Endocrine and reproductive outcome of men born with various degrees of hypospadias


Key messages
- 20% of hypospadias cases have reduced semen quality
- No difference in testosterone and LH levels was found between hypospadias cases and controls
- FSH and Inhibin B levels are not very reliable in predicting low sperm counts

INTRODUCTION

Background: Limited, small-scale studies have revealed that men with proximal hypospadias or with other signs of undermasculinisation (i.e. complex hypospadias) are at risk of reduced fertility and/or impaired testicular hormone synthesis. However, the extent of this phenomenon and if milder forms of isolated hypospadias are also affected, remains unclear.

Aims: To explore reproductive hormones and semen quality of young men (16-21 years old) born with all forms of non-syndromic hypospadias in comparison to healthy controls.

METHODOLOGY

Design: Cross-sectional assessment
Centers: Ghent University Hospital and Wien Medical University
Tests: Blood sampling between 8:00 and 9:00 AM for total and free testosterone, LH, FSH and Inhibin B. Spermiogram on two independent semen samples, according to the WHO 2010 criteria.
Statistics: IBM SPSS® 25.0 using an unpaired Student t-test or Mann Whitney-U test as appropriate.

PARTICIPANTS

<table>
<thead>
<tr>
<th>Hypospadias</th>
<th>N= 192</th>
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</thead>
<tbody>
<tr>
<td>Distal</td>
<td>132/192 (68,8%)</td>
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<tr>
<td>Midshaft</td>
<td>37/192 (19,3%)</td>
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<tr>
<td>Proximal</td>
<td>23/192 (12,0%)</td>
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<tr>
<td>Complex</td>
<td>20/192 (10,4%)</td>
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<tr>
<td>Controls</td>
<td>N=50</td>
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</tbody>
</table>

RESULTS

Spermiograms

Samples:
- Two semen samples: 83,9% and 93,8% of cases and controls, respectively

Results:
- Azoospermia in 7 (4,1%) cases
- Oligozoospermia in 25 (14,7%) cases and 2 (4%) controls
- Normal spermiogram: 86/170 (50,6%) cases; 30/50 (60%) controls
- In controls, mild astheno- and teratozoospermia were the most common causes of abnormalities

Androgens:
- Free / total testosterone & DHT levels
  - No differences:
    - Proximal / Distal / Controls
    - Complex / Isolated / Controls

Sertoli cell function:
- Higher FSH levels in complex hypospadias
- Isolated hypospadias (p<0,011); Controls (p=0,005)
- Lower inhibin B levels in complex hypospadias
- Isolated hypospadias (p=0,001); Controls (p=0,008)
- Both FSH and LH were poor predictors of oligo/azoospermia

CONCLUSION

In our cohort, over 20% of men born with hypospadias have reduced semen quality. Over 40% of complex and proximal hypospadias have oligo-/azoospermia as compared to 11,9% and 15,8% of distal and isolated hypospadias, respectively. There is no difference in testosterone or LH levels between hypospadias cases and controls. FSH and Inhibin B levels are not always predictive of a low sperm count.

Funding

European Society for Paediatric Endocrinology

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