



Assessment of the Impact of Nutritional Status on the Prognosis of FMF Patients

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ABSTRACT

Background: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease. A number of modifiers have been shown to influence inflammatory marker levels, as poor diet quality, being associated with elevated levels of circulating pro-inflammatory markers. Improved diet quality can beneficially affect inflammation. **Objectives of study:** Determine the effect of a set of nutritional modifications on the clinical symptoms and biochemical parameters of patients with familial Mediterranean fever. This may provide evidence of the value of nutritional intervention in the amelioration of the symptoms of FMF patients and pave the way for the integration of Dietary counseling in the routine management of patients with familial Mediterranean fever. **Patients and Methods:** Quasi experimental study carried out among 90 patients with Familial Mediterranean fever during the period from August 2021 to August 2022. Patients received nutritional education for six months. After that, they were divided into two groups: **Group A** patients who adhere to nutritional instructions, and **Group B** patients who did not adhere to nutritional instructions. Comparison between Group A and Group B was made, in terms of clinical symptoms and biochemical analyses, before receiving nutritional instructions and six months after receiving instructions. **Results:** Regarding clinical symptoms and biochemical analyses; In group A, there were statistically significant differences before the experiment and after the six-month. In group B, there were no statistically significant differences indicating improved health status. **Conclusion:** Following a healthy diet combined with drug therapy leads to reducing the severity and frequency of clinical symptoms and improving biochemical results.

Keywords: Familial Mediterranean fever (FMF), Autoinflammatory disease, Diet quality, Inflammation, Nutrition.

1. Introduction

Familial Mediterranean Fever (FMF) is the most common monogenic autoinflammatory disease (Poddighe *et al.*, 2021). A number of modifiers have been shown to influence inflammatory marker levels, as poor diet quality, being associated with elevated levels of circulating proinflammatory markers. So Improved diet quality can beneficially affect inflammation (Ekinici *et al.*, 2020).

This is accompanied by accumulating evidence suggesting that improved diet quality, using a diet approach focused on implementing healthy dietary patterns, such as the Mediterranean diet, which has beneficial effects on biomarkers of inflammation, including CRP and leptin. Further, the Dietary Inflammatory Index (DII), a tool established in 2009, is now frequently used in research to categorize individuals' diets on an anti- to pro-inflammatory continuum (Cowan *et al.*, 2020).

Studies have suggested an association between inflammation, diet and some dietary components. However, fruit and vegetable consumption has been associated with low levels of inflammation, while red meat, and food sources of SFA (Saturated Fatty Acids) have been shown to increase inflammation.

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The consumption of unhealthy foods in the form of industrialized foods rich in sodium, refined sugars, saturated fats and poor in fiber and whole grains and antioxidants can trigger an inflammatory process (da Silva *et al.*, 2021).

The ingestion of this type of food seems to activate an innate immune response due to the production of more proinflammatory cytokines than anti-inflammatory cytokines. On the other hand, greater adherence to the Mediterranean diet is associated with a decrease in inflammatory markers such as IL-6 and C-reactive protein (Yenokyan and Armenian, 2012).

The consumption of processed and culinary ingredients foods is suggestive of a more pro-inflammatory diet. There is a clear need for public policies that raise awareness on the importance of healthy food choices, especially because the adoption of a healthy dietary pattern is a crucial step in reducing inflammation-associated chronic diseases (da Silva *et al.*, 2021).

2. Patients and Methods

2.1. Study design, setting, participants and duration

A quasi-experiment design carried out among (90) patients with Familial Mediterranean fever (FMF) from the Clinical Genetics Department, National Research Center. Patients were diagnosed as having FMF by specialist physician. The data collection was initiated in August 2021 and completed in August 2022. The patients interviewed individually and each interview took about 45-60 minutes.

2.2. Nutrition education intervention:

Patients received Specific recommendations (a healthy diet rich in anti-inflammatory factors, plant and animal sources of iron and vitamin D and low in pro-inflammatory factors. In addition to healthy foods and drinks, the right cooking ways, foods that differ from one person to another and what the patient must follow during the seizure). Then they were followed up for 6 months as this period is sufficient for the effect of nutritional intervention to appear on clinical symptoms and biochemical analysis. During this period, five Patients come out. Patients were divided into two groups:

Group A (n=43): patients who adhere to nutritional instructions.

Group B (n=42): Patients who did not adhere to nutritional instructions.

2.3. Data collection

Data related to the clinical assessment (Number and duration of attacks in the last month and duration between attacks) and biochemical analyzes (Serum amyloid A level, hemoglobin level and Vitamin D) were collected before and 6 months after nutrition intervention in both groups.

3. Results

Comparison between group A and group B was made, in terms of clinical symptoms and biochemical analyses, before receiving nutritional instructions and six months after receiving instructions.

Regarding clinical symptoms and biochemical analyses; In group A, there were statistically significant differences before the experiment and after the six-month. In group B, there were no statistically significant differences indicating improved health status.

Table (1) shows that there were statistically significant differences in Serum amyloid A level before and 6 months after nutrition intervention in both groups. Shows also a significant increase in the levels of both hemoglobin and vitamin D ($P= 0.001$, $P= 0.001$) respectively, after 6 months nutrition intervention within normal limits in the results of group A, while there were no statistically significant differences in the results of group B, noting a slight decrease in their percentage.

Table (2) Shows there were no statistically significant differences in body temperature, number and duration of attacks in the last month and duration between attacks ($P= 0.001$ for both of them) in the results of group A, where the body temperature and number and duration of attacks decreased, and the period between one attack and the next increased. While there were no statistically significant differences in the results of group B.

Table 1: Laboratory assessment before and after 6 months in both groups.

	Group A (n=43) (Adherent group)		Group B (n=42) (Non-adherent group)	
	Before Mean \pm SD	After Mean \pm SD	Before Mean \pm SD	After Mean \pm SD
Amyloid percent	93.16 \pm 75.42	3.62 \pm 2.03	135.44 \pm 80.94	37.07 \pm 50.67
	P< 0.001*		P= 0.001*	
HB level	10.32 \pm 1.67	12.55 \pm 1.35	10.64 \pm 1.73	9.92 \pm 1.38
	P= 0.001*		P= 0.157	
Vitamin D level	23.29 \pm 5.83	33.39 \pm 6.00	23.12 \pm 5.02	22.25 \pm 1.66
	P= 0.001*		P= 0.081	

HB: hemoglobin level P: probability value of MC Nemar Test *: statistically significant

Table 2: Temperature, number and duration of attacks before and 6 months after nutrition intervention in both groups.

	Group A (Adherent group)		Group B (Non-adherent group)	
	Before Mean \pm SD	After Mean \pm SD	Before Mean \pm SD	After Mean \pm SD
Body temperature	39.24 \pm 1.47	37 \pm 0.12	38.65 \pm 1.39	38.67 \pm 1.38
	P= 0.001*		P= 0.157	
Number of attacks in the last month	4.74 \pm 6.23	0	2.7 \pm 1.52	3.21 \pm 1.66
	P= 0.001*		P= 0.081	
Duration of the attack	5.5 \pm 5.08	0	5.47 \pm 6.14	5.63 \pm 5.96
	P= 0.001*		P= 0.158	
Duration between attacks	18.36 \pm 19.51	180 \pm 0	14.14 \pm 20.39	12.65 \pm 12.77
	P= 0.001*		P= 0.094	

4. Discussion

Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease (Poddighe *et al.*, 2022). Our results showed that a proper controlled nutritional status could potentially dampen the inflammatory markers which agrees with previous studies (Ekinici *et al.*, 2020).

The progression of FMF is closely related to the levels of persistent inflammation characterized by the increase in serum amyloid A production (Lotfy *et al.*, 2016). In this work, a significant improvement in the clinical symptoms and the inflammatory biochemical parameters and with respect to duration and severity of attacks with the supplementation of an anti-inflammatory diet including vitamin D, flaxseed, curcumin intake, and foods rich in iron and omega 3. The dietary sources of omega 3 are salmon, sardines, mackerel, sunflower oil, rapeseed oil, flaxseed oil, grape seed oil and corn oil. Vitamin D protects cells against oxidative stress and inflammation through inhibiting reactive oxidant species (ROS) (Minich *et al.*, 2022). Curcumin has an antioxidant and anti-inflammatory potential (Zeng *et al.*, 2022). PUFAs have an important anti-inflammatory and antioxidant capabilities (Bahat *et al.*, 2022). This is consistent with previous researchers in that omega-3 PUFA alters the expression of inflammatory genes through transcription factor activate (Lopez *et al.*, 2004; Aggarwal and Harikumar, 2009). Accordingly, flaxseed, which is rich in omega-3 polyunsaturated fatty acids, is an effective anti-inflammatory and therapeutic agents (Lemos *et al.*, 2012). Our findings were supported by previous studies reported Turmeric is a powerful anti-inflammatory agent and neuroactive compound that reduces inflammation leading to improved general condition and reduced recurrence. Likewise, the diet has been shown to be low in fat, low in carbohydrates, and rich in fresh fruits and vegetables improving the general condition and modulating inflammation the inflammatory state of FMF and has a beneficial effect on health leading to a better prognosis and less complications. These bioactive compounds play an important role in mitigating the harmful effects associated with inflammation in FMF (Strimpakos and Sharma, 2008; Ren *et al.*, 2016). Our study revealed an improvement in clinical presentation and a decrease in CRP and serum amyloid A after this nutritional regulation.

5. Conclusion

Interventional nutrition including anti-inflammatory diet improves biochemical parameters and the clinical presentation with respect to duration, frequency and severity of the attacks. This nutritional strategy may help the development of therapeutic strategies to reduce mortality and improve the quality of life for these patients.

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