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Tissue fatty acid composition in obstructive sleep apnea and recurrent tonsillitis

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ABSTRACT

Objective: Tonsillar hypertrophy cells appear to have an altered lipid metabolism as evidenced by modulated inflammatory cytokines that affect tissue lipid metabolism. The aim of this study was to investigate differences in tissue fat composition between obstructive sleep apnea (OSA) and recurrent infective tonsillitis (RT) in children.

Methods: Tonsillar tissues were collected from 114 patients with OSA and 92 patients with RT, aged 4–10 years, during tonsillectomy. The tissue lipid extracts were analyzed by gas liquid chromatography for a comprehensive fatty acid profile.

Results: In the tonsillitis tissue, the levels of palmitoleic acid (16:1$n-7$; $P = 0.002$) and oleic acid (18:1$n-9$; $P = 0.003$) were higher, and the level of stearic acid (18:0; $P = 0.004$) was lower than that in the hyperplastic tonsillar tissue. Overall, tonsillar tissue of patients with RT had a significant increase in the total monounsaturated fatty acids (+9.9%; $P < 0.001$) and the fatty acid desaturation index (+20.5%; $P < 0.001$). Furthermore, oleic acid content of tonsillar tissue was positively correlated with BMI ($r = 0.20$, $P = 0.004$), snoring ($r = 0.16$, $P = 0.022$) and hypertrophy grade ($r = 0.18$, $P = 0.023$), which remain significant in the subgroup analysis by hypertrophy type.

Conclusions: The change in the fatty acid composition may be regarded as an indicator of altered lipid metabolism occurring *in vivo* during human tonsillar hypertrophy, which might be linked to the severity or type of the tissue damage.

1. Introduction

Tonsillar hypertrophy is one of the main problems in pediatric otolaryngology in terms of prevalence and the unreliable correlation between clinical features and behavior of this disease [1,2]. The most common indications for tonsillectomy are recurrent infective tonsillitis (RT) and the presence of hypertrophied tonsils occupying more than 75% of oropharyngeal space, with signs of obstructive sleep apnea (OSA) [3]. Mechanism of pathogenesis differs between these two subtypes of tonsillar hypertrophy, but little is currently known about their specific characteristics. Different morphology, proliferation and biological properties have already been reported [4,5].

Apart from being sources of energy, fatty acids are known to affect various aspects of cellular processes including membrane fluidity and signaling, which makes the evaluation of their status even more important [6,7]. Fatty acids *de novo* synthesis and their metabolic conversion to other fatty acids are catalyzed by intracellular lipogenic enzymes such as fatty acid synthase, desaturases and elongases [8]. These processes provide essential precursors for structural cell components and bioactive metabolites such as prostaglandins. It is recognized that hypertrophic cells have altered fatty acid metabolism and inflammatory cytokines [4,9,10] which may contribute to the pathogenesis of organ dysfunction and certain aspects of tissue behavior such as growth and response to therapy. Therefore, the proportions of specific fatty acids in the tonsillar tissue may also be related to tonsillar disorders, especially tonsillar hypertrophy.

Altered inflammatory cytokines have been shown in RT compared to OSA [11,12]. We have recently reported that RT patients had a significantly higher serum type II secretory phospholipase A2 (sPLA2 IIa) activity compared with OSA [13].

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Table 1
Clinical characteristics of study population.[a]

	Obstructive sleep apnea ($n=114$)	Recurrent tonsillitis ($n=92$)	P
Age, y	7.09 ± 1.85	7.40 ± 1.94	0.187
Gender, %women	39	47	0.239
Body mass index, kg/m^2	15.9 ± 3.5	16.6 ± 3.3	0.175
Oral respiration, %	94	89	0.211
Coughing, %	12	13	0.846
Dysphasia, %	20	26	0.294
Snoring, %	93	90	0.459
Grade of tonsillar hypertrophy	3.06	3.00	0.615

[a] Values are means ± SD or percentage with condition.

Although this indicated an altered lipid metabolism in tonsillar hypertrophy tissue, characterization of patients with tonsillar hypertrophy has not been undertaken. The aim of this study was to investigate tissue fatty acid composition in OSA and RT, and to compare the data obtained with clinicopathological parameters.

2. Materials and methods

2.1. Patients and tissue specimens

The study was approved by the ethic committee of Tabriz University of Medical Sciences, and all patients gave informed consent. Case and control subjects were identified as previously described [13]. Briefly, subjects were prospectively recruited from a patient population scheduled for tonsillectomy referred to ENT department of Tabriz University of Medical Sciences between 1 February 2010 and 30 February 2011. In present study, 206 patients (119 men and 87 women) were operated due to the presence of tonsil hypertrophy (114 OSA patients and 92 RT patients). RT was defined as the occurrence of at least three episodes a year of acute infection. The diagnosis of OSA was based on tonsil hypertrophy occupying more than 75% of the oropharyngeal space, with the signs of airway obstruction, but without any episodes of acute infection. Patients over 10 years of age and those with intercurrent infection for at least one month prior to surgery, current antibiotics medication, a previous diagnosis of congenital airway anomalies, asthma, endocrine diseases, allergic rhinitis; acute or chronic inflammatory disease were excluded to obtain a more homogeneous study population. Clinical characteristics such as oral respiration and coughing, dysphagia, snoring or grade of tonsillar hypertrophy were recorded. Snoring was considered positive if verified by parents as either often or always. All surgeries were performed according to a standardized procedure by the same surgeon, and all diagnostics were confirmed by histopathologic examination. The tonsillar tissue samples were dissolved in n-hexane and were stored at −70 °C in glass vials for ≤5 months until analysis.

2.2. Laboratory analysis

The solution of fat extract in hexane was evaporated under a stream of nitrogen to near dryness and the lipids were esterified with methanol during catalysis with acetyl chloride [14]. Fatty acid methyl esters were extracted and analyzed for fatty acid composition, as described previously by us [15].

2.3. Statistical analysis

The level of significance between groups was calculated according to t-test for continuous variables and χ^2-test for categorical variables. Pearson correlation test was performed to identify the relationship between variables. A P value of less than 0.05 was considered statistically significant. All analyses were carried out using SPSS for windows version 11.0 (SPSS Inc., Chicago, IL).

3. Results

The clinical details of the study subjects are presented in Table 1. Table 2 shows the level of fatty acids measured by gas liquid chromatography method in the hyperplastic tonsillar and tonsillitis tissue. Palmitic acid (16:0) was the major fatty acid in

Table 2
Fatty acid composition of tonsillar tissues in the studied groups.[a]

	Obstructive sleep apnea ($n=114$)	Recurrent tonsillitis ($n=92$)	P
14:0 (myristic acid)	1.20 ± 0.48	1.32 ± 0.64	0.14
16:0 (palmitic acid)	39.87 ± 2.58	40.05 ± 3.40	0.69
16:1n−7 (palmitoleic acid)	2.30 ± 0.99	3.00 ± 1.35	<0.01
18:0 (stearic acid)	23.74 ± 2.75	21.13 ± 2.80	<0.01
18:1n−9 (oleic acid)	18.13 ± 2.39	19.53 ± 2.95	<0.01
18:2n−6 (linoleic acid)	9.04 ± 2.19	9.19 ± 2.93	0.69
18:3n−9 (linolenic acid)	0.30 ± 0.17	0.30 ± 0.20	0.88
CLA (conjugated linoleic acid)	0.54 ± 0.24	0.59 ± 0.41	0.26
20:3n−6 (dihomo-γ-linolenic acid)	0.97 ± 0.47	1.07 ± 0.41	0.11
20:4n−6 (arachidonic acid)	2.91 ± 0.98	2.81 ± 0.97	0.52
20:5n−3 (eicosapentaenoic acid)	0.46 ± 0.18	0.48 ± 0.28	0.43
22:6n−3 (docosahexaenoic acid)	0.54 ± 0.40	0.50 ± 0.41	0.52
SFA (saturated FAs)	64.80 ± 3.95	62.62 ± 3.61	<0.01
MUFA (monounsaturated FAs)	20.43 ± 3.02	22.47 ± 3.44	<0.01
n−6 PUFA (polyunsaturated FAs)	13.46 ± 2.91	13.67 ± 3.61	0.65
n−3 PUFA (polyunsaturated FAs)	1.29 ± 0.59	1.28 ± 0.68	0.88
18:0/16:0	0.59 ± 0.08	0.53 ± 0.10	<0.01
18:1n−9/18:0	0.78 ± 0.21	0.94 ± 019	<0.01
20:4n−6/18:2n−6	0.33 ± 0.12	0.32 ± 0.12	0.66

[a] Values are expressed as means ± SD, $P<0.05$ (t-test); FAs, fatty acids.