

Optimal strategy for ovarian function assessment in girls with central precocious puberty before and during GnRH analogue treatment



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BACKGROUND

GnRH analogue (GnRHa) suppresses gonadotrophin secretion in girls with central precocious puberty (CPP); however, the extent of ovarian function suppression under GnRHa treatment has not been evaluated. Inhibin B, produced by granulosa cells in small antral follicles, is regulated by FSH and local factors and reflects follicular ovarian activity.

OBJECTIVE

To evaluate the ovarian acute response in terms of estradiol and inhibin B production to depot GnRH analogue in CPP girls, before and during treatment.

METHODS

CPP girls
Naïve of treatment

n=11

Depot Triptorelin 3.75 mg
First dose 4th dose 7th dose 13th dose

Samples

At Baseline LH, FSH, E₂ and INH-B

After 3 h depot Triptorelin = LH-3 h, FSH-3 h

After 24 h depot Triptorelin = E₂-24 h and INH-B-24 h

(pituitary response)

(ovarian response)

Assays

LH, FSH and E₂: ECLIA, Roche.

Inhibin B: ELISA, Inhibin B Gen II, Beckman Coulter Inc.

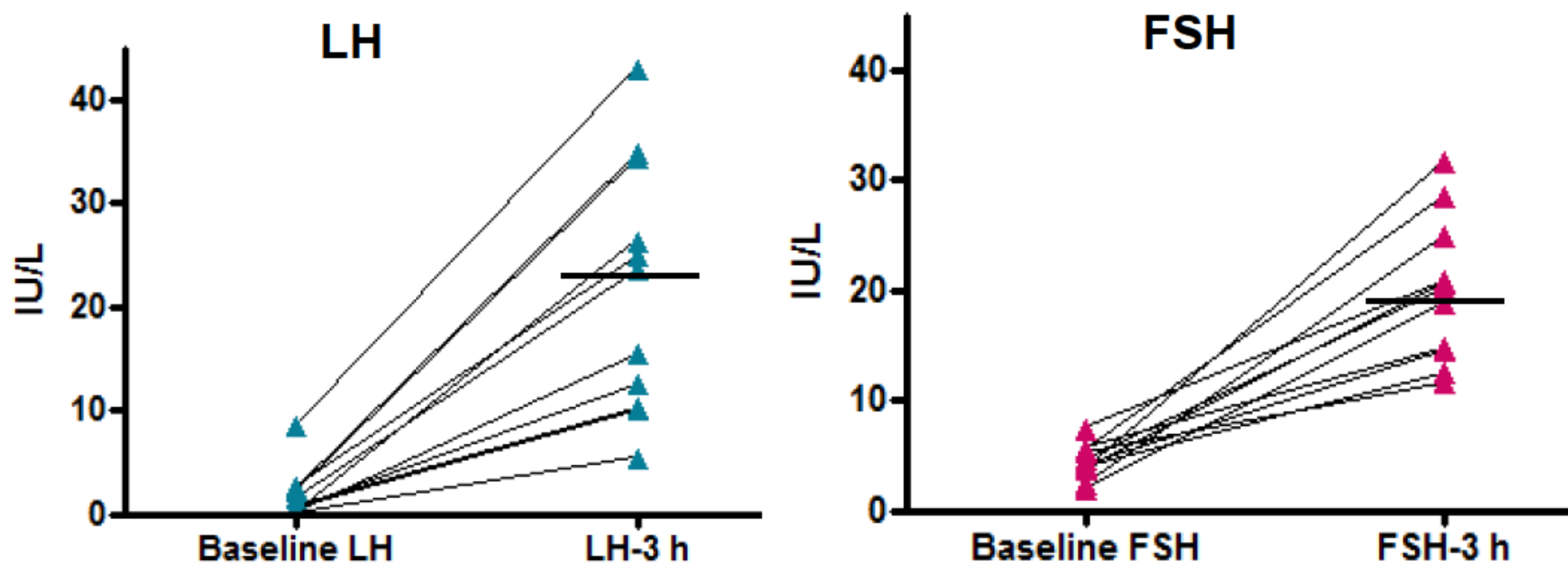
CVs were < 10%

Limit of quantification = 5 pg/mL.

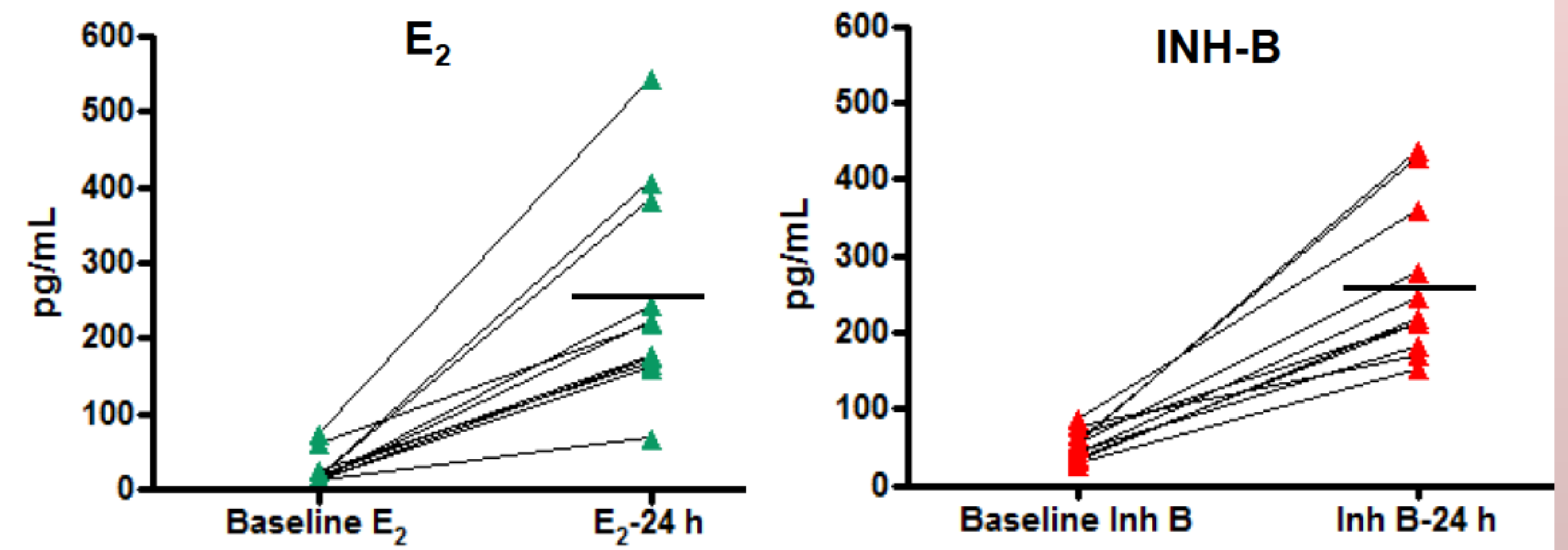
RESULTS

First depot GnRHa dose

Pituitary response at 3 h



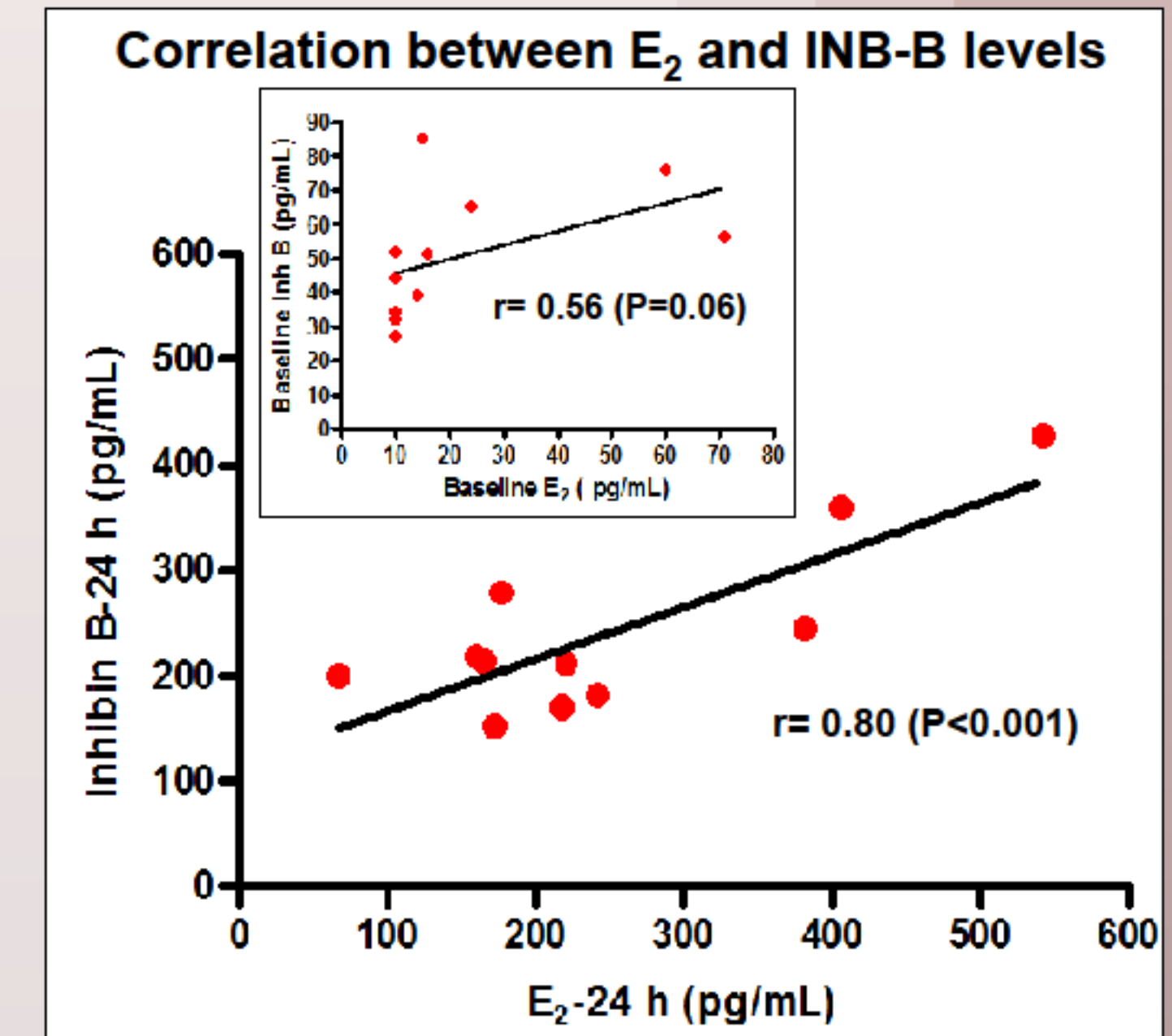
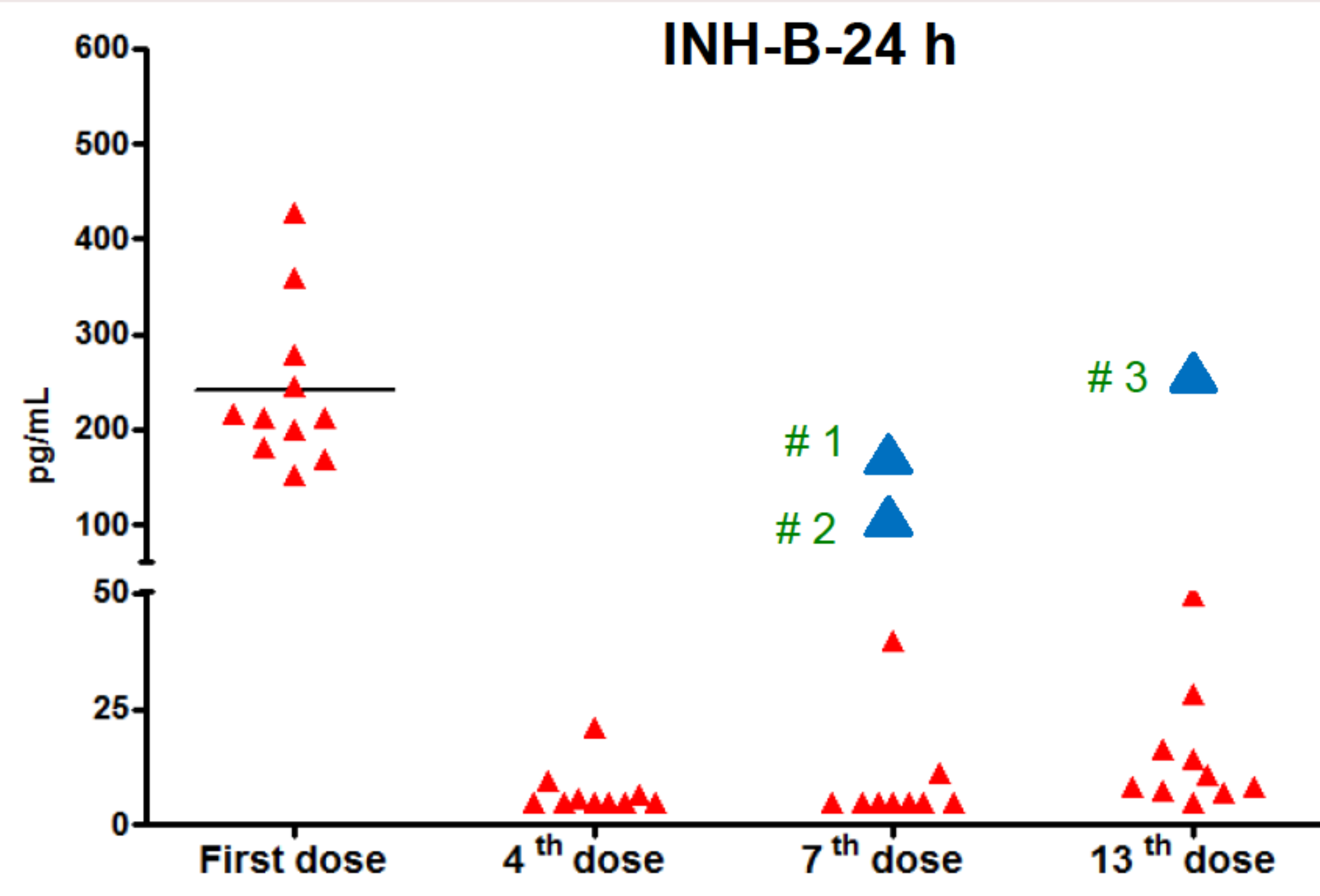
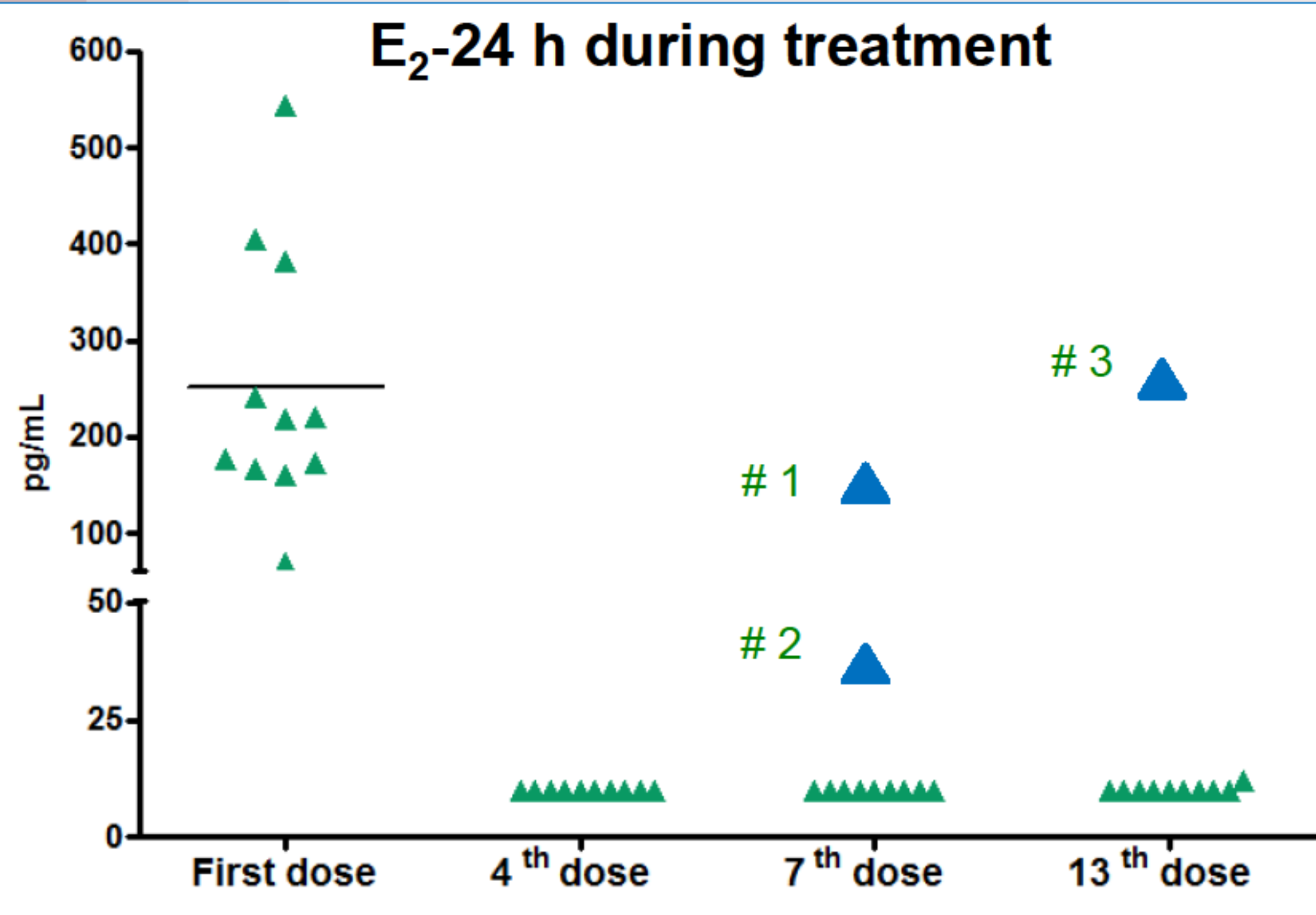
Ovarian response at 24 h



LH and FSH increased 10 and 5-fold over baseline after 3 h (mean ± SEM): 1.8 ± 2.4 to 22.2 ± 3.9 IU/L and 4.4 ± 1.5 to 19.9 ± 1.9 IU/L, respectively; p<0.001

E₂ and INH-B increased 10 and 5-fold over baseline after 24 h (24 ± 8 to 250 ± 42 pg/mL and 53 ± 5 to 263 ± 30 pg/mL, respectively, p<0.001)

During treatment - Ovarian response 24 h after depot GnRHa



E₂ and INH-B remained at very low levels after subsequent doses of GnRHa, in patients that concomitantly showed gonadotrophin suppression (LH-3 h < 4 IU/L and FSH -3 h < 6 IU/L)¹.

Pubertal E₂ and INH-B levels, concomitantly with unsuppressed gonadotrophins, were observed in 3 patients associated with irregular compliance to treatment.

Patient	LH-3h (IU/L)	FSH-3h (IU/L)
# 1	24	48.3
# 2	3	29.1
# 3	29.5	34.6

CONCLUSION

A similar profile of Inhibin B and estradiol levels were observed in CPP patients prior to and after depot GnRH analogue administration reflecting the activation and further suppression of the hypothalamic-pituitary-ovarian axis activity.

High Inhibin B and estradiol levels in response to the first dose of depot GnRH analogue, may suggest an increment in the number of granulosa cells and therefore, a marked follicular activity in CPP girls.

Sustained GnRH analogue administration induces gonadotrophin suppression and negligible ovarian endocrine activity.