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Original article

Evaluation of frequency and the attacks features of patients with colchicine resistance in FMF

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ABSTRACT

Introduction: Colchicine is the mainstay for the treatment of FMF, which is an auto-inflammatory disease mainly with relapsing polyserositis. Despite daily doses of 2 mg or more each day, approximately 5% to 10% of the patients continue to suffer from its attacks. In this study, we aimed to investigate the depression and attack features in patients with FMF who have colchicine resistance (CR).

Patients e Methods: CR was defined for FMF patients with 2 or more attacks within the last 6 months period while using 2 mg/day colchicine. Eighteen patients (9 Female/9 Male) were enrolled into the CR group and 41 patients were enrolled into the control group (12 Male/29 Female). Demographic, clinical e laboratory findings, treatment adherence, and *the Beck Depression Inventory (BDI)* scores were evaluated.

Results: The age of onset of FMF was significantly lower in the CR group (12.3 yrs. vs. 16.9 yrs, P = 0.03). Disease duration was longer in the CR group (P = 0.01). Abdominal and leg pain due to exercise were significantly more frequent in the CR group versus controls (83% vs. 51%; P = 0.02 e 88% vs. 60%; P = 0.04, respectively). Patients with BDI scores over 17 points were more frequent in the CR group compared to controls (50% vs. 34.1%; P < 0.001).

Discussion: We found that: (1) the age of disease onset was lower and (2) the disease duration was longer in CR group. Pleuritic attacks, hematuria e proteinuria were more frequent in CR patients. We propose that depression is an important factor to consider in the susceptibility to CR.

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Avaliação da frequência e aspectos dos ataques de pacientes com resistência à colchicina em febre familiar do Mediterrâneo (FFM)

RESUMO

Palavras-chave:
Febre familiar do Mediterrâneo
Resistência à Colchicina
Tratamento
Depressão

Introdução: Colchicina é a viga-mestra para o tratamento de FFM, que é uma doença autoin-flamatória com polisserosite recidivante como principal manifestação. Apesar de doses diárias de 2 mg ou mais/dia, aproximadamente 5%-10% dos pacientes continuam a sofrer de seus ataques. Neste estudo, objetivamos investigar os aspectos da depressão e dos ataques em pacientes com FFM apresentando resistência à colchicina (RC).
Pacientes e Métodos: Em pacientes com FFM, RC foi definida como dois ou mais ataques nos últimos seis meses, quando em medicação com colchicina 2 mg/dia. Dezoito pacientes (nove mulheres e nove homens) foram recrutados no grupo RC e 41 pacientes no grupo de controle (29 mulheres/12 homens). Foram avaliados os achados demográficos, clínicos e laboratoriais, a fidelidade ao tratamento e os escores do *Beck Depression Inventory* (BDI).
Resultados: A idade de surgimento da FFM foi significativamente menor no grupo RC (12,3 anos *vs.* 16,9 anos, P = 0,03). A duração da doença foi maior no grupo RC (p = 0,01). Dores abdominais e nas pernas em decorrência do exercício foram significativamente mais frequentes no grupo RC *versus* controles (83% *vs.* 51%; p = 0,02 e 88% *vs.* 60%; p = 0,04, res-pectivamente). Pacientes com escores BDI > 17 pontos foram mais frequentes no grupo RC *versus* controles (50% *vs.* 34,1%; p < 0,001).
Discussão: Verificamos que: (1) a idade do surgimento da doença foi mais baixa e (2) a duração da doença foi maior no grupo RC. Ataques pleuríticos, hematúria e proteinúria foram mais frequentes em pacientes com RC. Propomos que a depressão é fator importante a ser levado em consideração na sensibilidade à RC.

Introduction

Familial Mediterranean fever (FMF) is a hereditary and an auto-inflammatory disease predominantly characterized by repeated attacks of fever, abdominal pain, pleuritic chest pain, arthritis, and erysipelas-like erythema. The disease is most prevalent among non-Ashkenazi Jews, Arabs, Turks, and Armenians.[1] The pathogenesis is mainly based on the absence or insufficiency of pyrin production, which is a peptide involved in the inflammatory cascade that inhibits complement 5a (C5a). The main mechanisms that trigger FMF attacks have not been established. Colchicine is still the main-stay in the treatment of the disease. It completely or partially prevents FMF attacks and subsequent reactive amyloidosis that is regarded as the most dangerous complication of FMF.[2]

Interestingly, colchicine resistance (CR) is prevalent in nearly 10% of the FMF patients. The attack frequency or inten-sity may go on with similar or diminished frequency and severity. The CR patients could be divided into complete or partially non-responders. Many factors might be involved in the CR, including genetic predisposition as well as environ-mental and psychiatric conditions. Still, little is known about the absolute etiology of CR in FMF patients. Treatment adher-ence and potential reasons including demographic factors, socio-economic status, clinical and laboratory factors, and psychiatric dynamics are thought to be contributing factors.

The Beck Depression Inventory (BDI) was developed by Beck and colleagues (1979) and adapted to Turkish by Hisli (1988). The BDI is a self-report scale of 21 items measuring the emotional, somatic, cognitive, and motivational symptoms exhibited in depression. The scale is not designed to diag-nose depression but to objectively determine the severity of depressive symptoms. Correlation coefficients between the English and Turkish versions of the scale were calculated as 0.81 and 0.73 (language validity); split half reliability was 0.74, and criterion-related validity with MMPI-D (Minnesota Mul-tiphasic Personality Inventory) was 0.63. The BDI scores ≥ 17 were reported to discriminate depression that might require treatment with more than 90% accuracy. The score of each item ranges from 0 to 3, and the depression score is obtained by adding the score of each item. The highest obtainable score is 63.[3,4]

As a consequence, different therapeutic strategies are ongoing to limit CR in FMF patients. In this study, we aimed to investigate the depression and attack features in patients with FMF who have the CR.

Patients and methods

The study group was composed of 59 FMF patients with 18 CR (9 female / 9 male) and 41 (12 male / 29 female) complete colchicine responders. Patients having other accompanying diseases including infections, malignancies, autoimmune or metabolic diseases and patients who were diagnosed for depression previously and under-treatment with antidepres-sants were excluded. The diagnosis was checked one more time through the re-questioning of the patients in accordance with the Livneh criteria of FMF.[5]

CR was defined as two or more FMF attacks in a six-month period following a twelve-month regular therapy. Patients