ARTIGO ORIGINAL/ORIGINAL ARTICLE

Coffee Intake and Multiple Sclerosis Disability

Consumo de Café e Incapacidade na Esclerose Múltipla

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Abstract

Introduction: Previous studies on caffeine and risk of multiple sclerosis (MS) yielded different results; one study suggests a positive effect on disease progression. Our aim was to examine associations between coffee consumption, demographic and clinic characteristics.

Material and Methods: Questionnaires were applied to 126 MS patients. Severity was evaluated by EDSS, 9-HPT, T25-FW and SDMT. High coffee intake was considered ≥4 cups/day; lifetime consumption was calculated multiplying espressos per day by years of consumption.

Results: Our cohort had an average age of 45.3 years and 60.3% were women. Mean age of MS onset was 29.7 years and mean duration of disease 15.6 years. Seventy-nine percent had relapsing-remitting MS; 50% had EDSS 0-3.5, 35.7% EDSS=3.5-6.0, and 14.3% EDSS≥6.0. A third were current/past smokers. Regular coffee intake was observed for 78.6% and high coffee intake was present in 17.2%. Men had more high coffee intake (29% *vs* 10.3%, p=0.03) but total consumption was not different between genders (p=0.48). High coffee intake and total coffee consumption was associated with higher smoking habits (3.85 *vs* 0 pack-years, p=0.01; r=0.29, p<0.001). No significant association was found between EDSS and high intake or total coffee consumption (3 *vs* 3.5, p=0.79; r=0.06, p=0.48). Also, we did not find any differences regarding coffee intake and performance in 9-HPT, T25-FW and SDMT.

Conclusion: In our cohort, coffee consumption does not seem to have a role in progression of disability. Further studies are required to access this association and to evaluate the mechanisms by which coffee may be acting in MS.

Resumo

Introdução: Estudos prévios sobre o consumo de cafeína e risco de esclerose múltipla (EM) forneceram resultados diferentes; um estudo sugeriu um efeito positivo na progressão da doença. Propusemo-nos analisar a associação entre o consumo de café e as caraterísticas demográficas e clínicas.

Material e Métodos: Aplicação de questionários a 126 doentes com EM. A gravidade da doença foi avaliada através do EDSS, 9-HPT, T25-FW e SDMT. Consumo elevado de café foi considerado para ≥4 chávenas/dia; o consumo ao longo da vida foi calculado multiplicando o número de expressos por dia pelos anos de consumo.

Resultados: A nossa *cohort* tinha uma média de idades de 45,3 anos e 60,3 eram

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do género feminino. A média de idade de início da EM foi de 29,7 anos e a duração média da doença de 15,6 anos. Setenta e nove porcento tinha a forma surto-remissão da EM; 50% apresentava um EDSS de 0-3,5, 35,7% EDSS=3,5-6,0 e 14,3% EDSS≥ 6,0. Um terço era fumador atual ou prévio. Registamos um consumo regular de café em 78,6% e consumo elevado em 17,2%. Os homens tinham maior percentagem de consumo elevado de café (29% *vs* 10,3%, *p*=0,03), mas o consumo total não foi diferente entre géneros (*p*=0,48). Consumo elevado e total de café associaram-se a maior consumo de tabaco (3,85 *vs* 0 maços/ano, *p*=0,01; r=0,29, *p*<0,001). Não encontramos uma associação significativa entre o EDSS e o consumo elevado ou total de café (3 *vs* 3,5, *p*=0,79; r=0,06, *p*=0,48). Também não encontramos diferenças em relação ao consumo de café e a performance no 9-HPT, T25-FW e SDMT.

Conclusão: Na nossa *cohort*, o consumo de café não parece ter um papel na progressão da incapacidade. São necessários estudos adicionais para explorar esta associação e para avaliar os mecanismos pelos quais o café poderá atuar na EM.

Introduction

Multiple sclerosis (MS) is a multifocal inflammatory disease of the central nervous system, leading to demyelination and neuronal damage. Genetic predisposition only explains a fraction of the disease risk; lifestyle and environmental factors seem to be key contributors to the development of MS and some of them can be modified.[1]

Previous studies on caffeine and risk of MS have yielded different results[2-4] and one study suggests a positive effect on disease progression.[2-5]

Adenosine regulates a variety of physiological processes, including neuronal survival and suppression of inflammation.[6] A1 adenosine receptor (A1AR) expression and activity on macrophage/microglial cells may be diminished in MS patients compared with controls, with cytokine dysregulation.[6] In animal models of MS, caffeine was found to have a neuroprotective effect, potentially through A1AR upregulation.[6]

Our aim was to examine associations between coffee consumption, demographic and clinic characteristics in MS patients, namely disease severity.

Material and Methods

Questionnaires were applied to 126 MS patients that attended Neuroimmunology outpatient clinic between January and November of 2017. Only consumption of espressos and drinks with espresso was considered, in order to uniformize the comparison in terms of caffeine content. High coffee intake was considered for 4 cups or more per day; a numerical value of lifetime coffee consumption was calculated multiplying the number of cups of espresso per day by the duration of consumption in years. MS severity was evaluated by expanded disability status scale (EDSS), nine-hole peg test (9-HPT), timed 25-foot walk (T25-FW) and symbol digit modalities test (SDMT). To compare variables, Fisher exact test (categorical variables), Mann-Whitney test (categorical and continuous variables) and Pearson correlations (continuous variables) were used. Results were considered significant if $p<0.05$.

All participants provided informed verbal consent for participation in the study and publication. This form of consent was considered suitable given the preserved anonymity of all demographic and clinical data.

Results

Our cohort had an average age of 45.3 years (+/-11.9) and 76 patients (60.3%) were women. Mean age of MS onset was 29.7 years (+/-12.2) and mean duration of disease 15.6 years (+/-9.4).

Seventy-nine percent had relapsing-remitting MS, 15.1% primary-progressive MS and 5.56% secondary-progressive MS. Fifty percent had an EDSS between 0 and 3.5, 35.7% between 3.5 and 6.0 and 14.3% greater than or equal to 6.0.

A third of the patients were current or past smokers. Regular coffee intake was observed for 78.6% of the patients, and high coffee intake (≥4 cups/day) was present in 17.2%. The average daily caffeine consumption was 131.9 mg (in Portugal, one espresso has a mean caffeine content of 75 mg).[7]

Men had more high coffee intake (29% *vs* 10.3%, *p*=0.03) but the total coffee consumption was not diffe-

rent between genders ($p=0.48$). High coffee intake and total coffee consumption was associated with higher smoking habits (3.85 *vs* 0 pack-years, $p=0.01$; correlation coefficient=0.29, $p<0.001$).

No significant association was found between EDSS and high coffee intake or total coffee consumption (3 *vs* 3.5, $p=0.79$; correlation coefficient=0.06, $p=0.48$). Also, we did not find any differences regarding coffee intake and performance in 9-HPT, T25-FW and SDMT. Gender and smoking, possible confounders in what concerns MS progression, were not associated with the results in these tests nor with EDSS.

Discussion

Our study addressed a possible association between coffee consumption and disease severity in individuals with MS. The results obtained do not support a relation between caffeine intake and progression of disability.

We faced some limitations in interpreting our findings. The most obvious was the small sample size. Since information on exposure was gathered retrospectively, recall bias may also be a concern. Once we only included espressos and drinks with espresso as caffeinated beverages, caffeine intake may have been underestimated in some patients. For example, many different types of sodas may have a significant quantity of caffeine. Besides that, the amount of coffee consumed was assumed to be stable over time, which may not necessarily be true for all patients. In our cohort, the majority of the patients drinks coffee (78.6%) but only 17% reported high coffee intake; we can conclude there is not a significant difference in habits between them.

Men and patients with greater smoking habits were associated with higher coffee intake. These are recognized adverse factors in multiple sclerosis; however, we were able to demonstrate that those variables alone do not seem have an effect in MS severity, evaluated by EDSS, 9-HPT, T25-FW and SDMT.

To the best of our knowledge there is only one published case-control study reporting the association of coffee consumption with a reduced progression of disability in relapsing onset MS.[5] However, the possibility that the inverse relation between coffee consumption and progression of disability might be due to a reduced consumption in subjects with a higher disability cannot be completed excluded.

Caffeine seems to have an immunomodulatory action and is postulated to induce an anti-inflammatory state.[8] This knowledge not only provides a neurobiological basis for healthy usage of caffeine, but also opens up a possibility to develop methylxanthine-based treatments for MS.[9]

Conclusion

In our cohort, coffee consumption does not seem to have a role itself in the progression of disability. Further studies, namely prospective, are required to access this association and to evaluate the mechanisms by which coffee may be acting in MS. ■

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

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Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pelos responsáveis da Comissão de Investigação Clínica e Ética e de acordo com a Declaração de Helsínquia da Associação Médica Mundial.

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Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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