Original Article

# Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly

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ABSTRACT

*Introduction:* There is a substantial growth in the use of medical cannabis in recent years and with the aging of the population, medical cannabis is increasingly used by the elderly. We aimed to assess the characteristics of elderly people using medical cannabis and to evaluate the safety and efficacy of the treatment.
*Methods:* A prospective study that included all patients above 65 years of age who received medical cannabis from January 2015 to October 2017 in a specialized medical cannabis clinic and were willing to answer the initial questionnaire. Outcomes were pain intensity, quality of life and adverse events at six months.
*Results:* During the study period, 2736 patients above 65 years of age began cannabis treatment and answered the initial questionnaire. The mean age was 74.5 ± 7.5 years. The most common indications for cannabis treatment were pain (66.6%) and cancer (60.8%). After six months of treatment, 93.7% of the respondents reported improvement in their condition and the reported pain level was reduced from a median of 8 on a scale of 0–10 to a median of 4. Most common adverse events were: dizziness (9.7%) and dry mouth (7.1%). After six months, 18.1% stopped using opioid analgesics or reduced their dose.
*Conclusion:* Our study finds that the therapeutic use of cannabis is safe and efficacious in the elderly population. Cannabis use may decrease the use of other prescription medicines, including opioids. Gathering more evidence-based data, including data from double-blind randomized-controlled trials, in this special population is imperative.

## 1. Introduction

The use of medical cannabis in recent years is growing substantially [1–3], with varied indications such as: chronic pain, chemotherapy-induced nausea and vomiting, multiple sclerosis, Alzheimer's disease, anorexia nervosa, anxiety, dementia, dystonia, Huntington's disease, Parkinson's disease, post-traumatic stress disorder (PTSD), psychosis, Tourette syndrome, epilepsy and more [4–6]. The number of people aged 60 years and over is expected to double by 2025 worldwide and by 2050 in the United States [7–9]. Epidemiological data show that the older population constitutes a growing segment of medical cannabis users, ranging from approximately 7% to more than one third, depending on the country [10–12].

It is well known that aging is associated with substantial changes in pharmacokinetics and pharmacodynamics; for instance, hepatic drug clearance as well as renal elimination are both decreased in the elderly. Furthermore, aging is associated with increased body fat and decreased

lean body mass [13,14], which increase the volume of distribution for lipophilic drugs, such as cannabis. Only a small number of studies have evaluated the pharmacokinetics of cannabis and cannabinoids in the elderly population [15–17]. Interaction of cannabis and other drugs is also largely unknown, as the current evidence is scarce. Concomitant administration of cannabis with other drugs that influence the hepatic CYP family enzymes may greatly alter the metabolism of the cannabinoids. This issue is especially important in the elderly population, where polypharmacy is common [18,19]. Common adverse events patients experience due to cannabis use include dizziness, euphoria, drowsiness, confusion and disorientation [4,20]. These events are particularly important in the elderly population, which may suffer from conditions such as dementia, frequent falls, mobility problems, hearing or vision impairments [21,22]. Thus, studies conducted on younger adults cannot be simply extrapolated to the elderly population.

Despite the significant rise in use, the current evidence on the efficacy and safety of medical cannabis in elderly is scarce. Only a small

number of studies included elderly patients or analyzed them separately [20]. The aim of this study was to assess the characteristics of the older population receiving medical cannabis for a wide variety of diseases as well as evaluate the safety and efficacy of short and medium-term use.

## 2. Materials and methods

### 2.1. Study design and population

In Israel, most physicians who wish to prescribe medical cannabis for their patients send an authorization request to the Israel Medical Cannabis Agency (IMCA), a unit within the Israeli Ministry of Health (IMOH) [42]. Following the authorization for use patients are asked to contact one of the eight specified medical cannabis suppliers in Israel. To date, over 32,000 medical cannabis licenses were given in Israel, and approximately 33% of the patients receive their cannabis from "Tikun Olam Ltd.", the largest medical cannabis supplier in Israel.

The study included all the patients who initiated treatment with medical cannabis at "Tikun Olam" from January 20, 2015 to October 30, 2017, that were willing to answer the initial questionnaire and were 65 years of age or older at the initiation of treatment. The study was approved by the "Soroka University Medical Center" institutional review board (IRB) Committee. All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki. All the patients gave informed consent to participate in the study.

### 2.2. Data sources and collection

As part of the routine treatment process, every patient who begins treatment with medical cannabis from "Tikun Olam" receives thorough instructions from a certified nurse on the use of the drug, possible side effects, route of administration and the regulatory process that the use of medical cannabis entails. The medical cannabis license specifies two possible routes of administration: oil and inflorescence, delivered as flowers, capsules and cigarettes. During this intake session, following the patient's consent, the patient's medical history, medication use, habits, detailed symptoms list, quality of life assessment, indication for cannabis treatment and demographic data are evaluated by the nurse. At the end of the intake session the nurse recommends, out of the 15 available cannabis strains, specific strains suitable to the patient's condition. Every patient is eligible for either a single strain or several strains.

All the patients were followed up at one month and at six months from treatment initiation by a telephone interview. The interview after six months is extensive and includes an assessment of adverse events, treatment satisfaction, changes in symptoms and in drug regimens.

### 2.3. Study outcomes

For safety analysis, at six months of treatment, we assessed the occurrence and frequency of any adverse events and specifically the following: headache, dizziness, nausea, vomiting, stomach ache, dry mouth, somnolence, weakness, confusion and disorientation, restlessness, hallucinations, red eyes, palpitations, drop in sugar levels and cough. The patients were asked to provide details of the incidence, duration and severity of the reported adverse event.

For efficacy analysis, after six months of treatment, we assessed the following parameters:

- Quality of life – global assessment by the patient using the Likert scale with five options: very good, good, not good nor bad, bad or very bad.
- Pain intensity – assessment by the numeric visual analog scale with an 11-point scale (0 = no pain, 10 = worst pain imaginable).
- Perception of the general effect of cannabis – global assessment by using the Likert scale with seven options: significant improvement,

moderate improvement, slight improvement, no change, slight deterioration, moderate deterioration or significant deterioration.
- Treatment success – treatment success was defined as moderate or significant improvement in the patient's condition and compliance with the treatment.

### 2.4. Statistical analysis

Continuous variables with normal distribution were presented as means with standard deviation. Ordinary variables or continuous variable with non-normal distribution were presented as medians with an interquartile range (IQR). Categorical variables were presented as counts and percent of the total.

When appropriate, univariate comparisons were made using $\chi^2$-test or Fisher's exact test for categorical variables, and using Student's $t$-test or Mann–Whitney test for quantitative variables. Paired Wilcoxon test was used to compare ordinal variables.

A p-value of 0.05 or less (two-sided) was considered statistically significant. IBM SPSS software, version 24.0, was used for statistical analysis.

## 3. Results

### 3.1. Characteristics of the cohort

We identified 2736 patients over the age of 65 who initiated treatment with medical cannabis from "Tikun Olam" during the study period and were willing to answer the initial questionnaire. During the six months follow-up period, 564 patients died, 661 had been treated for less than six months, 297 stopped the treatment within six months and 28 patients switched to a different cannabis supplier. Thus, of the entire cohort, 1186 (43.3%) were eligible to answer the follow-up questionnaire after six months of treatment. Of the eligible patients, 901 (76.0%) responded to the questionnaire (Fig. 1). Of the entire population, 334 patients (12.2%) used medical cannabis from a different supplier prior to the initiation of treatment with "Tikun Olam". The elderly population comprises 34.2% of all the patients who initiated cannabis treatment with "Tikun Olam" in the study period (data not shown).

Table 1 shows demographic characteristics of the cohort. The mean age was 74.5 ± 7.5 years, with a slight female predominance (1463, 53.5%). The most common route of administration was oil (1022, 37.3%), followed by smoking (669, 24.4%) and vaporization (176, 6.4%).

Table 2 shows the indications for the medical cannabis. The most common indications were pain (1822, 66.6%) and cancer (1482, 60.8%), with a significant overlap between the two groups (cancer associated pain). All other indications comprise < 10% of the indications in the cohort. Cancer was also the most prevalent diagnosis at treatment initiation, followed by cardiovascular diseases (Supplementary data Table 1).

### 3.2. Strains of cannabis

Out of the 901 respondents at six months, 264 (29.3%) used one strain, 482 (53.5%) used two strains and 141 (15.6%) used between three to six strains. Most of the patients were using THC (tetrahydrocannabinol) rich strains of cannabis, whether the origin is from a *sativa* dominant species ("Erez" was used by 54.6% of the patients) or an *indica* dominant species ("Alaska" was used by 27.4% of the patients), regardless of the indication for cannabis use (Supplementary data Table 2). CBD (cannabidiol) rich strains were used by patients who suffer from pain (23.3%), chemotherapy side effects (30.9%), Parkinson's disease (45.7%) and inflammatory bowel disease (40%).