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The Metabolic Impact of Cannabis User on Biochemical Markers Among Bikaner Adults

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Abstract

Background—increased legalization of cannabis has resulted in renewed interest in its effects on body weight and cardiometabolic risk. There are limited data regarding the relationship between cannabinoids and metabolic processes. Epidemiologic studies have found lower prevalence rates of obesity and diabetes mellitus in cannabis users compared with people who have never used cannabis, suggesting a relationship between cannabinoids and peripheral metabolic processes. To date, no study has investigated the relationship between cannabis use and fasting insulin, glucose, and insulin resistance.

Objective—To assess the metabolic profile and cardiovascular risk factors as well as body weight and waist circumference among Bikaner adults cannabis users.

Methods—A cross sectional study design involving 100 male-subjects aged between 25 and 65 years. This study was conducted at Department of Biochemistry, Sardar Patel Medical College, Bikaner (Rajasthan) India. Study included Socio-demographic (age and race), laboratory, as well as clinical data such as blood pressure, weight, BMI, waist circumference, presence of diabetes, hypertension and hyperlipidemia were collected. Laboratory values were extracted from medical records and done within the past 3 months; they included total cholesterol, triglycerides (TG), LDL and HDL cholesterol, blood glucose, and hemoglobin A1C.

Results—Of the 100 patients surveyed, 100% were male. The mean (±SEM) age of the entire cohort was age range, 26–68 years. The mean body mass index (BMI) was 33.4 kg/m 2±0.74; SBP=127.7 mmHg±2.79; DBP=73.4 mmHg±1.58. Current five years cannabis users had the lowest waist circumference compared to one year cannabis user or never users respectively (40.1±1.50 vs. 35.9±0.88 vs. 33.4±0.74), $p<0.01$. Diastolic blood pressure in mmHg was significantly higher among one year cannabis users compared to current or never users, (80.0±2.13 vs. 82.3±3.42 vs. 73.4±1.58), $p<0.02$. Current cannabis users showed a tendency (not statistically significant) towards lower total cholesterol, Triglycerides (TG), High Density Lipoprotein (HDL)-cholesterol, Low Density Lipoprotein (LDL)-cholesterol, body mass index (BMI) and systolic blood pressure, compared to one year users or never users.

Conclusions: We found that cannabis use was associated with lower levels of fasting insulin and HOMA-IR, and smaller waist circumference.

Keywords: *Cannabis sativa* user; Metabolic risk factors; Body weight; Hypertension.

INTRODUCTION

Cannabis is the most commonly used illegal substance worldwide [1]. At least 160 million people or approximately 4.0% of the world's population between the ages of 15 and 64 years have been estimated to use cannabis at least once in the past year [2,3]. Emerging data from the 2013 National Survey on Drug Use and Health showed that adults older than 26 years reported marijuana use as the most frequently used drug, with a 5.6% current marijuana use rate [3]. Nearly twenty million individuals (aged 12 years old and above) used marijuana within the past month. Changes among adults aged 50 years and older show that the highest increase in reported current marijuana use was among 55–59 year olds [4].

Marijuana is associated with an acute increase in appetite and high caloric intake. For example, in the Coronary Artery Risk Development in Young Adults (CARDIA) study [5], using 15 years of longitudinal data from 3,617 participants with 1,365 reporting the use of marijuana, the more extensive use was associated with higher caloric intake. Interestingly, in this study, despite increased caloric intake, there was no increase in BMI, lipid or glucose values [5]. Furthermore, the increased caloric intake was largely attributed in this study to the associated increase in alcohol consumption [5]. Increased caloric intake was largely thought to be mediated through cannabinoid receptors type 1 (CB1) [6]. These findings led to the development of Rimonabant, a selective blocker of the cannabinoid receptor type 1 (CB1) for the treatment of multiple cardiometabolic risk factors, including abdominal obesity [7].

In the United States, some medications containing delta-9-tetrahydrocannabinol (THC) are approved by the Food and Drug administration (FDA) for treating chemotherapy and acquired immunodeficiency syndrome-induced anorexia and nausea [8]. The higher caloric intake among marijuana users, compared to non-users, was also demonstrated in other studies [2,8,9]. While some data suggest marijuana use to confer cardiometabolic benefits such as reductions in Lower Density Lipoprotein (LDL), fasting insulin, glucose, and hemoglobin A1C levels [2], Other studies show that marijuana users have a lower adipocyte insulin resistance index, lower plasma High Density Lipoprotein (HDL), and higher percent abdominal visceral fat, which are important risk factors for diabetes and cardiovascular disease [9,10]. Therefore, although marijuana is a frequently abused drug, its lasting effects on cardiovascular risk factors are not clear. Given the paucity of data on metabolic significance of marijuana use, particularly among the black population, the objective of the study was to investigate the potential effects of marijuana on metabolic risk factors and body weight among black patients.

MATERIALS AND METHODS

The present study was conducted on **100 male-subjects** aged between 25 and 65 years during the period of june 2009 to january 2011.They were randomly selected irrespective their caste and creed. Those individuals who were suffering from other inflammatory conditions like tuberculosis, leprosy, pregnancy, cancer, skin diseases,

gout, liver and kidney diseases were excluded to rule out any increase in inflammatory markers due to causes other than DM. Only those subjects included in the present study, who were taking 5 to 10 gm of cannabis per day and who was willing and able to sign an informed consent during the clinic visit. Socio-demographic (age and race), laboratory, as well as clinical data such as blood pressure, weight, BMI, waist circumference, presence of diabetes, hypertension and hyperlipidemia were collected. Laboratory values were extracted from medical records and done within the past 3 months; they included total cholesterol, triglycerides (TG), LDL and HDL cholesterol, blood glucose, and hemoglobin A1C. In addition, information on lifestyle behavior (physical activity, cigarette smoking, alcohol consumption, and drug as well as marijuana use history) was collected. Survey participants (SPs) answered "Yes" or "No" to the question "Have you ever, even once, used hashish / cannabis?" Five years cannabis user and current cannabis users were determined by the question "How long has it been since you last used marijuana or hashish?" with answers given as a numerical value in days, months or years. Frequency of marijuana consumption was assessed by asking the SPs "During the past 30 days, on how many days did you use marijuana or hashish?" Marijuana users who had smoked the drug within the last one year were categorized as current users, while individuals who had use marijuana at least once but not in the last 180 days were considered former users. And individuals who had not smoked marijuana at all were classified as never users.

STATISTICAL ANALYSIS:

Frequencies, proportions, means, and SDs were used to describe the overall sample, and the marijuana users and non-users. Student's t-test and chi-square tests were used to compare the descriptive statistics depending on data type. Data was analyzed using SPSS statistical package version 21 (SPSS, Inc, Chicago, IL).

RESULTS

The present study was conducted on 100 male-subjects aged between 25 and 65 years. The mean body mass index (BMI) 32.6 kg/m 2±0.64; SBP=122.0 mmHg±1.82; DBP=86.1 mmHg ± 1.21 (Table 1). Dyslipidemia was reported in 19% of the cohort, 11% had coronary heart disease and 22% were ex- smokers. Alcohol consumed over the past 3 months was reported in 08% of the cohort.Ten percent of the study cohort had diabetes, 16% had hypertension; while 14% suffered both diabetes and hypertension. Patients who have used cannabis in the past one year had a significantly higher waist circumference(inches) in inches than current users or never users respectively (40.1±1.50 vs. 35.9±0.88 vs. 34.4±0.74), $p<0.0175$; as well as significantly greater diastolic blood pressure in mmHg (82.3±3.42 vs. 80.0±2.13 vs. 73.4±1.58), $p<0.0245$ (Table 2). In addition, five years cannabis users had higher cholesterol levels in mg/dl (168.9±10.42) than one year cannabis user (189.0±8.10) and never users (181.8±6.97), this was marginally non-significant, $p<0.0569$. There

was no significant difference in the levels of HDL in mg/dL (52.3±4.65 vs. 57.6±5.05 vs. 54.6±3.90), p=NS; LDL in mg/dl (102.5±8.75 vs. 105.9±7.92 vs. 103.8±6.64), p=NS; BMI in Kg/m2 (32.5±2.22 vs. 31.1±1.17 vs. 29.6±1.00), p=NS; and triglyceride in mg/dl (95.9±10.58 vs. 133.0±15.0 vs. 120.3±12.30), p=NS; among using cannabis 5 to 10 gm per day for the last between five years, one year and never using cannabis respectively.(Table 2) Between the patients who had used cannabis at least once in their lifetime and non- users, there were no significant differences in any of the metabolic parameters examined (Table 3). The proportion of patients with diabetes was not significantly different among cannabis users and non-users, 26.7% versus 20.3%, P=0.57 for users and non-users respectively. There was also no significant difference in the mean ages of current, former, and never users, or the frequency of marijuana users by sex.

Table 1: Metabolic clinical characteristics of study participants

Parameters	**Mean**	**Std error**
Cholesterol (mg/dL)	194.6	5.98
Triglycerides (mg/dL)	128.8	9.43
LDL-cholesterol (mg/dL)	113.6	4.48
HDL-cholesterol (mg/dL)	60.5	4.69
Glucose (mg/dL)	118.0	4.90
Hemoglobin A1c (%)	5.87	0.24
BMI (Kg/m2)	32.6	0.64
Waist circumference (inches)	32.8	0.58
Systolic Blood Pressure (mm Hg)	122.0	1.82
Diastolic Blood Pressure (mm Hg)	86.1	1.21

Clinical features

Age	25 – 65 years
Hypertension %	16
Diabetes %	10
Hypertension and Diabetes %	14
Dyslipidemia %	19
Coronary Heart disease %	11
Former cigarette smokers %	22
Alcohol consumption over the past 3 months %	08

- LDL = low density lipoprotein,
- HDL = high density lipoprotein,
- BMI = body mass index (kg/m2)

Table 2: Comparison of metabolic markers Using Cannabis 5 To 10 gm Per Day For The Last between Five Years, One Year and never using Cannabis.

Using Cannbis 5 To 10 gm Per Day For The Last	**Five Years**	**(±SEM)**	**One Year**	**(±SEM)**	**Never Cannabis user**	**(±SEM)**	**p-value**
Cholesterol (mg/dL)	168.9	10.42	189.0	8.10	181.8	6.97	0.0569
Triglycerides (mg/dL)	95.9	10.58	133.0	15.00	120.3	12.30	0.1245
LDL-cholesterol (mg/dL)	102.5	8.75	105.9	7.92	103.8	6.64	0.5527
HDL-cholesterol (mg/dL)	52.3	4.65	57.6	5.05	54.6	3.90	0.4737
Glucose (mg/dL)	98.7	14.27	108.7	6.82	112.6	8.39	0.9287
Hemoglobin A1c (%)	6.8	1.20	6.4	0.39	6.5	0.30	0.6252
BMI (Kg/m2)	32.5	2.22	31.1	1.17	29.6	1.00	0.0906
Waist circumference (inches)	40.1	1.50	35.9	0.88	33.4	0.74	0.0175
Systolic Blood Pressure (mm Hg)	136.0	3.80	129.5	2.52	127.7	2.79	0.7593
Diastolic Blood Pressure (mm Hg)	82.3	3.42	80.0	2.13	73.4	1.58	0.0245

- LDL = low density lipoprotein,
- HDL = high density lipoprotein,
- BMI = body mass index (kg/m2)

Table 3: Metabolic markers in cannabis users and non-users

	Cannabis user		**Cannabis non-user**		
	Mean	**Std error**	**Mean**	**Std error**	**p-value**
Cholesterol	181.1	6.93	181.8	6.97	0.9529
Triglycerides	118.5	10.8	120.3	12.3	0.9186
LDL-cholesterol	102.9	6.09	103.8	6.64	0.9294
HDL-cholesterol	55.3	3.71	54.6	3.90	0.8956
Glucose	108.9	6.00	112.6	8.39	0.7093
HbA1C	6.6	0.40	6.5	0.30	0.8176
BMI	29.6	1.03	29.6	1.00	0.9745
Waist circumference (inches)	34.6	0.74	33.4	0.74	0.2692
Systolic Blood Pressure	128.0	2.16	127.7	2.79	0.9330
Diastolic Blood Pressure	77.9	1.62	73.4	1.58	0.0673

- LDL = low density lipoprotein,

- HDL = high density lipoprotein,
- BMI = body mass index (kg/m2)

DISCUSSION

Our study showed that current cannabis users have significantly smaller waist circumferences compared to former users, or non-users (Table 1). There was also tendency towards a lower BMI among current cannabis users, however, that did not reach statistical significance, likely due to the small sample size. These findings are quite important given the current epidemic of obesity and its attendant cardiovascular risk and the fact that waist circumference is an important predictor for cardiovascular risk, more so than BMI itself [10–13]. However, in our study we are unable to ascertain if the significantly lower waist circumference is due to a decrease in subcutaneous fat or intra-abdominal fat content. This is quite important since the increased cardiovascular risk associated with abdominal obesity is largely attributed to visceral fat [14–16]. To illustrate this point, a recent study that is well-conducted, at the National Institute of Health by Muniyappa et al. [10] on the metabolic effects of chronic cannabis smoking showed that chronic cannabis use, compared to control, is associated with visceral adiposity and insulin resistance in the adipose tissue [10]. This study is quite relevant to ours for enrolling a large percentage of blacks (73%) and it showed no association of cannabinoid use on total cholesterol, LDL- cholesterol, fasting glucose level or triglycerides [10]; data that is consistent with that shown here by our group (Table 1). Furthermore, our study also assessed hemoglobin A1c which is a surrogate measure of chronic (2–3 months) glucose control and there was no difference in A1c between the users and non-users of marijuana (Tables 1, 2). Interestingly, data from Muniyappa group [10] also showed lower HDL-cholesterol among cannabis users compared to non-users (49±14 versus 55±13 mg/dl, P= 0.02), our data showed a trend towards lower HDL- cholesterol among users of marijuana compared to former users or never users, however the difference did not reach statistical significance, again likely due to a small sample size (Table 1). Our data is also consistent with a large study by Penner et al. [2] that included 4,657 adult men and women from the National Health and Nutrition Examination Survey (NHANES) conducted between 2005 to 2010. In this study, Current cannabis use was significantly associated with smaller waist circumferences. However there was no significant dose-response identified [2].

Consistent with our study also, this large data set showed no differences among current, past, or never used marijuana groups in the cardiovascular parameters including systolic blood pressure, triglycerides, or HDL-cholesterol levels. In contrast to our study, however, there was statistically significant lower hemoglobin A1C among current marijuana users compared to past users or never users (5.4% versus 5.4% versus 5.5%, $P < 0.3$), for current, past and never marijuana users respectively [2]. This difference however is minimal and clinically insignificant and likely influenced by the large sample size of the study that also showed significantly lower BMI among current marijuana users [2], a finding that our study also demonstrated but

it did not reach statistical significance (Table 2). It is important, however to note that in contrast to our data which involves mainly a Black population, NHANES data set used by Penner et al. Contained, only 20% blacks with the majority (44%) of the population being Caucasians and 30% Hispanics [2].

Another study from the NHANES III, 1988–1994 data set conducted at the National Center for Health Statistics of the Centers for Disease Control and Prevention by Rajavashisth et al. [17] with 10,896 adult US population showed significantly lower odds of DM among marijuana users (adjusted OR 0.36, 95% CI 0.24 to 0.55; $p<0.0001$) [17]. This is in contrast to our study where we found no difference in diabetes rate among current, past, and never marijuana users. It is important to note that Rajavashisth et al. [17] concluded that a causal relationship could not be established and recommended against the use of marijuana to prevent diabetes.

Finally, it is important also to note that highest waist circumference in our study was observed among former marijuana users compared to current and never users (35.9 versus 32.1 versus 33.4 (inches), P 0.017) for former, current, and never users respectively. Former marijuana users also tended to have higher BMI, total cholesterol, LDL-cholesterol, and triglycerides; none of these metabolic parameters however reached statistical significance although certainly demonstrated a trend for unfavourable cardiometabolic profile among marijuana quitters. Therefore, our study suggests that marijuana quitting is associated with deleterious effects on waist circumference, weight, and other metabolic parameters that are consistent with the plethora of data on weight gain and other cardiovascular risk factors after cessation of cigarette smoking [18–22]; findings that are still of undetermined significance on cardiovascular outcomes compared to the effects of continued smoking that is certainly harmful [22].

CONCLUSION

Our study on the cardio-metabolic effects on marijuana use among Bikaner(Rajasthan) population from an inner city institution showed consistent results on the association of cannabis use with lower waist circumference that has been demonstrated previously among populations that are largely white. Our study is also consistent with data showing lack of cardio-metabolic benefits of cannabis use, as in the landmark Coronary Artery Risk Development in Young Adults (CARDIA) study where no beneficial effects of cannabis use were demonstrated.

Finally, while lower waist circumference has beneficial effects on cardiovascular risk, in the context of cannabis use this benefit is uncertain since the lower waist circumference appears to be primarily due to subcutaneous fat decrease as opposed to abdominal visceral fat which was actually higher in percentage among chronic marijuana users in a recently published study. Therefore, until further research is performed to determine the effects of cannabis on hard endpoints such as coronary artery disease, we do not recommend cannabis use for cardio-metabolic benefits; we also do not recommend cannabis for diabetes prevention or weight loss, given the uncertain and largely conflicting data shown in various studies.

Strength / Limitations

Our study adds to the growing literature on the value of cannabis in controlling metabolic syndrome. Consecutive family clinic patients were included in this series, thus limiting any selection bias because all patients who attended the clinic were offered the study questionnaire instrument to be part of the study Limitations of the study include the small sample size. Another important limitation relates to the fact that marijuana use was based on self-reported data and therefore subject to under-estimation or denial of illicit drug use. The study was performed at an inner city family medicine clinic, and the results are not generalizable to other communities. Future studies should examine whether other metabolic parameters such as LDL, HDL, glucose, hemoglobin A1c, BMI, or SBP would show significant effects in a larger sample size.

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