Effects of Therapy With Semi-occluded Vocal Tract and Choir Training on Voice in Adult Individuals With Congenital, Isolated, Untreated Growth Hormone Deficiency


INTRODUCTION

Voice and stature are fundamental features for self-confidence and social acceptance, and both are affected by growth hormone (GH) deficiency (GHD). In Itabaianinha County, in Northeast Brazil, there is a large cohort (105 subjects in 7 generations, 71 alive) of individuals with isolated GHD (IGHD) caused by a homozygous null mutation (c.57 +1G > A) in the GH-releasing hormone receptor (GHRHR) gene (GHRHR OMIM n. 139191). These individuals exhibit very low serum levels of GH and of its principal effector, the insulin-like growth factor I (IGF-I), throughout the life. The rest of their pituitary function (including gonadal axis) is normal. The most striking findings of these individuals are the proportionate short stature, the doll faces, the high-pitched voice, reduced muscle mass, and the central obesity. Although the last feature may be caused by a direct consequence of the lack of GH, the others reflect the lack of the synergistic effect of pituitary GH and IGF-I on bones, muscles, and cartilage. We have previously shown that these subjects with IGHD present more vocal abuse and higher values for roughness, breathiness, strain, laryngopharyngeal reflux signs, and laryngeal constriction than normal counterparts. In addition, they have higher values of fundamental frequency (f0) and most formant frequencies, suggesting smaller oral and pharyngeal cavities. Very interesting, these individuals seem to cope better with their short stature than with their voice, as their overall quality of life is excellent, whereas their quality of life related to voice is reduced. In other words, having a different and bad voice creates more challenges to social life for these subjects with IGHD, than presenting a severe short stature in this particular rural environment in Northeast Brazil.

Because of the high prevalence of IGHD in this community and the lack of obvious harmful consequences beyond short stature, these individuals with IGHD and their parents do not have special interest in GH replacement therapy. They consider themselves “shrunken long-lived people,” not patients. They are well accepted by the community, living and often marrying normal statured people.

Summary: Objectives. Voice is produced by the vibration of the vocal folds expressed by its fundamental frequency (Hz), whereas the formants (F) are fundamental frequency multiples, indicating amplification zones of the vowels in the vocal tract. We have shown that lifetime isolated growth hormone deficiency (IGHD) causes high pitch voice, with higher values of most formant frequencies, maintaining a prepuberal acoustic prediction. The objectives of this work were to verify the effects of the therapy with a semi-occluded vocal tract (SOVTT) and choir training on voice in these subjects with IGHD. We speculated that acoustic vocal parameters can be improved by SOVTT or choir training.

Study Design. This is a prospective longitudinal study without control group.

Methods. Acoustic analysis of isolated vowels was performed in 17 adults with IGHD before and after SOVTT (pre-SOVTT and post-SOVTT) and after choir training (post training), in a 30-day period.

Results. The first formant was higher in post training compared with the pre-SOVTT (p = 0.009). The second formant was higher in post-SOVTT than in pre-SOVTT (p = 0.045). There was a trend of reduction in shimmer in post-choir training in comparison with pre-SOVTT (p = 0.051), and a reduction in post-choir training in comparison with post-SOVTT (p = 0.047).

Conclusions. SOVTT was relevant to the second formant, whereas choir training improved first formant and shimmer. Therefore, this speech therapy approach was able to improve acoustic parameters of the voice of individuals with congenital, untreated IGHD. This seems particularly important in a scenario in which few patients are submitted to growth hormone replacement therapy.

Key Words: Growth hormone–Voice formants–Acoustic–Voice training–Singing.
Therefore, we asked if muscle function, soft tissue accommodation, or mandible position could be changed by any kind of vocal therapy, thereby improving their voice and probably their related quality of life, without GH replacement therapy. It is well known that choral singing produces positive effects in several physiological, psychological, social, and cultural aspects. To motivate the participation of a significant number of subjects with IGHD in this rural, humble environment, we thought of coupling the pleasant choir training to a therapy with a semi-occluded vocal tract (SOVTT). This technique is often used to produce normal vocal intensity with less mechanical trauma to tissues in people who suffer from the effects of long hours of daily speaking, such as teachers. We decided to employ SOVTT, by using the LaxVox tube. Although a spoken voice is generally natural and unconscious, a sung voice may have more benefits from both SOVTT and choir training to produce adjustments for effortless voice use. The objectives of this work were to verify the effects of SOVTT and choir training on voice in these subjects with IGHD.

SUBJECTS AND METHODS
A prospective longitudinal study assessed the effects of SOVTT and training on voice in subjects with IGHD in three sessions: pre-SOVTT, post-SOVTT, and post-choir training. They were recruited by word of mouth and by an advertisement placed in the local dairies’ association building, located in Itabaianinha County. Inclusion criteria were Portuguese language native speakers homozygous for the GHRHR c.57 + 1G > A mutation and having received no previous GH treatment. Exclusion criteria were as follows: age <20 years and obvious mental or speech deficiencies. Seventeen of 33 individuals with IGHD previously enrolled by Valença et al. volunteered for this study. The protocol was performed in four weekly sessions for 30 days. A fifth session was done in the Christmas of 2016, with the coral gala presentation.

We analyzed the acoustic measures: the f0 (Hz), which corresponds to the number of vocal fold vibration cycles in 1 second; jitter (J, %), which indicates the variability of f0 in the short run; shimmer (S, dB), which measures the phonation stability and indicates the variability of sound wave amplitude in the short run; and harmonic-to-noise ratio (dB), which relates the harmonic component to the noise component of the sound wave. In addition, we studied the pattern of vowel formant (F) frequencies (Hz), which represent regions of which harmonics present in the sound source are amplified. First formant (F1) reflects the characteristics of the posterior cavity, pharynx, second formant (F2) to the anterior oral cavity, third formant (F3) to the cavities above the vocal folds and around the inferior incisors, and fourth formant (F4) to the laryngeal tube length.

To analyze the effect of SOVTT, the sustained emission of the vowel [e] was recorded in a single frequency as recommended for jitter and shimmer analysis in a quiet room with <40 dB of noise. After training, 3-second sustained vowel emission was studied, using comfortable conversational pitch and loudness levels (SM58 microphone; Shure Inc., Niles, IL) kept at fixed distance of 5 cm from the subject’s mouth. Samples were digitally recorded with the software Sound Forge 10.0 (Professional Audio Program Sony Creative Software Inc., Madison, WI) in format data (wav extension), 22,050 Hz sampling frequency, 16 bit, and stored for acoustic analysis by software PRAAT (version 5.3.51, Paul Boersma and David Weenink, Phonetic Sciences, University of Amsterdam, Amsterdam, The Netherlands), with semiautomatic extraction.

The SOVTT protocol was composed of voice phonation exercises in a silicone tube with 35 cm of length and 0.9 cm of diameter, (LaxVox) initially submerged by 2 cm in the water contained in the 500 mL bottle of mineral water (half of the space filled with water), with the following sequence in 5 minutes (each series repeated three times): (1) emission in tone and usual volume of the vowel [u] in the tube, producing bubbles; (2) vocalization of the vowel “u” in the tube, with performance of ascending and descending scales from the lowest to the highest pitch, keeping pitch range at a comfortable level so that no laryngeal or vocal tract tension would occur; and (3) vocalization of the vowel [u] in the tube, following the same type of water immersion in the melody “Parabens para você” (Happy Birthday), breathing between the phrases. Then, the same exercises were performed with the variation of the depth of the tube immersion in the water. The rationale is, the deeper the tube in the water, the higher the resistance, and the vocal production system becomes more conditioned.

Four rehearsals were conducted for choir training, taught by a qualified singing teacher (G.C.M.), with more than 15 years’ experience, and two songs were practiced. It was started with the model of the second voice (bass), followed by the first voice (acute), a sequence more adapted to the subjects with IGHD. A method adapted to the repertoire was used, considering the prepuberal vocal pattern of these subjects.

The Institutional Review Board of the Federal University of Sergipe approved the protocol, and written informed consent was obtained from all participants.

Statistics
The Kolmogorov-Smirnov test was used to verify the normal distribution of variables, expressed as mean (standard deviation), and non-normal distribution, expressed as median (interquartile range). Analysis of variance or Kruskal-Wallis test was used to analyze the three conditions (pre-SOVTT, post-SOVTT, and post-choir-training) with normal and non-normal distributions, respectively. Bonferroni posttest was used. Levene test for the equality of variances was also used. Multivariate analysis of covariance, with f0 and the formants as dependent variables and condition as covariable, was used to estimate the effect of the condition in those dependent variables. The statistical analysis was processed by the SPSS Statistics 17 (PC Inc. Program, Chicago, IL).

RESULTS
Ten of the 17 individuals with IGHD were women. Their age and height were 49.8 (13.7 years), range 26–73, and 124.2 (8.8) cm, range 108–137 cm, respectively. As we assessed the effects of SOVTT and training comparing these individuals with
themselves in three time points, we preferred to use, for this analysis, the data of pooled genders, instead of separating them, which would reduce the number of the sample.

Table 1 shows the analysis in the three studied conditions, before and after SOVTT (pre-SOVTT and post-SOVTT, respectively), and post choir training of the \( f_0 \), the formants \( F_1 \), \( F_2 \), \( F_3 \), and \( F_4 \) (Hz), jitter (%), shimmer (dB), and harmonic-to-noise ratio (dB). There was significant difference in \( F_1 \) (\( P = 0.011 \)), \( F_2 \) (\( P = 0.049 \)), and shimmer (\( P = 0.022 \)). Table 2 shows the multiple comparisons (Bonferroni post hoc test) to the variables with significant differences among the conditions. \( F_1 \) was higher in post-choir training than in pre-SOVTT (\( P = 0.009 \)). \( F_2 \) was higher in post-SOVTT than in pre-SOVTT (\( P = 0.045 \)). There was a trend of reduction in shimmer in post-choir training in comparison with pre-SOVTT (\( P = 0.051 \)), and a reduction in post-choir training in comparison with post-SOVTT (\( P = 0.047 \)).

There was no difference in jitter among the three conditions. Levene test for the equality of variances shows that their variances (not the means) were lower in both post-SOVTT (\( P = 0.043 \)) and post-training (\( P = 0.028 \)) in comparison with pre-SOVTT. Multivariate analysis of covariance revealed that \( F_1 \) differs between pre-SOVTT and post-choir training (\( P = 0.011 \)), with an effect of 0.202, partial eta squared, and observed power of 0.790; and \( F_2 \) differs between pre-SOVTT and post-SOVTT (\( P = 0.018 \), with an effect of 0.830 partial eta squared and observed power of 0.734).

### Table 1

**Analysis in the Three Studied Conditions, Before and After SOVTT (pre-SOVTT and post-SOVTT, Respectively) and Post-choir Training**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-SOVTT</th>
<th>Post-SOVTT</th>
<th>Post-choir Training</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( f_0 )</td>
<td>196.91 (39.46)</td>
<td>173.39 (33.39)</td>
<td>193.3 (36.58)</td>
<td>0.143</td>
</tr>
<tr>
<td>( F_1 )</td>
<td>610.13 (73.90)</td>
<td>657.88 (65.20)</td>
<td>698.61 (102.41)</td>
<td><strong>0.011</strong></td>
</tr>
<tr>
<td>( F_2 )</td>
<td>2025.97 (449.26)</td>
<td>2404.71 (375.69)</td>
<td>2239.14 (479.52)</td>
<td><strong>0.049</strong></td>
</tr>
<tr>
<td>( F_3 )</td>
<td>3547.07 (290.22)</td>
<td>3299.16 (349.54)</td>
<td>3254.61 (424.55)</td>
<td>0.207</td>
</tr>
<tr>
<td>( F_4 )</td>
<td>4093.69 (374.58)</td>
<td>4262.05 (449.04)</td>
<td>4819.06 (408.48)</td>
<td>0.392</td>
</tr>
<tr>
<td>Shimmer</td>
<td>0.29 (0.14)</td>
<td>0.29 (0.12)</td>
<td>0.186 (0.09)</td>
<td><strong>0.022</strong></td>
</tr>
<tr>
<td>Jitter</td>
<td>0.29 (0.29)</td>
<td>0.27 (0.29)</td>
<td>0.201 (0.15)</td>
<td>0.313</td>
</tr>
<tr>
<td>HNR</td>
<td>18.28 (8.32)</td>
<td>18.64 (7.17)</td>
<td>20.14 (4.06)</td>
<td>0.521</td>
</tr>
</tbody>
</table>

One-way ANOVA for fundamental frequency (\( f_0 \)), formants \( F_1 \), \( F_2 \), \( F_3 \), and \( F_4 \) (Hz) and shimmer (dB) expressed in mean (standard deviation) and Kruskal-Wallis H test for jitter (%) and harmonic-to-noise ratio (HNR) (dB) expressed in median (interquartile range). Abbreviation: SOVTT, voice therapy with a semi-occluded vocal tract. Significant differences are shown in bold.

### Table 2

**Multiple Comparisons (Bonferroni Post Hoc Test) With the Variables With Significant Differences Between the Conditions, Before and After SOVTT (pre-SOVTT and post-SOVTT, Respectively) and Post Choir Training**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Conditions</th>
<th>Difference</th>
<th>Standard Error</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( f_0 )</td>
<td>Pre-SOVTT</td>
<td>Post-SOVTT</td>
<td>23.52353</td>
<td>12.54141</td>
</tr>
<tr>
<td>Post-choir training</td>
<td>3.88235</td>
<td>12.54141</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>( F_1 )</td>
<td>Post-SOVTT</td>
<td>Post-choir training</td>
<td>–19.64118</td>
<td>12.54141</td>
</tr>
<tr>
<td>Pre-SOVTT</td>
<td>–47.74928</td>
<td>28.14594</td>
<td>0.289</td>
<td></td>
</tr>
<tr>
<td>Post-choir training</td>
<td>–88.47439</td>
<td>28.14594</td>
<td><strong>0.009</strong></td>
<td></td>
</tr>
<tr>
<td>( F_2 )</td>
<td>Post-SOVTT</td>
<td>Post-choir training</td>
<td>–40.72511</td>
<td>28.14594</td>
</tr>
<tr>
<td>Pre-SOVTT</td>
<td>–378.74483</td>
<td>149.89203</td>
<td><strong>0.045</strong></td>
<td></td>
</tr>
<tr>
<td>Post-choir training</td>
<td>–213.17218</td>
<td>149.89203</td>
<td>0.484</td>
<td></td>
</tr>
<tr>
<td>( F_3 )</td>
<td>Post-SOVTT</td>
<td>Post-choir training</td>
<td>165.57265</td>
<td>149.89203</td>
</tr>
<tr>
<td>Pre-SOVTT</td>
<td>–210.74564</td>
<td>123.13695</td>
<td>0.280</td>
<td></td>
</tr>
<tr>
<td>Post-choir training</td>
<td>–166.20298</td>
<td>123.13695</td>
<td>0.550</td>
<td></td>
</tr>
<tr>
<td>( F_4 )</td>
<td>Post-SOVTT</td>
<td>Post-choir training</td>
<td>44.54266</td>
<td>123.13695</td>
</tr>
<tr>
<td>Pre-SOVTT</td>
<td>–168.35447</td>
<td>141.25475</td>
<td>0.718</td>
<td></td>
</tr>
<tr>
<td>Post-choir training</td>
<td>–169.94129</td>
<td>141.25475</td>
<td>0.705</td>
<td></td>
</tr>
<tr>
<td>Shimmer</td>
<td>Pre-SOVTT</td>
<td>Post-SOVTT</td>
<td>–1.58682</td>
<td>141.25475</td>
</tr>
<tr>
<td>Post-choir training</td>
<td>–0.001294</td>
<td>0.042073</td>
<td><strong>0.051</strong></td>
<td></td>
</tr>
<tr>
<td>Post-SOVTT</td>
<td>0.10535</td>
<td>0.042073</td>
<td><strong>0.047</strong></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: SOVTT, voice therapy with a semi-occluded vocal tract. Significant differences are shown in bold.
DISCUSSION

The GH/IGF-I axis may influence several aspects of voice, namely the power source (lungs), the sound source (vocal folds), and the sound modifiers (vocal tract). Indeed, we have previously shown that adults with lifetime untreated IGHD from the Itabaianinha kindred present more vocal abuse and higher values for roughness, breathiness, strain, laryngopharyngeal reflux signs, and laryngeal constriction than normal counterparts. In addition, their high values of fundamental frequency and formants suggest smaller oral and pharyngeal cavities. The voice of subjects with IGHD reflects structural features in hard (bones) and soft tissues (muscles), reflecting peculiar effect of GH or IGF-I deficiency in these tissues. For instance, the doll facies result from a less accentuated reduction of the cephalic perimeter than of the facial height, causing a disproportionate between the calvarium and the face, and the reduction of the maxillary length is similar to the stature. The reduction of the muscle mass may interfere with the power and the sound source. Therefore, we asked if SOVTT and choir training could change muscle function, soft tissue accommodation, or mandible position in these subjects with IGHD.

The principal findings of the present paper were the increase of F1 in post-choir training compared with the pre-SOVTT and of F2 in post-SOVTT in comparison with pre-SOVTT. In addition, there was a trend of reduction in shimmer in post-choir training in comparison with pre-SOVTT, and a reduction in post-choir training in comparison with post-SOVTT. Although changes in a particular area of the vocal tract can impact multiple formants, we will discuss our personnel interpretation of these changes, and thereafter the shimmer data.

Although F0 is dependent of the cephalic perimeter; formants depend on size and shape of the vocal tract and its constrictions, tongue, and lip position. The net effect of SOVTT was the increase of F2, whereas the effect in F1 may combine effects of SOVTT and choir training. F2 reflects the shape of anterior oral cavity and the horizontal tongue displacement. F1 is influenced by the shape of the posterior cavity, mandibular opening, and vertical displacement of the tongue. It is possible that the anterior oral cavity (soft tissue) is more sensitive to SOVTT than the posterior cavity (soft and hard tissue represented by the mandibular opening) and that the latter requires a combination of SOVTT and choir training to achieve better muscular fitness and new positioning of the jaw. Accordingly, orthognathic surgery promotes functional changes in the resonating system, leading to the need for further speech and voice adjustments.

Choir training was particularly relevant to the shimmer reduction. Shimmer changes with the reduction of glottal resistance and mass lesions on the vocal cords, and is correlated with the presence of noise emission and breathiness. Subjects with IGHD have higher values for roughness, breathiness, and strain and signs of laryngeal constriction. We speculate that the shimmer reduction indicates an improvement in these parameters, resulting in a voice with less effort.

We did not find difference in jitter in our protocol, but that their variances (not the means) were lower in both post-SOVTT and post-training than in pre-SOVTT. Jitter is affected mainly by the lack of control of vibration of the vocal cords, and consequently the voices of subjects with pathologies often have a higher percentage of jitter. We wonder if the reduced variance in both post-SOVTT and post-choir training may reflect more homogeneity of their voices, even without a significant effect of both approaches in this measure.

SOVTT is beneficial for voice therapy because it heightens the interaction between the source and the filter. Such interaction can increase vocal intensity, efficiency, and economy. Several results may be obtained; change in vocal folds shape, contraction of the thyroarytenoid muscle, and adjustments in the epilaryngeal tube shape, glottis, and oral cavity. Which of these mechanisms is involved in the improvement of the voice in the IGHD subjects is presently unknown.

The increase of F1 and reduction in shimmer in our subjects with IGHD suggest positive effects of choir training, thereby improving the conscious control of the physiological use of one’s own voice and the degree of strain. Singing activities, in normal volunteers, have been found to improve the respiratory support, the adjustment of the sound source, and the configurations of the vocal tract (sound modifiers).

The increase of F2 and reduction of shimmer in adult subjects with IGHD is also reported in dysphonic teachers and in singers without vocal complaint, probably because of the improvement in the folds’ vocal adduction, by the action of the cricothyroid muscle, increasing intraoral pressure. Although it is difficult in our approach to identify specific changes because of choir training and SOVTT, this later speech therapy technique is each more used in patients with neurologic disorders such as Parkinson disease, hyper- or hypofunctional dysphonia, chronic laryngitis, or vocal nodules, reducing the effort and vocal fatigue. Now, we included an unpublished indication. SOVTT coupled with choir training improved acoustic analysis of a typical high-pitched voice of subjects with congenital untreated isolated GHD.

Our work has some limitations. First, the relatively short period in which SOVTT and choir training were administered. Second, the absence of a control group. Third, an eventual warm-up effect cannot be definitively eliminated in our protocol. Finally, although F2 effects seem to be ascertained to SOVTT and shimmer effects to choir training, respectively, the other changes can combine effect of the two approaches. Ongoing studies are analyzing these topics. Nevertheless, this is the first report of SOVTT and voice training in adult subjects untreated for IGHD. This double approach improved one of the most impressive phenotypic features of these individuals, their high-pitched voice, without need of GH replacement therapy.

CONCLUSIONS

A speech therapy approach using SOVTT and choir training for 30 days was able to improve acoustic parameters of the voice of adult individuals with severe, untreated IGHD.

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REFERENCES


