EVALUATING THE DIAGNOSTIC VALUE OF BASAL LUTEINISING HORMONE AND LHRH TEST IN PREDICTING PROGRESSION INTO PRECOCIOUS PUBERTY IN GIRLS

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Introduction

Central precocious puberty (CPP) in girls:

- considered the onset of true puberty before 6-8 years of age
- current gold standard for diagnosis is luteinising hormone-releasing hormone (LHRH) testing

There is an absence of clear established diagnostic cut offs.[1]

Current recommendations for CPP:

- LHRH test: positive for puberty if stimulated LH >5.0 IU/L[2]
- Basal LH: pubertal progression if >0.3 IU/L[2]

Objectives and hypothesis

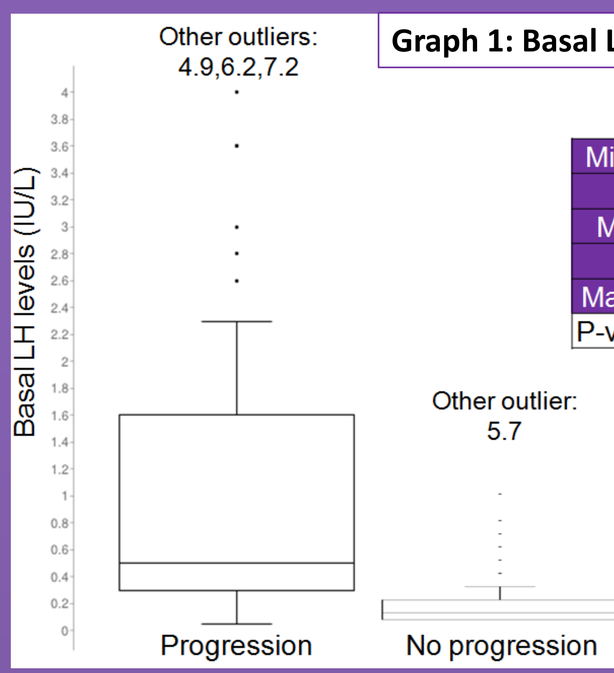
1) Test efficacy of using basal gonadotropin levels for predicting CPP in girls
2) Establish diagnostic cut-offs for LHRH tests for CPP in girls

Method

- Retrospective data collection of LHRH test results from a regional paediatric centre between 1st January 2005 to 31st December 2013
- 172 girls: aged 2 to 10 years old
- Measure of progression into puberty was based on clinician's judgment following LHRH testing
  - 56 girls in progression group
  - 116 girls in non-progression group
- Compare differences between the two groups

Results

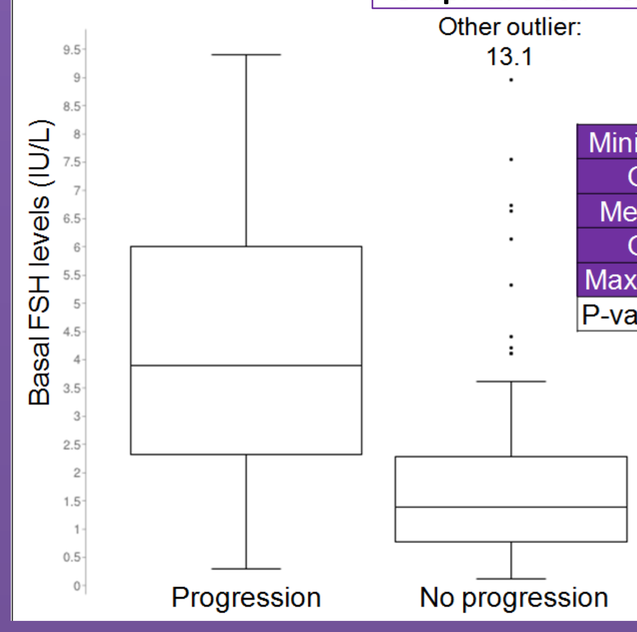
Graph 1: Basal LH (IU/L)



	Progression (n=56)	No progression (n=116)
Minimum	<0.1	<0.1
Q1	0.3	<0.1
Median	0.5	0.1
Q3	1.9	0.2
Maximum	7.2	5.7
P-value (Mann-Whitney U test): <0.0001		

Correlation coefficient
- between basal LH and median stimulated LH (up to basal LH of 2.0)
  - 0.74

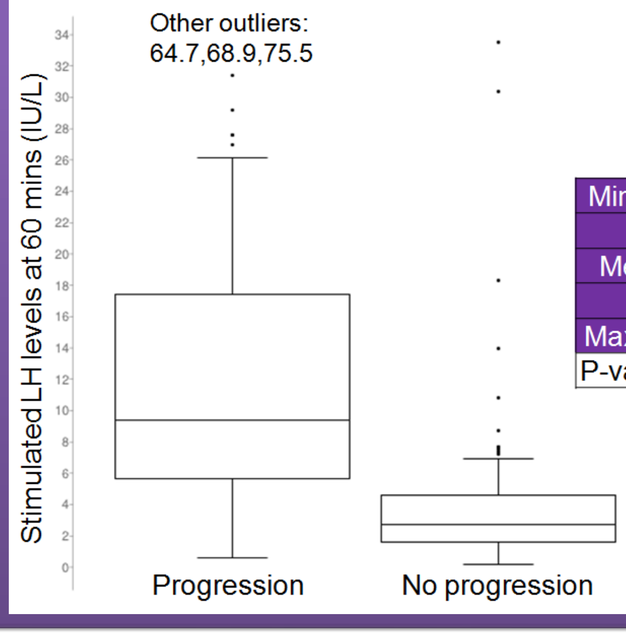
Graph 2: Basal FSH (IU/L)



	Progression (n=56)	No progression (n=116)
Minimum	0.3	0.3
Q1	2.3	0.9
Median	3.9	1.5
Q3	6	2.4
Maximum	9.4	13.1
P-value (Mann-Whitney U test): <0.0001		

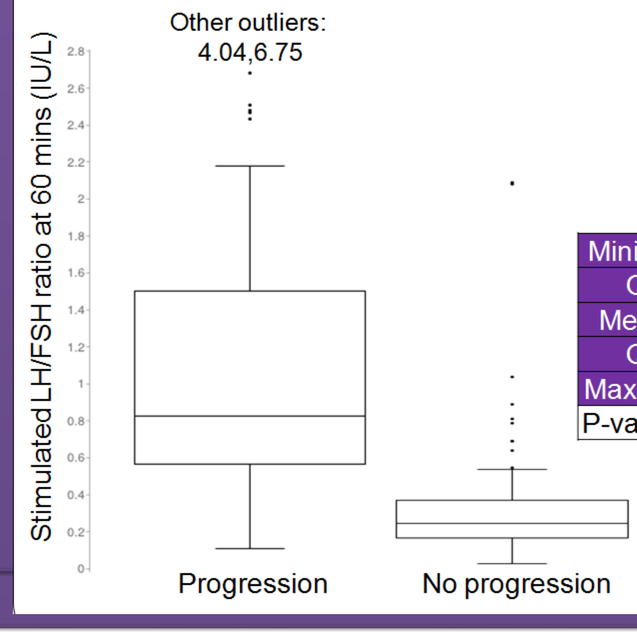
Correlation coefficient:
- between basal FSH and median stimulated FSH (up to basal FSH of 5.0 IU/L)
  - 0.62

Graph 3: Stimulated LH at 60 mins



	Progression (n=56)	No progression (n= 116)
Minimum	0.7	0.2
Q1	5.9	1.6
Median	11.1	2.7
Q3	20.7	4.55
Maximum	75.5	33.5
P-value (Mann-Whitney U test): <0.0001		

Graph 4: Stimulated LH/FSH ratio at 60 mins



	Progression (n=56)	No progression (n=116)
Minimum	0.11	0.02
Q1	0.57	0.16
Median	0.88	0.24
Q3	1.5	0.36
Maximum	6.75	2.08
P-value (Mann-Whitney U test): <0.0001		

	Sensitivity (95% CI)	Specificity (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
Basal LH ≥ 0.3 IU/L	**78.6% (65.6% - 88.4%)**	**85.3% (77.6% - 91.2%)**	**72.1% (59.2% - 82.9%)**	**89.2% (81.9% - 94.3%)**
Basal FSH ≥3.4 IU/L	58.9% (45.0% - 71.9%)	**86.2% (78.6 %– 91.9%)**	67.4% (52.5% - 80.0%)	**81.3% (73.3% - 87.8%)**
Basal LH ≥ 0.3 **and** basal FSH ≥3.4	58.9% (45.0% - 71.9%)	**92.2% (85.8% - 96.4%)**	78.6% (63.2% - 89.7%)	**82.31% (74.6% - 88.4%)**
Peak LH at 30 mins ≥ 5.4 IU/L	**86.4% (75.7% - 93.6%)**	**81.9% (73.7% - 88.4%)**	73.1% (61.8% - 82.5%)	**91.4% (84.2% - 96.0%)**
Peak LH at 60 mins > 4.1 IU/L	**91.1% (80.4 – 97.0)**	73.5% (64.6% - 81.2%)	62.2% (50.8% - 72.7%)	**94.5% (87.6% - 98.2%)**
Peak LH/FSH at 30mins >0.63	**89.3% (78.1% - 95.9%)**	**85.5% (77.8% - 91.3%)**	74.6% (62.5% - 84.5%)	**96.2% (90.4% - 98.9%)**
Peak LH/FSH ratio at 60 mins >0.88	50.0% (36.3% - 63.7%)	**97.4% (92.7% - 99.4%)**	**90.3% (74.2% - 97.9%)**	**80.3% (72.8% - 86.5%)**

Table 1: Table showing the clinical utility of different diagnostic cut-offs

Conclusion

Using basal LH and FSH levels together is a useful screening test to rule out precocious puberty in the majority of girls. If an LHRH test is required, we have reported novel cut-offs for LH levels at 30 and 60 minutes, and have shown how the LH/FSH ratio has overall greatest diagnostic value.

Recommendations: Pre-pubertal

1) Basal LH < 0.3 IU/L
2) Basal FSH <3.4 IU/L
3) Stimulated LH at 30 mins <5.4 IU/L
4) Stimulated LH at 60 mins <4.1 IU/L
5) Stimulated LH/FSH ratio at 30 mins <0.63
6) Stimulated LH/FSH ratio at 60 mins <0.88

Pubertal response

1) Basal LH ≥ 0.3IU/L
2) Stimulated LH at 30 mins ≥ 5.4 IU/L
3) Stimulated LH at 60 mins > 4.1 IU/L
4) Stimulated LH/FSH ratio at 30 mins ≥ 0.63
5) Stimulated LH/FSH ratio at 60 mins ≥ 0.88

References

[1]Carel JC et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*. 2009 Apr;123(4):e752-62
[2]Harrington J, Palmert MR, Hamilton J. Use of local data to enhance uptake of published recommendations: an example from the diagnostic evaluation of precocious puberty. *Arch Dis Child*. 2014 Jan;99(1):15-20