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Ocular Effects of Marihuana Smoking

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Before 1972 there was little information available regarding the ocular effects of marihuana smoking. Observations of redness and dry sensation of the eyes were common among users of marihuana, but scientific studies were lacking. In fact, there were statements of frank misinformation, including alleged pupillary dilatation, decrease in visual acuity, altered depth perception, and impaired peripheral vision.

In December, 1972, Hepler, Frank, and Ungerleider reported actual observations of the eyes and of visual function. For instance, the conjunctiva was photographed before and after intoxication, documenting the striking engorgement of conjuctival vessels that occurs with the smoking of marihuana. They used a standard ophthalmologic test for tear secretion, the Schirmer's test, which measures quantitatively the amount of soaking of a standardized strip of filter paper placed over the lid margins into the conjuctival cul-de-sacs. A normal individual totally soaks the filter paper, while subjects intoxicated with marihuana soaked only a few millimeters. Neither the fact that the eyes became red nor that they became dry came as a surprise, since these observations were well known to marihuana users. However, the pupillary findings were unexpected. Rather than an obvious dilatation, the only change in pupillary size was a slight pupillary constriction. There was preservation of normal pupillary reactivity to light and near-stimulation. Also observed was a consistent decrease in intraocular pressure in normal, healthy subjects (Hepler et al., 1972).

In the past 2 years additional observations of the ocular effects of marihuana and of some marihuana derivatives have been made. Enough normal subjects have been studied to provide statistically large samples. Drug effects in normal rabbit eyes have been studied, and ocular effects in human glaucoma patients have been recorded.

NORMAL HUMAN STUDIES

Acute Effects

Adult males between the ages of 21 and 29 returned for a total of eight outpatient sessions in each of which they received one dose of one of the following, administered in a double-blind protocol: (1) Natural marihuana with standard-

ized Δ^9-tetrahydrocannabinol (Δ^9-THC) content of 1.0, 2.0, or 4.0% of weight of plant material. The amount of smoking material was kept constant: 7 mg/kg body weight. (2) Synthetic Δ^9-THC blended into placebo marihuana material (referred to as "THC-spiked placebo") smoked in comparable dosages. (3) Oral THC: Synthetic Δ^9-THC dissolved in sesame oil and administered in capsules. (4) Placebo: Marihuana plant material free of Δ^9-THC.

All subjects were experienced marihuana smokers. Before acceptance into the study each subject's suitability was evaluated utilizing general physical examination, psychiatric assessment, and basic laboratory blood analysis. Each subject underwent ophthalmological evaluation to rule out past history of ocular disease or injury, or any demonstrable abnormality on ocular examination. All subjects had normal central visual acuity and peripheral visual fields, ocular movements and fusion, intraocular pressures, and fundoscopic examination. Amblyopia ex anopsia, however slight, disqualified a subject as did refractive errors greater than five diopters. Testing procedures, protocols for supervision, and other aspects of materials and methods were similar to those used by other members of the UCLA Marihuana Research Group as reported elsewhere in this volume. The opthalmologic aspects of examination have been reported previously by Hepler et al. (1972). However, it should be pointed out that procedures were carried out in a standardized manner with respect to time of day, nature of instrumentation, and experience of examiner. Tonometry (measurement of intraocular pressure) was performed by the same experienced technician throughout, utilizing the same Goldmann applanation tonometer. Both the technician and tonometer were checked periodically to assure accuracy. Pupillography utilized an infrared pupillograph constructed in the laboratories of Dr. Irene Loewenfeld, as described by Hepler et al. (1972).

Results

Pupils. There was a slight, statistically nonsignificant constriction of the pupils at 5 min, with preservation of normal light and near-stimulus sensitivity. The initial slight constriction returned gradually toward normal during the course of approximately 3 hr. This pupillary phenomenon was observed in patients smoking natural marihuana, THC-spiked placebo, and in subjects ingesting Δ^9-THC (Figs. 1 and 2).

Intraocular pressures. Tables 1 and 2 indicate the dose-related and statistically significant effect in reducing acutely the intraocular pressure following smoking or ingesting marihuana or THC. The amount of pressure drop was in the range of 30% for 2% THC and natural marihuana. The placebo also showed consistent mild pressure drop, the effect approximating 10% pressure reduction. Since we subsequently observed pressure-reducing effects with cannabinoids other than THC, our THC-eluted marihuana may have contained significant amounts of other active agents.

Higher dosages of oral THC were given to a very small group of normals. There

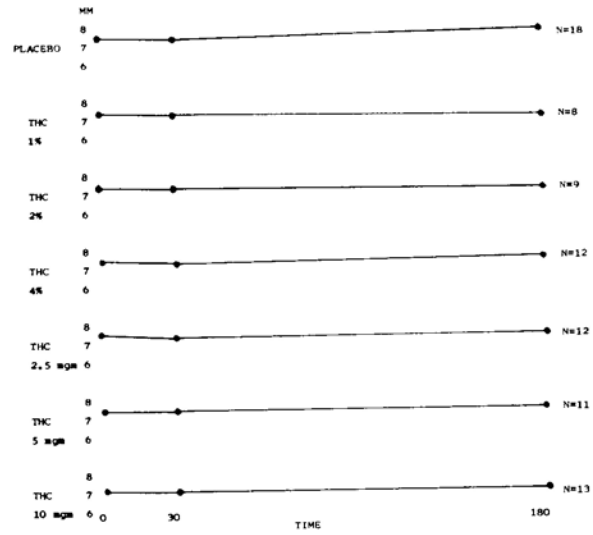

FIG. 1. Mean pupil size at rest after smoking THC-spiked placebo and oral THC. Times are in minutes post drug.

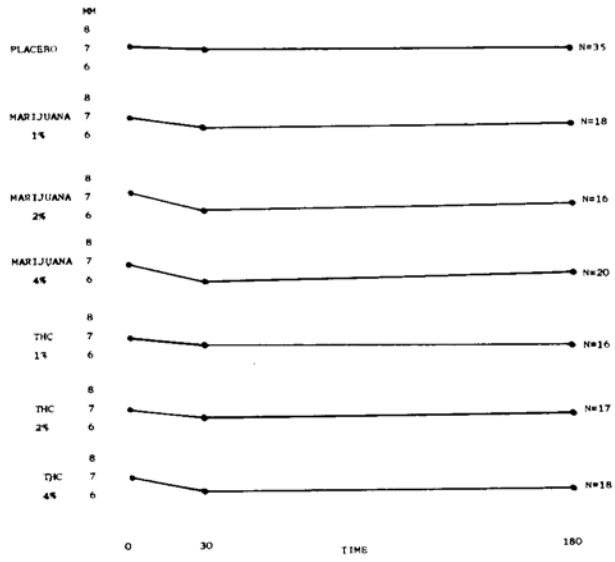

FIG. 2. Mean pupil size at rest after smoking natural marihuana and THC-spiked placebo. Times are in minutes post drug.

TABLE 1. *Intraocular pressure after smoking marijuana and THC*

Drug	Presmoking pressure (mm Hg)	Postsmoking pressure (mm Hg)	
		30 min	180 min
Placebo			
$N = 86$	14.26 ± 2.3	13.20 ± 2.2	12.87 ± 2.5
1% Marihuana			
$N = 44$	14.72	10.31[a]	11.42[b]
2% Marihuana			
$N = 46$	14.10	10.55[a]	11.63
4% Marihuana			
$N = 48$	14.86	9.80[a]	11.45[b]
1% THC			
$N = 40$	14.14	12.04	11.88
2% THC			
$N = 40$	13.86	10.63[a]	11.24[b]
4% THC			
$N = 40$	13.98	10.58[a]	10.64[b]

[a] Significant at $p < 0.01$ level.
[b] Significant at $p < 0.05$ level.

TABLE 2. *Intraocular pressure after oral THC (L, M, H) and smoking (%THC)*

Drug	Preingestion and presmoking pressure (mm Hg)	Postingestion and postsmoking pressure (mm Hg)	
		30 min	180 min
Placebo			
$N = 18$	15.36 ± 2.5	14.17 ± 2.6	13.75 ± 2.1
1% THC			
$N = 9$	15.17	12.75[a]	12.36[a]
2% THC			
$N = 9$	14.75	13.11	11.89[a]
4% THC			
$N = 12$	14.98	12.25[a]	12.27[a]
(L) THC			
$N = 12$	15.25	13.77	13.18
(M) THC			
$N = 12$	14.52	12.98[a]	12.02[a]
(H) THC			
$N = 13$	15.23	12.77[a]	11.77[a]

[a] Significant at $p < 0.05$ level.
L = 5 mg oral THC, approximately 0.062 mg/kg body weight.
M = 10 mg oral THC, approximately 0.125 mg/kg body weight.
H = 20 mg oral THC, approximately 0.250 mg/kg body weight.

TABLE 3. *Intraocular pressure after oral THC*

Dose (mg)	N	Pre-ingestion	Postingestion (min)			Change (%)
			60	120	180	
15	2	14.75	11.00	10.25	12.00	18.65
30	3	13.67	12.83	11.42	9.00	34.17
40	3	16.08	14.25	14.00	asleep	12.94 (60 min)

appeared to be a pressure-reducing effect, but recovery of data was incomplete because of the marked sedative effect of this dosage (Table 3). Our subjects were sometimes too sleepy to permit measurement of intraocular pressures, at least by Goldmann applanation tonometry, 3 hr after intoxication.

Chronic and Cumulative Effects

Nineteen hospitalized subjects were observed for 35 days, and another 29 subjects were observed as in-patients for a total of 94 days to study cumulative effects. (The 94-day study is still in progress.)

Results

Pupils. During this prolonged period of observation, pupillary findings showed no cumulative effects.

Intraocular pressures. Twelve-hour observations of 34 subjects were made after smoking placebo, 1% and 2% natural marijuana. Intraocular pressures were measured for an initial 5 hr to form a stable baseline. After intoxication at approximately 3:30 P.M., pressures were measured for another 5 hr. There was a consistent drop in intraocular pressure, around 30% for 2% marijuana, and the reduction appeared to last between 4 and 5 hr (Table 4 and Fig. 3).

Eighteen hospitalized subjects were permitted to smoke marijuana *ad libitum* during a 5½-hr period. The average number of joints smoked was 5, with a range between 2 and 22. All subjects demonstrated a substantial drop in intraocular pressure, a typical change being from 16 mm Hg before smoking to 9 mm after smoking. Figure 4 shows representative data from two such subjects, one of whom smoked two joints, the other 22. Curiously, there did not seem to be much cumulative effect shown by those who smoked more than two joints.

In hospitalized subjects observed for 35 or 94 days the daily base-line intraocular pressure showed a prompt drop as soon as the subjects began to smoke. There were no indications of cumulative effects upon the intraocular pressure response.

Other ocular observations. All subjects observed for 35 or 94 days were examined repetitively to elicit any changes in visual function that might be related to chronic drug administration. The categories of examinations performed and the

TABLE 4. *Intraocular pressure in chronic study*[a]

Drug	*N*	8 A.M.	10 A.M.	12 A.M.	2 P.M.	4 P.M.	5 P.M.	6 P.M.	7 P.M.	8 P.M.	9 P.M.
Placebo	6	13.71	13.88	13.96	13.58	13.08	12.58	12.85	12.79	12.92	12.83
1% Marihuana	13	13.73	13.54	13.42	13.42	11.92	11.31	11.17	11.09	11.65	11.96
2% Marihuana	15	13.92	13.80	13.72	13.30	11.18	10.35	10.42	10.67	11.53	11.77

[a] Subjects intoxicated at 3:30 P.M.

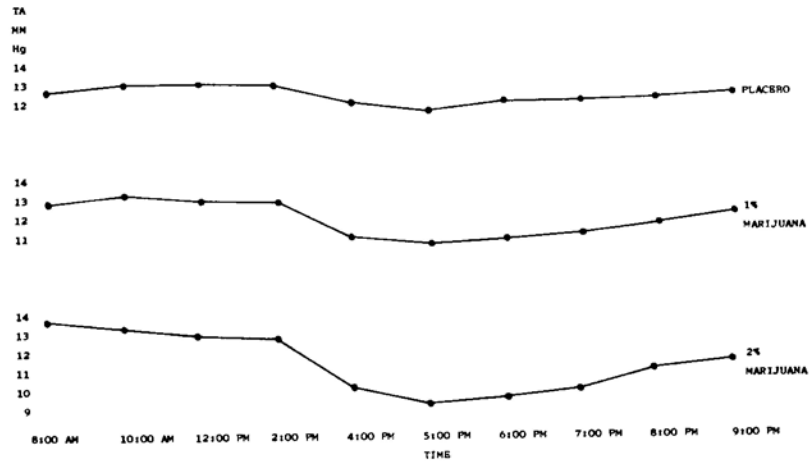

FIG. 3. Intraocular pressure in chronic study. Subjects were intoxicated at 3:30 P.M.

results include: (1) basic ocular examination, including central visual acuity and peripheral visual fields: no changes; (2) orthoptic evaluation to determine whether there were any subtle changes in depth perception and fusion: no changes; (3) Doppler ultrasonography, in which blood flow in arteries was estimated without entering the arteries: no changes; (4) tonography, a means of providing a continuous 4-min recording of intraocular pressure: consistent decrease in amplitude

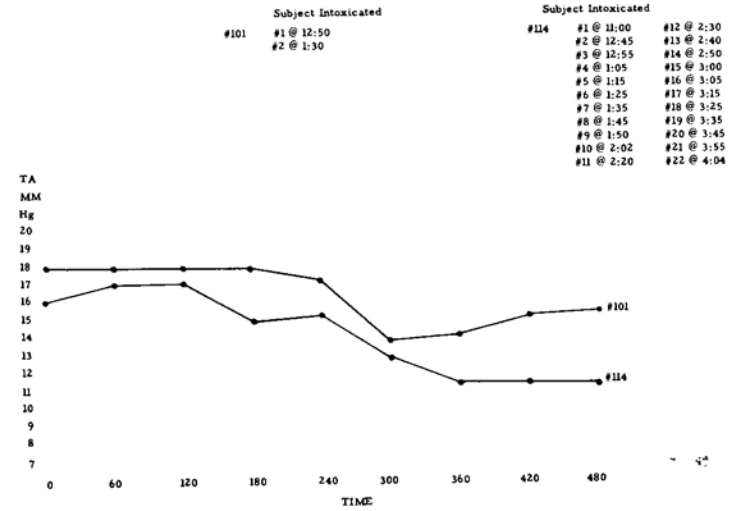

FIG. 4. Intraocular pressure on day 52 in two subjects smoking 2.2% natural marihuana cigarettes of about 0.9 g. Time on abscissa is given from the start of the first cigarette.

of pulse pressure transmitted to the intraocular contents; (5) ophthalmodynamometry (performed on a few of the hospitalized subjects): no changes; (6) electroetinography (ERG): no changes.

GLAUCOMA PATIENT STUDIES

Human patients with glaucoma have been recruited to determine whether they also demonstrate intraocular pressure-lowering effects of marihuana smoking as do experienced young smokers without glaucoma. It might be noted that obtaining suitable subjects who met reasonable criteria for human patient experimentation was difficult. Some of the requirements for selection included: age: no older than 60; fertility: female subjects must be incontrovertibly sterile; character of

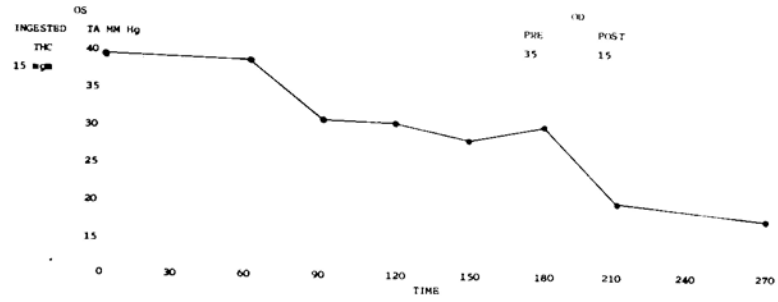

FIG. 5. Intraocular pressure in a glaucoma patient after oral ingestion of Δ^9-THC.

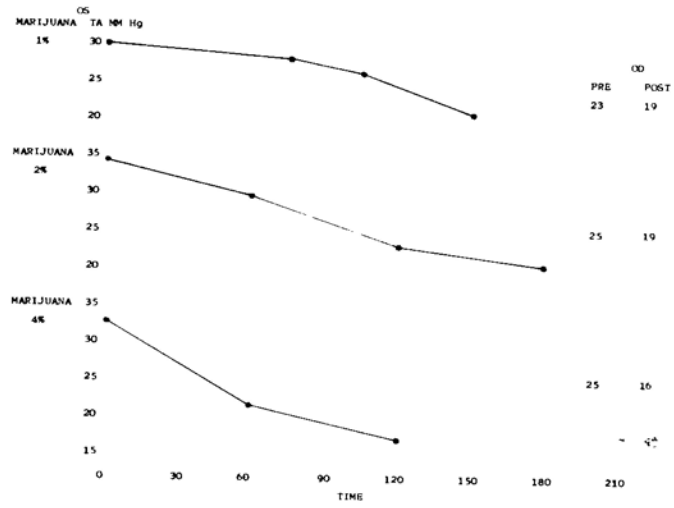

FIG. 6. Intraocular pressure in a glaucoma patient after smoking natural marihuana cigarettes.

glaucoma: must be chronic simple type (open angle), not secondary to injury or other ocular disease, not operated upon; general health: must be stable with no history of cardiorespiratory disease, no history of use of medications that might affect autonomic nervous system functions (antispasmodics, antihypertensives). Of 11 patients so studied, seven have demonstrated what appears to be a substantial drop in intraocular pressure averaging around 30%. However, the remaining four out of the 11 seemed not to demonstrate drug effect, although there are reservations as to whether these individuals mastered the technique of marihuana-smoking sufficiently to become intoxicated.

Figures 5 and 6 illustrate typical pressure-lowering effects in one glaucoma patient. The intraocular pressure data are given as measured periodically after drug administration at time $T=0$.

EXPERIMENTAL ANIMALS

Animal experimentation in our unit has been limited to observations in rabbits. A pump and delivery system capable of intoxicating rabbits with marihuana smoke has been devised. In small numbers, we have demonstrated a substantial decrease in intraocular pressure following the smoking of marihuana that appears to correspond to the observations of Green and Podos (1974) who administered THC to rabbits intravenously. Furthermore, topical application of a solution of THC placed on the rabbit cornea also leads to a drop in intraocular pressure. So far, there are insufficient observations to draw statistical inferences.

DISCUSSION

Glaucoma is the second leading cause of legal blindness in the United States. The term glaucoma refers to a group of ocular disease states that have in common elevated intraocular pressure, with eventual production of optic nerve damage and associated loss of visual field. If intraocular pressures are not controlled sufficiently, blindness eventually results. Like diabetes mellitus, the most common categories of glaucoma are never cured, only controlled by medical and occasionally surgical therapy. Periodic medical follow-up is necessary throughout the patient's lifetime.

Antiglaucomatous medications presently available are effective in regulating intraocular pressures in many but far from all patients with glaucoma. Furthermore, even when effective in lowering pressure, present medications often have side effects that can be annoying at best and seriously damaging to the health of the patient, at worst. Some of these side effects, grouped according to the class of drug to which they most often pertain, include:

Miotics. They can cause blurred vision during the day and impaired vision in reduced illumination, due to ciliary body spasm and pupillary miosis. Miotics are strongly suspected of contributing toward the development of cataracts. These drugs may predispose the patient to uveitis and retinal detachment.

Epinephrine. It causes local ocular irritation and discomfort and chronic redness of the eyes. It may create or potentiate cardiac arrhythmias and hypertension.

Carbonic anhydrase inhibitors. These drugs bring on electrolyte imbalance, fatigue, anorexia, weight loss, and renal stones.

Even if patients are able to tolerate the side effects of the foregoing major classes of agents, the combined therapeutic effects are not always sufficient to control pressure adequately. For such patients, the present alternatives are filtering surgery (with distinct and potentially serious risks) or eventual blindness.

So far it has been shown that marihuana smoking induces a substantial decrease in intraocular pressure in normal young males. The magnitude of the effect is greater than that which would be expected to occur utilizing currently accepted medications (miotics, epinephrine, or carbonic anhydrase inhibitors) in normals. Preliminary results indicate that as great or greater responses may occur in glaucoma patients. There are no indications so far of any deleterious effects of marihuana smoking on visual function or ocular structures. There is reason to suspect that the mechanism of pressure reduction induced by marihuana smoking may differ from the mechanism of action of standard antiglaucoma drugs presently in use. Therefore marihuana may provide a crucial additive effect for presently uncontrolled glaucoma patients. It is hoped that a derivative of marihuana or a modified form of administration will provide a means of obtaining beneficial effects without the psychotropic and other side effects of marihuana itself.

ACKNOWLEDGMENTS

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