Improved somatic growth following adenoidectomy and tonsillectomy in young children. Possible pathogenetic mechanisms

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ABSTRACT
The effect of Adenotonsillectomy on somatic growth was studied prospectively in 57, randomly selected children (31 boys, 26 girls), aged 5.03±1.32 (mean±1SD) years. The indication for surgery was adenotonsillar hypertrophy with or without recurrent infections. Weight, height, triceps skinfold thickness, and Body Mass Index were measured prior to the operation and 6-13 months afterwards. Weight was significantly improved following T&A in all children. The improvement in height was significant only for children under 5 years. In an attempt to uncover the pathogenetic mechanisms, lactic acid, pyruvic acid, somatomedin-C (IGF-I), growth hormone (GH), insulin, glucose, pH, hemoglobin (Hb), and white cell count (WBC) were also determined in the last 18 children, prior to and 6-8 months post operatively. For the comparison of pre and post operative values the paired t test was applied. Although the values of GH and IGF1 did not significantly increase post-op the IGF-1/GH ratio increased, possibly indicating improved IGF1 generation. There was also a rise in Hb values and a lowering of WBC, probably reflecting the lower frequency of infections. All other metabolic indices did not change. In conclusion, linear grow post-Adenotonsillectomy improved in children aged <5 years and was associated with improved IGF-1/GH ratio, increased Hb values and decreased in WBC.

Keywords: Growth retardation, Adenotonsillectomy, Growth hormone, IGF1

INTRODUCTION
The major indications for adenotonsillectomy (T&A) have remained the same for many years and include, recurrent pharyngotonsillitis and its complications, excisional biopsy, management of chronic ear disease, and chronic upper respiratory obstruction.¹⁻⁵ Currently, the most frequent indication for T&A is upper airway obstruction due to hypertrophy of the tonsils and adenoids.⁵ Chronic upper airway obstruction can lead to obstructive sleep apnea syndrome (OSAS) with chronic alveolar hypoventilation, cor pulmonale, cardiac failure⁶⁻¹⁵ sleep disor-
ders,16-19 behavioral changes, learning disability, enuresis, and retarded growth.1,8,14,20-23 Published data on the influence of T&A on somatic growth refer to case reports,24-27 or include small number of patients,6-8,28 younger than 3 years, primarily affected by OSAS. In these studies, most of the children were underweighted pre-operatively (pre-op), and presented “catch-up” growth after T&A. Other trials29,23 looked retrospectively to the improvement of somatic growth. A small number of prospective studies, have been published in which, OSAS was mainly correlated to changes in growth post-op. Results concerning the influence of recurrent tonsillitis on somatic growth are controversial.20,30,31 There are reports28,8 which show that only tonsillectomy had a positive influence on somatic growth post-operatively (post-op), while others found that adenoidectomy is as effective as tonsillectomy or T&A. The pathogenetic mechanism involved have not been elucidated. In the present study the influence of T&A on height and weight was studied prospectively in children aged 5.03–1.32 years, who were operated upon for various indications. An attempt was also made to look into pathogenetic mechanism responsible for the alteration in growth pattern, following T&A.

PATIENT SELECTION AND METHODS

Fifty seven children, 31 boys (54.3%) and 26 girls (45.6%) were studied. The age of the patients at entrance to the study was 5.03±1.32 years, who were operated upon for various indications. An attempt was also made to look into pathogenetic mechanism responsible for the alteration in growth pattern, following T&A.

The weight, height, and triceps skinfold thickness were measured the day prior to surgery, between 9-10 am and the body mass index was estimated using the formula: weight (kg)/height (m).2 The measurements were carried out by the same person, following an identical procedure, i.e. the children were weighted in their indoor clothing and without shoes, using a stable balance. The height was measured as length up to the age of five years (lying down) and as height (upright position) past the age of 5 yrs, using the Harpenden stadiometer. The triceps skinfold thickness was measured using the Holtain skinfold caliper. Six to thirteen months after operation, the children were once again measured following the same protocol. For the statistical analysis the paired t test was applied. For the auxologic data the standardized weight and height (z scores) and their percentiles were used while for the other parameters the actual values were used.

In the last 18 children of this series the following parameters were additionally determined: lactic acid (Monotest Boehringer), pyruvic acid (Combination test Boehringer), somatomedin-C/IGF-I (Radioimmunoassay-RIA, Nichol’s reagents), growth hormone (RIA), glucose (glucose oxidase), insulin (RIA), pH (venous blood), haemoglobin (Hb), and white cell count (WCC) by routine methodology, prior to the operation and 6-8 months post operatively.

Parents were asked to report on changes in the activity, the appetite and frequency of infection of their children following the operation.

RESULTS

Weight (Table I)

The weight standardized value (z score) for the total group significantly increased following the operation (pre-op value 0.2481±1.26, post-op value 0.8793±1.43, p=0.0001) and the mean percentile value also increased form the 54th percentile, to the 68th (p=0.0001). No difference was observed in these changes between boys and girls.

There was also no difference in the changes observed whether the pre-op weight was above or below the 50th percentile.
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of five, while for the group of children over five (28 children), no significant changes in either standardized value, or percentile were observed (p=0.2019, 0.133 respectively). Boys grew somewhat better than girls (Table II).

There was no difference in the changes observed whether the pre-op height was above or below the 50th percentile.

The changes observed according to the type of operation were as follows: Significant increase for those who underwent T&A and A (p<0.001 for both), but not, for those who underwent T (p>0.1). In the latter however, as we mentioned before, the sample was small (5 children).

**Skinfold thickness (SFT)**

The SFT also increased significantly post-op (mean pre-op and post-op values 10.6±3.3mm and 11.4±3.7mm, respectively p<0.01).

Body Mass Index (BMI) values increased from a pre-op value of 15.85±1.7 to 16.7±2.1 post-op (p<0.001).

**Hormonal and other hematologic parameters**

Concerning the search for pathogenetic mechanisms the following changes between pre-op and post-op values were observed (Table III): IGF-I form 0.69±0.3 to 0.91±0.7, growth hormone form 4.1±4.5 to 2.1±3.7, lactic acid from 17.69±5.04 to 20.07±7.14, pyruvic acid from 0.37±0.18 to

### Table I. Pre, and post-op mean values for body Weight expressed in z scores and percentiles

<table>
<thead>
<tr>
<th></th>
<th>All children</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Pre-op</td>
<td>Post-op</td>
<td>p</td>
</tr>
<tr>
<td>Percentile</td>
<td>57</td>
<td>54.3</td>
<td>67.9</td>
</tr>
<tr>
<td>z score</td>
<td>57</td>
<td>0.2481</td>
<td>0.8793</td>
</tr>
</tbody>
</table>

### Table II. Pre, and post-op mean values for Height expressed as z scores and percentiles

<table>
<thead>
<tr>
<th></th>
<th>All children</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Pre-op</td>
<td>Post-op</td>
<td>p</td>
</tr>
<tr>
<td>Percentile</td>
<td>57</td>
<td>65.1</td>
<td>69.6</td>
</tr>
<tr>
<td>z score</td>
<td>57</td>
<td>0.4994</td>
<td>0.6578</td>
</tr>
</tbody>
</table>

### Table III. Pre, and post-op mean values for the hormonal and other hematological parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>n</th>
<th>Pre-op</th>
<th>Post-op</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGF-I (IU/L)</td>
<td>18</td>
<td>0.69±0.3</td>
<td>0.91±0.7</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>G.H. (mg/ml)</td>
<td>18</td>
<td>4.1±4.5</td>
<td>2.1±3.7</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>IGF1/GH</td>
<td>18</td>
<td>0.56±0.54</td>
<td>1.38±1.53</td>
<td>P&lt;0.025</td>
</tr>
<tr>
<td>Lactic acid (mg/dl)</td>
<td>17</td>
<td>17.6±5</td>
<td>20.0±5</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Pyruvic acid (m/dl)</td>
<td>17</td>
<td>0.37±0.18</td>
<td>0.38±0.2</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>18</td>
<td>91.2±1.5</td>
<td>98.7±17</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Insulin (µU/mg)</td>
<td>18</td>
<td>14.6±12.7</td>
<td>18.3±15.3</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>pH (venous)</td>
<td>16</td>
<td>7.33</td>
<td>7.33</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Hb (gr/dl)</td>
<td>18</td>
<td>12.2±0.8</td>
<td>12.6±0.95</td>
<td>0.037</td>
</tr>
<tr>
<td>White cell count</td>
<td>18</td>
<td>11558</td>
<td>9036</td>
<td>0.005</td>
</tr>
</tbody>
</table>
0.38±0.2, glucose from 91.2±15.6 to 98.7±17.1, in-
sulin from 14.6±12.7 to 18.3±15.03 and pH didn’t
change (7.33). The above changes were not statisti-
cally significant. The ratio IGF1/GH increased from
a pre-op value of 0.56±0.54 to 1.38±1.53 post-op
(p<0.025).

A significant difference was found between pre-
op and post-op values of hemoglobin (pre-op
12.2±0.87 and post-op 12.6±0.95, p=0.037) and
white cell count (WBC) (11558.3±3295.5 pre-op,
and 9036.6±2812.3 post-op, p=0.005).

According to the parent’s opinion the majority
of the children had a better appetite and activity 6-
13 months after the operation and, reportedly, less
frequent infections post-op.

**DISCUSSION**

In this prospective study, somatic growth, as re-
lected in height, weight, BMI and skinfold thick-
ness, were significantly increased after T&A in the
total group. The improvement in height (z score)
was highly significant only in children under five
years, irrespective of the indication for surgery, and
the pre-op z score. The underlying mechanisms for
this improvement are not known. In the present
study, parameters related to impaired oxygenation
(lactic acid), growth (IGF1, GH) and infection (H\(\beta\)
and WBC) were evaluated in an attempt to clarify
the pathogenetic mechanisms involved.

Growth hormone (GH) is released in pulsatile
fashion during a 24 hours period, mainly during
sleep\(^3^2\) but the highest GH\(^3^3\) values are associated
with the onset of slow wave sleep (SWS). It has been
shown that sleep disturbances and specifically a de-
crease in the amount of SWS occur in children with
adenotonsillar hypertrophy. This effect is expected
to decrease sleep associated GH secretion. The ef-
fect of GH on skeletal growth appear to be mediated
through the somatomedins. The somatomedins
or IGF factors are a family of insulin like peptide
growth factors modulated by insulin and nutrition
as well as by GH. Deficient growth in the presence
of adequate GH secretion could occur because of
decreased somatomedin generation, increased so-
matomedin inhibitors, or changes in the responsive-
ness of the target organ. In children who do not have
GH deficiency, the presence of low somatomedin
levels would suggest nutritional insufficiency, chronic
illness or genetically impaired IGF1 generation.\(^3^4\)

Based on the above data we measured values of
GH, IGF-1 and other parameters, possibly related
to impaired growth. The values of GH IGF1, insu-
lin and glucose did not statistically change post-op,
whereas the IGF1/GH ratio significantly increased.
With regard to GH, only single values in the morn-
ing were measured. A 24-hour integrated concen-
tration of GH or provocative testing would have
been more informative than basal values\(^3^3,3^5\) since it
is quite possible that GH secretion pattern during
sleep could be decreased pre-op. For obvious rea-
sons, however, such an experimental design could
not be materialized.

Other investigators have also attempted to in-
terpret the increase in growth post T&A. Thus,
Marcus et al\(^3^6\) attributed the growth improvement
post T&A to the lowering of energy expenditure
which they observed, during sleep, post-op.

Bar et al\(^3^7\) found that IGF1 values but not IG-
FBP3 increased post T&A in association with pro-
longation of slow wave sleep period. They infer that
GH was increased post-op, but actual values of GH
were not determined.

In another study, higher values of IGF1 and IG-
FBP3 were found.\(^3^8\) Based on these findings, the au-
thors speculated that the GH values had improved.
Two other studies also found higher IGF1 and IG-
FBP3 values post T&A.\(^3^9,4^0\)

In our study, besides IGF1, GH values were also
determined in 18 subjects, under basal conditions.
Contrary to expectations, the basal GH values tend-
ed to be higher pre-op although not statistically sig-
nificant. As mentioned previously, basal GH values
do not adequately reflect sleep associated or 24 hour
GH secretion. Nevertheless, the data are not in fa-
vor of lower GH values pre-op. It is quite interest-
ing and provocative that the IGF1 to GH ratio was
higher post-op suggesting an improvement in IGF1
generation by GH. This phenomenon is not unex-
pected, as it may be encountered in other situations
of growth inhibition in which inflammatory respons-
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es predominate. In such cases, GH may be normal, whereas IGF1 levels are low. Supporting evidence for such a phenomenon is derived from the information that infections were less frequent, the Hβ values were higher and the WBC was lower post T&A. Moreover, in another study IL-1beta and IL6 values were significantly lower post T&A. An increase in Hβ values post T&A was also detected by Elverland et al.

In conclusion, body weight improved in all children post-op. Height was improved only in children under the age of five. For the latter observation two explanations can be offered. The “catch-up” growth in children over five had already occurred, because the organism itself managed to overcome the pathological condition (escape phenomenon) or “catch-up” growth is not possible if the abnoxious factors are not removed early in life. Growth was improved post-op, irrespective of the pre-op percentile for weight and height. Gender was not an important factor. A significant difference in the IGF1/GH ratio was detected post-op possibly indicating improved IGF1 generation. Among the possible pathogenetic mechanisms involved, as emerged from our study, was an impairment in IGF1 generation possibly as a result of better nutrition and or decrease in the frequency of infections.

REFERENCES

25. Everett AD, Koch WC, Saulsbury FT, 1987 Failure to


