Associations Between Fatty Acid Amide Hydrolase Variants and Response to Cannabis Use for Pain Management in Rheumatoid Arthritis

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A genetic variant in FAAH is associated with 5× greater odds of effective pain management among cannabis users with RA

FORWARD
The National Databank for Rheumatic Diseases

BACKGROUND

- Fatty acid amide hydrolase (FAAH) is a serine hydrolase that breaks down the endocannabinoid/cannabinoid receptor agonist anandamide[a]
- Variants in the FAAH gene have previously been separately associated with pain susceptibility, cannabis use, and arthritis[b, c, d]
- Objective: to examine the relationships between FAAH variants and cannabis use as well as real-world effectiveness in pain management for individuals with RA

METHODS

- Data were provided by adults with RA participating in FORWARD, who provided blood samples and answered questions about cannabis use
- Genotyping was performed with the Illumina Infinium Global Screening Array platform and non-silent common FAAH variants were included in this study
- Logistic regression models were utilized to examine the association between FAAH variants (by presence or absence of the minor allele) and cannabis use as well as self-reported effectiveness in arthritis pain management among cannabis users

RESULTS

- A total of 365 participants met inclusion criteria, 129 (35.3%) of whom reported cannabis use as a treatment for arthritic pain (Table 1)
- Among users, 52% reported that cannabis was helpful in reducing their pain, 30% reported that it was not helpful, and 18% reported that they were not sure
- Genotype distributions of both variants are presented in Table 2
- In multivariable models for each of the two variants that met inclusion criteria (Figure 1), one (rs324419 C→T) was associated with cannabis use (OR [95% CI] 1.9 [1.1, 3.3]; p=0.03) and the other (rs324420 C→A) was associated with self-reported effectiveness of cannabis in treating arthritic pain (5.2 [1.6, 16.7]; p<0.01).

Table 1. Characteristics of study participants by cannabis/CBD use status (nonuser vs user) and by self-reported effectiveness of cannabis in arthritis pain management.

Characteristic	Nonuser n=236	User n=129	Not Effective n=38	Effective n=65
Age, years, mean (SD)	68.6 (11.1)	65.4 (11.0)	69.4 (8.2)	62.4 (12.1)
Female, %	86.7	93.0	94.6	92.3
White race, %	93.2	91.4	94.7	90.6
Hx cigarette smoking, %	34.3	39.5	34.2	43.1
RA duration, years, mean (SD)	26.8 (14.6)	23.5 (13.1)	23.1 (15.2)	24.8 (12.2)
BMI, kg/m^2, mean (SD)	27.6 (6.9)	28.7 (6.6)	29.7 (6.2)	27.5 (6.2)
Glucocorticoid use, %	25.1	20.6	36.8	12.7
NSAID use, %	25.1	34.9	28.9	38.1
Opioid use, %	16.7	23.0	21.1	22.2
RDCI, 0-9, mean (SD)	2.2 (1.8)	2.3 (1.8)	2.4 (1.9)	2.2 (1.9)

BMI=body mass index; NSAID=non-steroidal anti-inflammatory drugs; RDCI=Rheumatic Disease Comorbidity Index

Table 2. Genotype distributions of the variants investigated and frequency of cannabis use and reported cannabis effectiveness for managing arthritic pain by genotype.

Variant	Genotype	Genotype n (%)	Cannabis User n (%)	Reported Effective n (%)
rs324419	CC	263 (72.1)	84 (31.9)	43 (51.2)
	CT	94 (25.8)	42 (44.7)	21 (50.0)
	TT	8 (2.2)	3 (37.5)	1 (33.3)
rs324420	CC	227 (62.2)	76 (33.5)	31 (40.8)
	CA	120 (32.9)	47 (39.2)	30 (63.8)
	AA	18 (4.9)	6 (33.3)	4 (66.7)

Percent genotype is of the total N. Percent cannabis users is of n per genotype. Percent reported effective is of n cannabis users per genotype.

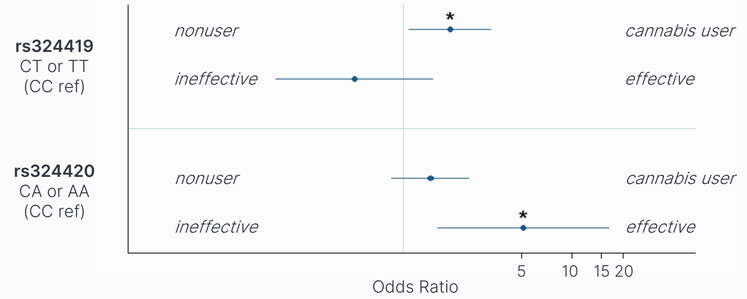

Figure 1. Odds ratios and 95% confidence intervals for each variant's association with cannabis use and with self-reported effectiveness of cannabis in treating RA-related pain. Each model was adjusted for age, sex, white race, cigarette smoking history, calendar year, RA duration, BMI, glucocorticoid use, NSAID use, opioid use, and Rheumatic Disease Comorbidity Index (RDCI). Associations marked with an asterisk (*) are statistically significant (p<0.05).

CONCLUSION

- Individuals with RA and the genotype CT or TT at rs324419 are twice as likely to use cannabis for arthritis pain management compared to those with the genotype CC
- Cannabis users with RA and the genotype CA or AA at rs324420 have five times greater odds of finding cannabis effective in reducing their pain (CC genotype reference)
- FAAH has previously been implicated in pain perception[b], in cannabis use[c], and in reduction of arthritis severity in mouse models[d], but this is the first study linking FAAH variants with cannabis use and real-world pain management in RA

DISCLOSURES

- KW, JZ, SK, and KM have no disclosures to declare. TS is a consultant for Bristol-Myers Squibb and for Janssen Pharmaceuticals.

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