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Histological analysis of palatopharyngeal muscle from children with snoring and obstructive sleep apnea syndrome

Isabela Mattos De Vuono [a,*], Edmar Zanoteli [b], Acary Souza Bulle de Oliveira [b], Reginaldo Raimundo Fujita [a], Shirley Shizue Nagata Pignatari [a], Gilberto Ulson Pizarro [a], Márcia Lurdes de Cássia Pradelle-Hallinan [c], Gustavo Antônio Moreira [c]

[a] *Department of Otorhinolaryngology and Head and Neck Surgery, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil*
[b] *Department of Neurology, UNIFESP, São Paulo, Brazil*
[c] *Department of Sleep Medicine and Biology, UNIFESP, São Paulo, Brazil*

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Summary Obstructive sleep apnea syndrome (OSAS) is an upper airway obstruction that occurs during the sleep. One of the suggested mechanisms involved in this process is a neuromuscular abnormality of the palatal muscles. Whether children with OSAS develop into OSAS adults, or children and adult OSAS are two distinct disorders occurring at different ages are questions to be answered. Here, we made the histological analysis of palatophryngeal muscle in 34 oral-breathing children of both genders, aged 5—12 years old, with hypertrophic tonsils and adenoids. According to the polysomnographic study the participants were divided into children without sleeping disorders (group I) and children with primary snoring (group II) or apnea (group III). The main histological findings were fiber size variability in 70% cases from groups II and III and in 71% from group I; perimysial connective tissue infiltration in 48% children from groups II and III and in 71% from group I; intracytoplasmatic mitochondrial proliferation in 63% cases from groups II and III and in 57% cases from group I. Muscle necrosis was only observed in one case, in association with subglandular inflammation. Others findings observed in all groups included fibers with internal architecture alteration, such as moth-eaten and lobulated fibers, type 2 fiber predominance, and small areas of fiber type grouping. The presence of similar histological findings in the palatopharyngeal muscle in children with primary snoring or apnea but also in children without sleeping disorders indicate that such changes

* Corresponding author. Tel.: +55 11 55397723.
E-mail address: ivuono@uol.com.br (I.M.D. Vuono).

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could be a normal histological feature of this muscle rather than a neurogenic or myopathic pathology.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a breathing disorder characterized by upper airway obstruction with an abnormal sleep pattern [1]. Childhood OSAS is relatively common, with a prevalence of 2% in children aged 2—18 years [19]. The natural course of OSAS in children is still to be determined, and whether OSAS children develop into OSAS adults, or both are two distinct breathing pathologies is not clearly known [16].

In children, palatine and pharyngeal hypertrophy have been associated with OSAS [11,5], and most of the cases have been successfully treated with adenotonsillectomy [22]. However, the surgical treatment of OSAS has been proved not effective in patients in whom the only risk factor for OSAS is the adenotonsillar hypertrophy [22,14,18]. In addition, it has been shown that OSAS is most probable caused by a combination of structural and neuromuscular factors [16,15].

The pathophysiological mechanism for the collapse of upper airways during inspiration and sleep in patients with heavy snoring and OSAS is not clear. Many studies have suggested that OSAS is probably the final stage of a progressive disease, starting with simple snoring [9]. One of the mechanisms suggested to be involved in this process is the neurogenic lesion of the palatal muscles [7,13]. As the functional activity of the muscles of the upper airway is of vital importance to maintain the stability and patency of the upper airway during inspiration, a muscle dysfunction might be one of the causes of OSAS [7,13,20,4,23].

A previous study has shown that the degree of neurogenic process on palatopharyngeal muscle of adult patients was associated with the degree of sleep breathing disorder [9]. The authors compared adults with habitual snoring and upper airway obstruction to normal individuals and found that the degree of histological abnormalities correlated significantly with the degree of obstructive breathing. They suggested that a progressive local neurogenic lesion caused by the trauma of snoring might be a potential contributory factor to the upper airway collapsibility [9]. The determination of the presence of neurogenic muscular alteration in children with OSAS could indicate a genetic risk factor for the condition.

The aim of this work was to detect the presence of possible myopathic or neurogenic changes on palatopharyngeal muscle in children with OSAS.

2. Patients and methods

2.1. Patients

Thirty-four consecutive children (16 males and 18 females, mean age 7 years old, range 5—12) scheduled for tonsillectomy participated in the present study. The patients presented with mouth breathing for at least 6 months, palatine tonsils hypertrophy grades III and IV [3], and adenoid hypertrophy occupying at least 70% of the nasopharynx, assessed by clinical examination and nasofibroscopy. According to their polysomnographic study and based on the American Thoracic Society Criteria [1], the children were divided into three groups: group I (normal nocturnal polysomnography), group II (habitual snoring) and group III (OSAS) (Table 1). None of the subjects had clinical signs or symptoms of neuropathy or neuromuscular disorder. This study received the approval of the institutional ethics committee.

2.2. Muscle biopsy

The muscle biopsies were obtained from the cranial part of the palatopharyngeal muscle. Every surgery was performed under general anesthesia, without the use of local anesthetic. Each specimen was quickly frozen in liquid nitrogen and stored in a deep freezer at −75 °C. Cryosections (5—8 μm, −25 °C) were stained with hematoxylin—eosin (H&E), modified Gomori trichome (GO), NADH-tetrazolium reductase (NADH-tr), succinate dehydrogenase (SDH), and myofibrillar adenosine triphosphatase (ATPase) after alkaline (pH 9.6) and acid (pH 4.6 and 4.3) preincubations [6].

The blind evaluation of histopathological changes of palatopharyngeal muscle was performed by two specialists (EZ, ASBO) in agreement, and the main histological abnormalities included for analysis were: fiber type variability, endomysium and perimysium connective tissue proliferation, nuclei positioning, muscle necrosis, endomisyum and perimysium inflammation, atrophic rounded fibers, hypertrophied fibers, subsarcolemal and/or intracitoplasmatic mithocondrial proliferation, mouth-eaten appearance, fiber splitting, nuclear bags and