a superior safety profile in comparison to many other line 1 or 2 conventional medications used for chronic pain, and no reports witnessed deaths in case of overdose, due to the lack of CB1 receptors in the brainstem or cardiorespiratory centers [15]. THC-mediated side effects are dose-dependent and are rate-limiting. Gradual increase in dose and concentration, when combining CBD with THC, better reduce adverse effects; quick tolerance to psychoactive effects of cannabis is also obtained within days, without concomitant tolerance to the benefits, and therefore maintenance of the same daily dose uninterrupted is most efficacious [16]. This is in stark contrast to opioids where treatment protocols need recurrent augmentations.

Finally, the reason for prescribing the patient with the mixture of THC 20%/CBD 4% was her earlier exposure to that mixture. The rationalization was that it would be pharmacologically unwise to prescribe her with lower concentrations after her brain has already been reliant on that therapeutic protocol. Had the earlier "introduction" of the patient to marijuana not taken place, it would have been more prudent to start treatment with a lower concentration and quantity ("start low, go slow"). Also, a combination of both compounds is recommended: there is synergy between

THC and CBD, the latter enhancing the analgesic potential of THC by means of potent inverse agonism at CB2 receptors [17]. In addition, CBD may modulate the potential unwanted effects of THC by means of antagonism at CB1 receptors [18] thus enhancing the safety profile for the THC+CBD composition. Lastly, we do not know whether cannabis is as effective in males as in females; the current report is based on only one female who presented at the clinic due to long COVID-19 symptoms.

3. Conclusions

Medical marijuana, at a mixture of THC 20% and CBD 4%, administered at a daily dose of 15 mg/kg, proved an optimal protocol for attenuating post-COVID-19 physical and mental sequelae, without evoking adverse effects. The worldwide COVID-19 pandemic will probably be around for the unforeseeable future, thus various doses and compositions of medical marijuana should be tested, aiming at reaching the optimal therapeutic protocol for post-COVID-19 syndrome, especially for malaise and depression.

Conflict of Interest Statement

The author declares no conflict of interest.

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