Abstract

In infants and children, follicle stimulating hormone (FSH) concentrations rise shortly after birth and then fall to very low concentrations by 6 months in boys and 1 to 2 years in girls. Later, concentrations begin to rise again before the beginning of puberty and the development of secondary sexual characteristics. FSH and luteinizing hormone are used to diagnose delayed or precocious puberty in children. Measurement of FSH is also used to evaluate pituitary function and aid in diagnosis of pituitary or hypothalamic disorders. A pediatric reference interval study was conducted for FSH using the Roche Diagnostics Modular E170 analyzer. Subjects undergoing elective surgical procedures were assessed for enrollment by a Physician Assistant prior to the administration of general anesthesia. Blood was collected into serum separator tubes allowed to clot for 30 minutes at room temperature, and centrifuged. Aliquots were stored in liquid nitrogen prior to testing. An aliquot was thawed, mixed, and centrifuged prior to analysis. The results were analyzed and partitioned by age and gender. When no statistically significant differences were observed, gender and/or age groups were combined. The proposed reference intervals are summarized in Table 1. Significant differences were observed between males and females. For females, there was a significant difference observed between the age groups 6 months to 2 years, 3 to 4 years and 5 to 6 years. No significant difference was observed between age groups for males, therefore all male subjects were combined to establish the reference interval. Reference intervals for FSH should be gender-specific throughout life. Establishment of pediatric reference intervals for FSH should be useful in evaluating pituitary function and aid in diagnosis of pituitary or hypothalamic disorders. In infants and children, FSH concentrations rise shortly after birth and then fall to very low concentrations by 6 months in boys and 1 to 2 years in girls. Later, concentrations begin to rise again before the beginning of puberty and the development of secondary sexual characteristics. Gender differences in reference intervals have been observed from infancy to adulthood. Reference intervals established for FSH, LH, prolactin, TSH, T4, T3, free T4, free T3, T-uptake, IgE, and ferritin. Clin Biochem 1995; 28:150-62.

Introduction

Follicle stimulating hormone (FSH) is a gonadotropin that is secreted by the gonadotropic cells of the anterior pituitary gland. It is regulated by estrogens and inhibin in the female and testosterone and inhibin in the male. Primary functions include regulation of sexual development and reproductive function. FSH and luteinizing hormone are used to diagnose delayed or precocious puberty in children. Measurement of FSH is also used to evaluate pituitary function and aid in diagnosis of pituitary or hypothalamic disorders. In infants and children, FSH concentrations rise shortly after birth and then fall to very low concentrations by 6 months in boys and 1 to 2 years in girls. Later, concentrations begin to rise again before the beginning of puberty and the development of secondary sexual characteristics. Gender differences in reference intervals have been observed from infancy to adulthood. Reference intervals established for prepubertal females are higher than those in prepubertal males. Mean concentrations of FSH have shown to increase significantly in both boys and girls with each stage of puberty. In infants and children, concentrations of FSH have shown to increase significantly in both boys and girls with each stage of puberty. In addition, results from different immunoassay systems have been reported to differ by more than 50%, even when calibrated with the same reference preparation. Therefore, it is necessary to evaluate reference intervals for FSH by gender and method.

Table 1. Pediatric reference interval summary for FSH.

<table>
<thead>
<tr>
<th>Gender(s) Age Range</th>
<th>N</th>
<th>Lower Limit</th>
<th>90% CE</th>
<th>Median</th>
<th>Upper Limit</th>
<th>90% CE</th>
</tr>
</thead>
<tbody>
<tr>
<td>F 6 months-2 year</td>
<td>100</td>
<td>1.4</td>
<td>1.0-1.8</td>
<td>2.3</td>
<td>2.0</td>
<td>1.7-2.4</td>
</tr>
<tr>
<td>F 3-4 years</td>
<td>124</td>
<td>0.6</td>
<td>0.4-1.0</td>
<td>2.1</td>
<td>2.0</td>
<td>1.5-2.6</td>
</tr>
<tr>
<td>F 5-6 years</td>
<td>123</td>
<td>0.5</td>
<td>0.3-0.6</td>
<td>3.5</td>
<td>3.2</td>
<td>2.9-3.4</td>
</tr>
<tr>
<td>M 6 months-6 year</td>
<td>448</td>
<td>0.3</td>
<td>0.2-0.3</td>
<td>7.0</td>
<td>6.2</td>
<td>5.7-6.6</td>
</tr>
</tbody>
</table>

No significant differences were observed for males 6 months to 6 years, therefore all male subjects were combined.

Materials and Methods

• Testing for FSH was performed on the Roche Modular Analytics E170.
• Subjects were assessed for enrollment by a Physician Assistant prior to undergoing elective surgical procedures. Eligible subjects were enrolled after obtaining parental permission.
• Subjects were excluded for known medical conditions, medication use, or if the parent did not provide consent.
• Approval for use of specimens from human subjects was obtained from the University of Utah Institutional Review Board (Salt Lake City, UT).
• The study included 407 females and 446 males from 6 months through 6 years of age who were nearly all Caucasian.
• Blood was collected from fasting subjects through an intravenous catheter by the anesthesiologist prior to the administration of general anesthesia. Blood was transferred into three 4 mL serum separator vacutainers (Becton Dickinson) and allowed to clot at room temperature for 30 minutes then centrifuged at 480g for 3 minutes. Samples were refrigerated for a maximum of 5 hours before being separated into aliquots and stored in liquid nitrogen (<-180°C).
• Prior to testing, an aliquot was thawed, mixed, centrifuged at 2090g for 5 minutes, and analyzed by the E170.
• Non-parametric reference intervals were established using EP Evulator Release 8 software (Olim Innovations). The results were analyzed and partitioned by age and gender. When no statistically significant differences were observed, age groups were combined.

Results and Conclusions

• The proposed reference intervals are summarized in Table 1.
• Significant differences were observed between females and males.
• For females, there was a significant difference observed between the age groups 6 months to 2 years, 3 to 4 years, and 5 to 6 years.
• No significant differences were observed for males 6 months to 6 years, therefore all male subjects were combined.
• Reference intervals for FSH should be gender-specific throughout life.

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References


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