Medical use of cannabis in the Netherlands

Abstract—The authors investigated the indications for cannabis prescription in the Netherlands and assessed its efficacy and side effects. A majority (64.1%) of patients reported a good or excellent effect on their symptoms. Of these patients, approximately 44% used cannabis for ≥ 5 months. Indications were neurologic disorders, pain, musculoskeletal disorders, and cancer anorexia/cachexia. Inhaled cannabis was perceived as more effective than oral administration. Reported side effects were generally mild.

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Robert W. Gorter, MD, PhD; Mario Butorac, MA; Eloy Pulido Cobian, MD; and Willem van der Sluis, PhD

There has been renewed interest in the medical use of *Cannabis sativa* and its main constituent, δ -9-tetrahydrocannabinol (THC), for conditions like anorexia and cachexia in cancer and AIDS,^{1,2} movement disorders and multiple sclerosis (MS),^{3,4,5} migraine, spinal cord injuries,⁶ and pain.

In 1997, 112 patients with MS in the USA and the UK were asked in an anonymous questionnaire about their medical use of cannabis for relief of symptoms. After cannabis consumption, there was a strong improvement of spasticity at the onset of sleep and upon awakening in the morning as well as a reduction in pain and tremor. Patients also reported improvement in the ability to walk, in recovery of balance, and in sexual function. There was only minor improvement in memory loss, fecal incontinence, and constipation.⁷

In another 1997 study, 7,407 members of the Dutch Society of Multiple Sclerosis received an anonymous questionnaire to investigate knowledge and use of cannabis among patients. The response rate was 68.1%. Almost half of all respondents knew about the possible benefits of cannabis in MS. Most patients who used cannabis for relief of symptoms were elderly and lived in cities with a population of $\geq 100,000$. In Amsterdam, relatively more patients with MS over age 40 used cannabis vs the city's general population. In the Netherlands as a whole, approximately 5% of the population above age 12

used cannabis occasionally vs 13% of all patients with MS who responded.⁸

In the Netherlands, recreational use of cannabis is illegal, but consumption of small amounts under certain conditions is condoned. Medical use of cannabis was legalized in 2003, so physicians now prescribe cannabis to patients through pharmacies. Founded in 1995, Maripharma, a nonprofit patient-oriented organization, delivers "medical-grade cannabis" (MGC) on prescription to pharmacies throughout the country. When a patient presents a prescription for MGC, the pharmacy forwards the prescription to Maripharma, which delivers units of 25 or 5 g of standardized, sterile, and vacuum-packed MGC to the pharmacy. The THC content in MGC is standardized at 10.2%.

Methods. We developed a standardized questionnaire about the medical use of cannabis in the Netherlands to obtain information from patients and physicians prescribing MGC. We documented the indications for which MGC was taken, the duration, whether the patient had any side effects, and whether the patient was content with the effects of cannabis. Each shipment of MGC was accompanied by two questionnaires, which were to be completed by both patient and prescribing physician, along with self-addressed envelopes with prepaid postage.

The physician was asked to document his/her name, office address, and specialty and the patient's diagnosis, date of birth, weight, gender, and duration of intake. The physician was also asked to rate the efficacy of the therapy with cannabis as "not at all," "somewhat," "good," or "excellent" and indicate how the cannabis was administered (orally, by inhalation, or both). The patient was asked about the occurrence of 12 side effects (eye irritation, feeling "high," short-term memory loss, sleepiness, hunger, loss of concentration, decrease in motivation, anxiety, euphoria, depression, dry mouth, and difficulties in coordination), the frequency of the symptoms, and intensity of the symptoms (see table E-1 on the *Neurology* Web site at www.neurology.org). The questionnaires were to be returned to the International Institute for Oncological and Immunologic Research in Amsterdam. The first 107 questionnaires, returned during the period October 1997 to February 1999, were analyzed.

Results. Questionnaires were included with 300 shipments of MGC, from which 107 patients (35.7%) completed and returned their questionnaires. Forty-eight (45%) were men, median age was 58.0 years (52.5 years for men, 60.0 years for women), median body weight was 70.0 kg (men 74.5 kg, women 65.0 kg), and mean duration of cannabis (MGC) intake was 5.4 months (men 7.3 months, women 3.9 months) (table 1). Patients were located in all parts of the country, with a slightly higher prevalence in larger cities in the western part of the Netherlands.

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From the International Institute for Oncological and Immunological Research (Drs. Gorter and Cobian, M. Butorac), Cologne, and University Witten/Herdecke Medical School (Dr. Gorter), Germany; University of California San Francisco Medical School (Dr. Gorter) and Institute of Holistic Studies (Dr. Gorter), San Francisco State University, CA; School of Pharmacy (Dr. Gorter), University of the Western Cape, Cape Town, South Africa; and School of Pharmacy (Dr. van der Sluis), University of Utrecht, the Netherlands.

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Address correspondence and reprint requests to Dr. R.W. Gorter, International Institute for Oncological and Immunological Research, Hohenstaufenring 30-32, 50674 Cologne, Germany; e-mail: robert.gorter@cancer-society.org

Table 1 Reported diagnoses sorted by frequency

Diagnoses	Frequency	Percentage
Neurologic disorders	45	38.8
Musculoskeletal/connective tissue disorders	24	20.7
Malignant tumors and symptoms thereof	16	13.8
Other	31	26.7
Pain	10	8.6
HIV	5	4.3
Stroke	3	2.6
Diabetes mellitus	2	1.7
Hypertension	2	1.7
Other cerebrovascular diseases	2	1.7
Asthma	1	0.9
Depressive episode	1	0.9
Emotional shock or distress	1	0.9
Emphysema	1	0.9
Glaucoma	1	0.9
Ménière disease	1	0.9
Sarcoidosis	1	0.9
Total	116	100.0

Prescribing physicians were internists, oncologists, neurologists, and family practitioners in private practice. Specialists tended to prescribe cannabis at the request of their patients, whereas family practitioners, on their own initiative, tended to discuss the possible benefits of cannabis with their naive patients before it was prescribed.

The main reported diagnoses for which MGC was prescribed were neurologic disorders like MS and spinal cord injuries ($n = 45$; 38.8%), musculoskeletal/connective tissue disorders ($n = 24$; 20.7%), and malignant tumors for symptoms like anorexia/cachexia and fatigue ($n = 16$; 13.8%) and “other,” which were often HIV infection, cerebrovascular accident, and pain ($n = 31$; 26.7%) (see table 1).

In 19 cases (18.4%), no positive effects of cannabis were reported (table 2). These patients stopped taking cannabis at between 1 and 4 months. In contrast, a good or excellent effect was documented in 66 cases (64.1%). Twenty-nine of

these patients had taken cannabis for ≥ 5 months at the time of the survey. Sixteen patients took it for >10 months. The perceived efficacy by the patient correlated positively with the duration of the intake of *C sativa* (Spearman $r = 0.52$, $p < 0.01$).

There was a correlation between side effects and the duration of MGC use at the time of the survey. Of the 12 listed side effects, only “dry mouth” (27.4%) was reported as present regularly or always. This might be because most patients inhaled cannabis vs taking it orally. Other side effects mentioned were “sleepiness” (13.9%), “euphoria” (13.3%), “loss of concentration” (11.7%), and “feeling high” (10.6%).

Negative experiences were more frequent in the first few months of intake (see table E-1). Positive experiences accumulated more when time progressed. There are two explanations: Those patients who experienced side effects or no efficacy stopped after 1 to 4 months, or the perceived efficacy of cannabis took time to develop. Perceived efficacy was better in the group who inhaled only (68% of all patients) vs those who took MGC orally only (32% of all patients). Thus, efficacy of MGC was better when inhaled (Mann–Whitney U Test, $Z = 4.7$, $p < 0.01$).

Discussion. In the Netherlands, patients and physicians are aware of the possible benefits of cannabis for certain medical conditions. Main indications are neurologic disorders (MS, spinal cord injuries), musculoskeletal and connective tissue disorders, cancer and AIDS (anorexia/cachexia and fatigue), and various forms of pain. Interestingly, patients with more chronic pain documented less benefit than patients with more acute pain (e.g., migraine).

Of the 107 questionnaires evaluated in this study, 66 patients (64.1%) documented a good or excellent effect for their symptoms. Of these patients, 44% used cannabis for ≥ 5 months. It is likely that benefiting patients continued taking cannabis for the relief of their symptoms, while others, not experiencing a benefit during the first few weeks to months, might have stopped within 1 to 4 months. In addition, lack of efficacy experienced in the first few months might be attributed to certain medicinal effects of cannabis that take a while to take effect, such as appetite stimulation, weight gain, and mood elevation. The evaluations of efficacy and side effects by physician

Table 2 Correlation between estimated efficacy and duration of cannabis intake

Months	Estimated efficacy									
	Not at all		Somewhat		Good		Excellent		Total	
	Frequency	%	Frequency	%	Frequency	%	Frequency	%	Frequency	%
0–1	13	38.2	10	29.4	8	23.5	3	8.8	34	33.0
2–4	5	13.9	5	13.9	20	55.6	6	16.7	36	35.0
5–10	0	0.0	2	12.5	13	81.2	1	6.2	16	15.5
>10	0	0.0	1	6.2	7	43.8	8	50.0	16	15.5
Total*	19	18.4	18	17.5	48	46.6	18	17.5	103	100.0

* One missing.

and patient were similar. Therefore, it is likely that both patients and physicians were equally content or disappointed with regard to the medicinal effects of the cannabis.

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NeuroImages

Figure. (A) Axial unenhanced head CT. Several round hypodensities compatible with fat in the interpeduncular cistern (arrow) and the left temporal horn (arrowhead) of the lateral ventricle are observed. (B) Axial T1-weighted MRI of the brain. Bilateral round hyperintensities in the frontal horns with chemical shift artifact consistent with the magnetic resonance characteristics of lipid (arrows). The fat particles are seen in a nondependent location compatible with its chemical composition. Brain and spine MRI both before and after procedure failed to demonstrate evidence of dermoid/epidermoid.

Intracranial fat embolization due to baclofen pump

Y. Qian, BS; B.M. Ances, MD, PhD; A. Pruitt, MD; B. Choi, MD; and G. Moonis, MD, Philadelphia, PA

A 38-year-old woman presented with sudden headaches, hyperacusis, and photophobia 3 months after baclofen pump placement for spasticity due to multiple sclerosis. CT demonstrated hypoden-

sities within the basilar cisterns and temporal horn of the lateral ventricles (figure, A and B). MRI of the neural axis showed fat along the tract of the baclofen pump. These lesions were not consistent with dermoid or epidermoid tumors.¹ Intracranial fat seen in this case suggests that pump placement in addition to multiple lumbar punctures can lead to fat dissemination.²

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Address correspondence and reprint requests to Dr. Gul Moonis, Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA 19103-4283; e-mail: gul.moonis@uphs.upenn.edu

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Y. Qian, B. M. Ances, A. Pruitt, et al.

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