Original Article

Cephalometric evaluation of children with familial Mediterranean fever

Ahmet Yalcin Gungor[a]; Vefik Arica[b]; Ozge Gungor[c]; Murat Tutanc[b]

ABSTRACT

Objective: To test the null hypothesis that no differences exist in craniofacial morphology between patients with familial Mediterranean fever (FMF) and the healthy population.

Materials and Methods: Standardized lateral cephalograms of 32 FMF patients (mean age, 11.50 $\pm$ 2.72 years) and 32 healthy controls (mean age, 11.86 $\pm$ 2.19 years) were obtained. Cranial and dentofacial parameters were measured using a cephalometric analysis program (Nemoceph Imaging Cephalometric and Tracing Software S.L., Spain). All statistical analyses were conducted using SPSS version 17.0.0 (SPSS Inc., Chicago, Ill). Descriptive statistics were calculated for all measurements, and the independent *t*-test was used to evaluate intergroup differences.

Results: The ANB angle was significantly greater in the FMF group ($P < .05$). Differences in SNA and SNB angles were insignificant. Anterior ($P < .001$) and posterior ($P < .05$) face heights were significantly shorter in the FMF group. Mandibular body length ($P < .001$) and condylion to gnathion ($P < .05$) measurements were significantly shorter in the FMF group. The upper lip was more protrusive in the FMF group ($P < .05$). U1–NA (mm; $P < .001$) and L1–NB (mm; $P < .05$) measurements were significantly shorter in the FMF group.

Conclusion: The hypothesis is rejected. Significant differences exist between the craniofacial morphology of patients with FMF and the healthy population. (*Angle Orthod.* 2012;82:552–555.)

KEY WORDS: Cephalometric; Autoinflammatory; FMF

INTRODUCTION

Familial Mediterranean fever (FMF) is a systemic autoinflammatory disorder characterized by seemingly unprovoked recurrent episodes of fever and synovial, serosal, or cutaneous inflammation.[1] FMF is an autosomal recessive hereditary disease that most commonly occurs in multiple populations from the eastern Mediterranean basin, particularly Jews, Armenians, Turks, and Arabs.[2] FMF is characterized by short recurrent bouts of fever and localized inflammation usually involving the peritoneum, pleura, joints, or skin.[1,3]

Two phenotypes of FMF have been reported based on clinical features. Patients with typical clinical features who have been genetically confirmed to have MEFV mutations are defined as phenotype I. Other patients develop amyloidosis without any previous attacks of typical FMF; they are defined as phenotype II patients.[4]

The FMF gene (MEFV), which is located on the short arm of chromosome 16, encodes a protein termed *pyrin* or *marenostrin*; most of the pathogenic MEFV mutations are located near the C-terminal half, which is a clear clue to the functional importance of this domain.[5,6] The estimated prevalence of FMF in Turkey is 1/1000, and the carrier rate is 1:5.[6] Continuous subclinical inflammation in FMF patients may lead to a decrease in bone mineral density and osteoporosis in this group of patients. Recent studies showed decreased bone mineral density levels in children patients with FMF.[2,7] In addition, arthritis is commonly seen in FMF patients.[4]

Altered body composition and growth impairment, including disturbed bone development, are complications of autoinflamatory disorders.[8–13] Patients with autoinflamatory disorders show decreased bone and muscle mass, and the reduction in bone mass may represent secondary bone loss.[9,11] Many studies

[a] Assistant Professor, Department of Orthodontics, Faculty of Dentistry, University of Akdeniz, Antalya, Turkey.

[b] Assistant Professor, Department of Paediatrics, Faculty of Medicine, University of Mustafa Kemal, Hatay, Turkey.

[c] Assistant Professor, Department of Pediatric Dentistry, Faculty of Dentistry, University of Akdeniz, Antalya, Turkey.

Corresponding author: Dr Ahmet Yalcin Gungor, Akdeniz Üniversitesi, Dishekimligi Fakultesi, Ortodonti A.D. Kampus, Antalya, Turkey
(e-mail: aygungor@gmail.com)

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demonstrated that continuing inflammation decreases the bone mineral density and causes retardation of growth and development.[8–13] Furthermore, Bechtold and Roth[11] concluded that a decrease in muscle mass and force is a major contributing factor to the deficits in bone mass. Gorska et al.[8] evaluated the levels of serum markers of bone formation and resorption in juvenile idiopathic arthritis and found that a longer duration of disease proves a pathogenesis of disorders of bone formation and resorption occurring in childhood and adolescence. Many of the authors who evaluated bone mineral density and bone formation in FMF found that FMF patients have lower levels of bone mineral density and other bone formation markers.[13–15] Therefore, in our study, we intend to investigate if there are any differences in craniofacial development between FMF patients and a healthy population.

The present study aimed to cephalometrically evaluate the children with FMF and to find out whether significant differences exist in dentofacial structures of healthy controls. The null hypothesis to be tested stated that no difference exists in craniofacial morphology between patients with FMF and the healthy population.

MATERIALS AND METHODS

Records of FMF patients and heath individuals (control group) were selected retrospectively from the archives of Mustafa Kemal University, Faculty of Medicine research hospital. Selection criteria included no previous orthodontic treatment and having cephalometric films and records for FMF.

The exclusion criteria for the FMF patients were as follows:

- Having any missing teeth
- Being younger than 8 years
- Having severe periodontitis

A control group was selected from records of Class I malocclusion patients with no systemic disease who came to the dentistry clinic of Mustafa Kemal University, Faculty of Medicine, research hospital.

Standardized lateral cephalograms of 32 FMF patients (22 girls, 10 boys) and age and sex-matched 32 healthy individuals that had been taken with the same digital cephalometric imaging system (Blue X Imaging Srl, Assango, Italy) in a natural head position[16] were selected. Mean ages were 11.50 $\pm$ 2.72 years for the FMF group and 11.86 $\pm$ 2.19 years for the control group. Cranial and dentofacial parameters were measured using a cephalometric analysis program (Nemoceph Imaging Cephalometric and Tracing Software S.L., Spain). A total of 23 measurements were performed on the lateral cephalograms. Cephalometric landmarks were marked and digitized by one of the authors. In 10 subjects, all of the measurements were repeated 2 weeks later to determine the measurement error, which was .994 or greater for all parameters.

Statistical Method

All statistical analyses were conducted using SPSS version 17.0.0 (SPSS Inc, Chicago, Ill). Significance for all statistical tests was predetermined at $P < .05$. Descriptive statistics were calculated for all measurements, and the independent *t*-test was used to evaluate intergroup differences.

RESULTS

The results of the descriptive statistics and intergroup comparisons of cephalometric variables are presented in Table 1. ANB angle was significantly greater in the FMF group ($P < .05$). Differences in SNA and SNB angles were insignificant. Anterior ($P < .001$) and posterior ($P < .05$) face heights were significantly shorter in the FMF group. Mandibular body length ($P < .001$) and condylion to gnathion ($P < .05$) measurements were significantly shorter in the FMF group. The upper lip was more protrusive in the FMF group ($P < .05$). U1–NA (mm; $P < .001$) and L1–NB (mm; $P < .05$) measurements were significantly shorter in the FMF group.

DISCUSSION

The present study aimed to compare the cephalometric characteristics of FMF patients with healthy subjects and to determine possible relationships between these cephalometric measurements. To increase the comparability of the two groups and minimize the contribution of growth and development, we selected age- and sex-matched patients from the archives for the control group. To our knowledge, this is the first study that compares the cephalometric characteristics of FMF patients, so we were not be able to compare the results of this study to similar studies.

In the FMF group, no statistically significant differences were found in the positions of the maxillary and mandibular base relative to the cranial base. However, the mandible was found to be significantly retrusive relative to the maxilla. In the FMF group, the mandible was significantly smaller according to the mandibular body and condylion to gnathion measurements. The ramus height was also shorter but insignificant in the FMF group. Reduction in the size of the mandible may be associated with arthritis and/or reduced bone turnover on mandibular condyle due to FMF. Reed et al.[17] stated that active inflammation reduces the rate

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Table 1. Comparison of the Cephalometric Variables[a]

Parameter	Patients With FMF				Healthy Individuals				*P*
	Mean	SD	Lower	Upper	Mean	SD	Lower	Upper	
ANB (°)	5.04	1.21	3.00	7.10	4.23	1.36	1.90	7.10	*
SNA (°)	79.90	3.86	75.90	92.80	80.88	4.45	72.80	89.80	
SNB (°)	74.88	3.89	69.50	86.90	76.64	4.72	67.70	84.90	
GoGn-SN	36.93	4.87	24.20	44.70	36.63	6.54	25.80	51.80	
Anterior face height (NaMe)	99.33	5.93	91.00	109.70	105.90	6.31	92.50	117.30	***
Posterior face height (SGo)	62.44	5.74	55.20	77.80	65.52	4.89	57.50	74.40	*
P-A face height (%)	62.88	4.50	51.40	75.30	61.97	4.50	54.20	70.70	
Lower anterior facial height	56.59	4.00	50.10	63.20	60.34	4.91	49.00	68.80	**
Ramus height	37.34	5.72	26.00	47.80	38.06	4.14	32.00	45.60	
Mandibular body	56.70	6.04	49.70	70.70	63.38	4.38	53.90	71.40	***
Condylion to point A	74.00	5.53	65.70	87.00	74.40	4.86	66.60	84.70	
Anterior cranial base length	59.85	2.49	54.60	63.40	60.70	3.70	51.20	64.90	
Condylion to gnathion	93.72	8.44	80.60	112.80	97.87	5.46	86.20	108.20	*
Nasolabial angle	120.78	9.59	109.30	142.30	110.70	11.01	93.70	131.50	***
Upper lip protrusion	0.14	1.30	−2.20	2.40	−0.99	2.46	−5.50	3.80	*
Lower lip protrusion	0.51	1.50	−1.80	2.60	0.84	1.83	−1.30	5.00	
Wits	0.21	1.44	−3.20	2.60	−0.62	2.00	−4.50	2.90	
Interincisal angle	125.04	6.43	116.40	136.00	121.58	8.91	108.90	140.40	
U1–NA (mm)	2.13	1.52	−0.30	4.40	4.17	1.58	1.00	7.00	***
L1–NB (mm)	4.96	1.97	1.20	7.50	6.28	1.97	2.20	11.10	*
U1–NA (°)	21.93	5.35	14.10	35.30	23.51	5.91	10.10	37.60	
L1–NB (°)	27.99	5.41	17.30	35.90	30.69	5.58	23.10	41.30	
Pog–NB (mm)	1.01	1.16	−2.00	3.10	0.96	2.36	−6.60	4.80	

[a] FMF indicates familial Mediterranean fever. Independent *t*-test.
* $P < .05$; ** $P < .01$; *** $P < .001$.

of bone formation. Bakkaloglu[4] stated that arthritis is seen in 45% of the FMF patients. Gorska et al.[8] concluded that children with higher degrees of joint destruction have reduced bone turnover. Many authors who studied bone turnover and bone growth in children with juvenile rheumatoid arthritis found that disturbed linear growth occurs frequently in these children.[9–12] Therefore, continuing inflammation on the condyle could cause retardation of growth and development of the mandible.

Contrary to the mandible, there was no difference found in the size of the maxilla and anterior cranial base. Besides, there is no defined mechanism to affect this structure.

Anterior and posterior face heights were shorter in the FMF group. This may be due to reduced alveolar growth caused by an unknown mechanism. As expected, there was no difference found in P-A face height ratio and GoGn-SN angle because of the simultaneous reduction of anterior and posterior facial heights.

Upper and lower incisors were more retrusive in the FMF group. Teeth and their supporting bone are in a position of balance between the lips and tongue. A retruded and lower-positioned tongue, due to a smaller size of the mandible, could be the reason for the retrusive incisors.

Although the upper incisors were more retrusive, the upper lips were more protrusive to the E-plane and the nasolabial angle was wider in the FMF group. Because the E-plane is a line between the tip of nose and chin, the protrusive position of the upper lips could be due to the retruded position of the chin.

The weakness of this study is that it is a cross-sectional study, and further studies are needed to confirm these findings and examine the growth pattern of patients with FMF.

CONCLUSIONS

- Significant differences exist in the craniofacial morphology of patients with FMF and the healthy population.
- FMF patients showed reduced posterior and anterior facial heights and mandibular body length.
- Positional relationships of the maxilla to the cranial base and to each other are similar between the FMF patients and healthy subjects.
- The results of the study indicated that characteristics of children with FMF should be considered, especially during functional treatment of mandible.

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