Association between adenotonsillar hypertrophy and sickle cell disease in adolescents

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ABSTRACT

Aim of the study: To assess the association between sickle cell disease and adenotonsillar hypertrophy in adolescents.

Material and methods: The study group consisted of adolescents aged between 12 and 16 years with sickle cell disease. The control group consisted of adolescents of the same age group who did not have this disorder. The adolescents underwent oropharyngoscopy and transnasal endoscopy. The palatine tonsils were classified according to Brodsky’s criteria, and those with grade three or four were considered hypertrophic. Regarding the pharyngeal tonsil, two criteria were adopted. It was considered obstructive when there was minimal occlusion of the choanae of 50%, and when the obstruction was equal to or greater than 70%. Adenotonsillar hypertrophy was diagnosed when the pharyngeal tonsils and/or palatine tonsils were obstructive.

Results: In the study group, 31.3% of the adolescents had hypertrophic palatine tonsils, and in the control group, 2.6% exhibited that condition ($p < 0.001$). With respect to the pharyngeal tonsils, when the criterion of minimal obstruction of the choanae was 50%, 54.2% of the adolescents of the study group and 15.8% of the control group were diagnosed with hypertrophy ($p < 0.001$). When the criterion for minimal occlusion of the choanae was 70%, the frequency was 35.4% in the study group, and 7.9% in the control group ($p = 0.004$). Regarding adenotonsillar hypertrophy, when the criterion of the occlusion of the choanae was 50%, it occurred in 58.3% of the adolescents of the study group and 18.4% of the control group ($p < 0.001$). When the criterion for minimal obstruction of the choanae was 70%, it was observed that adenotonsillar hypertrophy occurred in 45.8% of the adolescents of the study group and in 10.5% of the control group ($p < 0.001$).

Conclusions: Adenotonsillar hypertrophy was associated with sickle cell disease in adolescents.

KEY WORDS: adolescent, hypertrophy, palatine tonsil, sickle cell, adenoids.

INTRODUCTION

Waldeyer’s ring is of extreme importance for local and systemic immunity. It consists of the pharyngeal tonsils (also known as adenoids), palatine tonsils, tubal tonsils, and lingual tonsils [1]. The pharyngeal and palatine tonsils are the largest. They are located at the entrance of the airways and the digestive tract. They represent the first site of contact with a variety of microorganisms and other antigens present in ingested food and inhaled air [2].

Adenotonsillar hypertrophy (ATH) is the term commonly used to describe abnormal enlargement of the pharyngeal tonsils (adenoid vegetations) and palatine tonsils. The causes of ATH have not yet been fully elucidated.
However, chronic or acute recurrent inflammation seems to be involved, given that children undergoing these processes usually exhibit abnormal growth of cervical and pharyngeal lymphoid tissue [3].

Sickle cell disease (SCD) is a genetic anomaly, characterised by progressive damage of several organs. It is considered one of the most serious common monogenic diseases. This name was given because of the sickle-shaped red blood cells of the patients. Sickle cell anaemia is the most common form, and refers specifically to the homozygosity of the β S-globin allele, which leads to the production of a particular type of haemoglobin, i.e. haemoglobin S (HbS). There is also sickle cell haemoglobinopathy, due to the relationship between the β S-globin allele and the β C-globin allele with β-thalassaemia allele, resulting from the combination of the β S-globin allele with the β-thalassaemia allele, causing Hbs/β-thalassaemia [4].

ATH is apparently more frequent and tends to be a long-lasting disorder in children and adolescents with SCD. There are three main hypotheses suggested for its association with SCD, namely: a) compensation for self-splenectomy; b) a consequence of recurrent infections in the upper respiratory tract due to failure of opsonisation of pathogenic bacteria; and c) the functioning of the pharyngeal and palatine tonsils as haematopoietic centres due to haemolysis. ATH can lead to sleep-disordered breathing, ranging from snoring to obstructive sleep apnoea syndrome [5, 6]. The objective of the present study was to assess the association between SCD and ATH in adolescents.

MATERIAL AND METHODS

The present study was conducted from October 2017 to August 2018. The study group consisted of adolescents aged between 12 and 16 years, attending the specialised outpatient clinic of the university public service (a regional reference), recruited by the researcher during routine consultations. The control group consisted of healthy adolescents who belonged to the same age group and were attending the childcare outpatient clinic for adolescents in the same public service during the same period. Patients of both groups were recruited via convenience sampling.

The inclusion criteria for the study group were: having been diagnosed with SCD, confirmed by the quantitative analysis of haemoglobin, performed through haemoglobin electrophoresis or high performance liquid chromatography; and being clinically stable. The inclusion criteria for the control group were: not having a diagnosis of SCD; and not being in the period of an acute infectious process. The exclusion criteria for the two groups included: craniofacial malformations; debilitating diseases; recent craniofacial traumas; adenoidectomy surgery and/or previous palatine tonsillectomy; and use of systemic therapy with corticosteroids during the research.

Parents and/or guardians of the adolescents, who were willing to collaborate in the study signed an informed consent form. The adolescents were then submitted to oropharyngoscopy with frontal lighting and a tongue depressor, and trans-nasal video endoscopy, using a 3.2 mm flexible endoscope (Machida®) coupled to a Lumen® LED light source. We also used a Pro-HD II® digital micro camera to record the images to be subsequently analysed.

The palatine tonsils were classified according to Brodsky’s criteria, namely: grade 0 = palatine tonsils located inside the tonsillar fossa; grade 1 = tonsils located beyond the tonsillar fossa, occupying less than 25% of the oropharynx space; grade 2 = tonsils occupying more than 25% and less than 50% of the oropharyngeal space; grade 3 = tonsils occupying more than 50% and less than 75% of the oropharyngeal space; and grade 4 = tonsils occupying more than 75% of the oropharyngeal space [7]. Palatine tonsils grade 3 or 4 were considered obstructive. Pharyngeal tonsils (adenoids) were considered obstructive when they met the following two criteria: 1) minimal occlusion of the choanae of 50% [8]; and 2) the minimal obstruction should be 70% of the choanae [9]. The adolescents with obstructive adenoids and/or palatine tonsils were diagnosed with ATH [8].

The variables were described by means of absolute frequency and relative percentage. The associations were tested using Fisher’s exact test and Pearson χ² test estimated asymptotically or via Monte-Carlo method. The significance level was 5%, and the software used was R Core Team 2018. The project was approved by the Research Ethics Committee of the institution (Opinion No. 2,256,897).

RESULTS

The study group was composed of 48 adolescents (26 males and 22 females) considered eligible. Of them, 46 had a diagnosis of sickle cell anaemia, and two had sickle cell haemoglobinopathy. The control group consisted of 38 adolescents (15 males and 23 females). There were no statistically significant differences between the groups regarding sex (p = 0.198) and age (p = 0.767).

Among the 48 adolescents of the study group, 15 (31.3%) had hypertrophic palatine tonsils, whereas only one adolescent (2.6%) of the control group had this condition. This difference was statistically significant (p < 0.001). Regarding the pharyngeal tonsils, considering hypertrophic those that led to a minimal obstruction of the choanae of 50%, 26 adolescents (54.2%) of the study group and six (15.8%) of the control group exhibited this condition. In this case, there was statistical significance between the groups (p < 0.001). When pharyngeal tonsils were considered hypertrophic, causing a minimal occlusion of the choanae of 70%, the frequency was 17 (35.4%) adolescents in the study group and three (7.9%) in the control group. This difference was statistically significant (p = 0.004).

Regarding the presence of ATH, when we used the criterion that considered pharyngeal tonsil obstruction...
with occlusion of the choanae of at least 50%, it was observed that it occurred in 28 adolescents of the study group (58.3%) and in seven (18.4%) of the control group, with a significant difference between the frequencies of the two groups \( p < 0.001 \). When we used the criterion of minimal obstruction of the choanae of 70%, it was observed that ATH occurred in 22 adolescents of the study group (45.8%) and in four (10.5%) of the control group, representing a significant difference between the frequencies of the two groups \( p < 0.001 \).

Table 1 indicates that there was an association between ATH and age in the study group, both when using the criterion of minimal obstruction of 50% \( (p = 0.001) \) and when the criterion used was 70% \( (p = 0.011) \), with the highest ATH frequency occurring among 12-year-old adolescents. On the other hand, there was no association between ATH and age in the control group, regardless of whether the obstruction criterion was 50% \( (p = 0.646) \) or 70% \( (p = 0.648) \).

### DISCUSSION

The results indicated that the groups were comparable, given that both of them had similar sex and age distribution. Primary follicles are already present in human tonsils around the 16th gestational week; however, the formation of germinal centres does not occur until birth, indicating the need of being exposed to antigens for their development. The proliferation of lymphoid tissue leads to the growth of the tonsil, which achieves its peak in the head and neck in patients with and without SCD. The authors used magnetic resonance imaging (MRI) to compare the dimensions of the lymphatic systems of the head and neck in patients with and without SCD.

Although the measurement scale was not the same as the one used in our study, a previous study found palatine tonsil hypertrophy in 55% of 53 patients with SCD, whose age ranged from 1.9 to 16.5 years [13]. A Brazilian study assessed children and adolescents with SCD, aged between two and 19 years, and found an ATH frequency of 55.3%. In this case, the criterion adopted for the diagnosis of ATH was the presence of palatine tonsils grade 3 or 4 according to Brodsky's criteria, as well as pharyngeal tonsil with an occlusion of at least 50% of the choanae [8]. Thus, the ATH frequency was very close to that observed in the present study, although the age range that we assessed was considerably more restrictive, given that only adolescents aged between 12 and 16 years were eligible for the study. The choice of this age group was due to the fact that the age of 12 years is the milestone for the involution of Waldeyer's ring [14], whereas the upper end of 16 years was adopted because the present research is part of a larger study using the Sleep Disturbance Scale for Children, which was originally validated for children and adolescents aged six to 16 years [15].

Regarding the degree of obstruction of the pharyngeal tonsil, some authors believe that it can be considered hypertrophic when occlusion of the choanae reaches 50% or over [8, 16]; whereas other authors use the threshold of 70% of obstruction for the diagnosis of adenoid hypertrophy [9]. Therefore, we chose to work with the thresholds of 50% and 70% of occlusion. As for palatine tonsil hypertrophy, there is a consensus in considering Brodsky's grades 3 and 4 as hypertrophic [7].

A study used magnetic resonance imaging (MRI) to compare the dimensions of the lymphatic systems of the head and neck in patients with and without SCD. The au-

### TABLE 1. Age distribution of patients with adenotonsillar hypertrophy, according to the criterion of minimal occlusion of the choanae of 50% and 70% in the study group and control group

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Study group minimal occlusion 50% n (%)</th>
<th>Control group minimal occlusion 50% n (%)</th>
<th>Study group minimal occlusion 70% n (%)</th>
<th>Control group minimal occlusion 70% n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>15 (53.6)</td>
<td>2 (28.5)</td>
<td>13 (59.1)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>13</td>
<td>2 (7.1)</td>
<td>3 (42.9)</td>
<td>2 (9.1)</td>
<td>2 (50)</td>
</tr>
<tr>
<td>14</td>
<td>6 (21.4)</td>
<td>1 (14.3)</td>
<td>4 (18.2)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>15</td>
<td>4 (14.3)</td>
<td>0 (0)</td>
<td>2 (9.1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>16</td>
<td>1 (3.6)</td>
<td>1 (14.3)</td>
<td>1 (4.5)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Total</td>
<td>28 (100)</td>
<td>7 (100)</td>
<td>22 (100)</td>
<td>4 (100)</td>
</tr>
</tbody>
</table>

\( p \)-value 0.001 0.646 0.011 0.648
authors observed that they were significantly increased in patients with SCD, including the palatine and pharyngeal tonsils [5]. However, the goal of the present study was to assess the association between SCD and obstructive ATH, and not only the relative increase of lymphoid tissues in patients with SCD.

The highest frequency of ATH observed in the present study occurred in 12-year-old adolescents with SCD, whereas in the control group there was no predominance of any age regarding ATH. However, given that our sample was of limited size, it was not possible to infer whether there would be a trend of tonsil involution in patients with SCD after that age.

A recent study conducted by the same group that performed the present study did not observe a significant increase in the prevalence of ATH among children with SCD, aged two to six years [17]. This fact makes it possible to speculate that the growth of the tonsils in patients with SCD can occur even after preschool age, which would be explained by immunological deficiency inherent to SCD. Some authors believe that this hypertrophy may occur due to self-splenectomy, which would also be in accordance with a higher incidence of ATH in adolescence than in infancy in patients with SCD [18, 19].

One limitation of the present study was that we did not assess the consequences of ATH in adolescents’ sleep, which was due to the difficulty in performing polysomnography in the service. It is known that ATH is the main cause of snoring and obstructive sleep apnoea syndrome in this age group, and that respiratory sleep disorders may aggravate the clinical picture of SCD [10]; however, one study has indicated that the effect of pharyngeal tonsil hypertrophy in obstructive sleep apnoea syndrome was significantly reduced in adolescents [20].

It is also possible that the use of topical and systemic corticosteroids may transiently affect the degree of naso-obstruction and even tonsillar dimensions [21, 22], although this hypothesis has been refuted by some authors [23]. Following the methodology of other studies [8, 17], we decided to consider only the use of systemic corticosteroids during the otorhinolaryngological evaluation period as an exclusion criterion, given that there was great difficulty in obtaining reliable information about the recent use of medications from parents and/or guardians, and there was no consensus in the medical literature regarding the duration of effects of various corticosteroids on the palatine and pharyngeal tonsils.

REFERENCES


CONCLUSIONS

In the present study, we found that ATH was associated with SCD in adolescents.

DISCLOSURE

The authors declare no conflict of interest.