

GONADOTROPIN FLARE WITH DIFFERENT DEPOT GNRH AGONISTS: COMPARATIVE ANALYSIS



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INTRODUCTION

Central precocious puberty (CPP) is effectively treated by inhibition of GnRH signaling through GnRH receptor desensitization with depot GnRH agonists (dGnRHa), but the **first injection** is associated with a **surge in LH and FSH (flare)** that proportionally **increases estradiol levels**. When estradiol levels drop, usually within a fortnight, vaginal bleeding may be seen in a small number of girls.

Although dGnRHa that use higher, longer-acting doses are increasingly being used in girls with CPP, as they reduce the number of injections/year, **the magnitude of the flare** caused by each of them **has not been compared**.

One concern that pediatric endocrinologists may have when administering higher doses of dGnRHa is the possibility of greater flare with unwanted consequences such as vaginal bleeding.

AIM

To compare gonadotropin levels during the flare in the first dose of two dGnRHa preparations that differ in dose, intervals, and route of administration in girls with CPP

METHOD

29 CPP girls from our center were included.

They received as first dose of treatment :

- n=17 Triptorelin 3.75 mg intramuscular route monthly (Trip 3.75)¹

- n=12 Leuprolide 45 mg subcutaneous route biannually (Leu 45) (data of Leu 45 were obtained from TOL2581A trial)²

The patients were not randomized to treatment.

LH and FSH levels were measured (by ECLIA) **at 3 hrs (Trip 3.75 group) and at 4 hrs (Leu 45 group)**. Clinical characteristics and gonadotropins levels were assessed

RESULTS

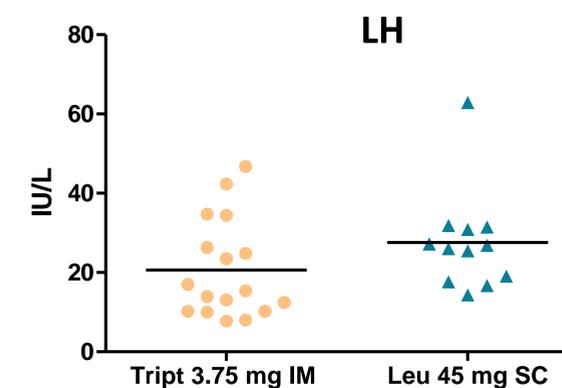
Chronological age (CA), bone age (BA), BA-CA, growth velocity (GV), BMI and breast Tanner stage, were comparable between groups

	Tript 3.75 IM n=17	Leu 45 mg SC N=12	P
CA(years)	8.2 ± 0.6	8.0 ± 0.5	NS
BA(years)	10 ± 0.8	10.5 ± 0.6	NS
CA - BA (years)	1.7 ± 0.7	2 ± 0.65	NS
GV (cm/year)	8.1 ± 1.9	9.3 ± 2	NS
BMI	18.5 ± 2.4	17.8 ± 2	NS
Breast Tanner stage	3	11 (90%)	NS
n (%)	4	0	1 (10%)

No patients experienced vaginal bleeding.

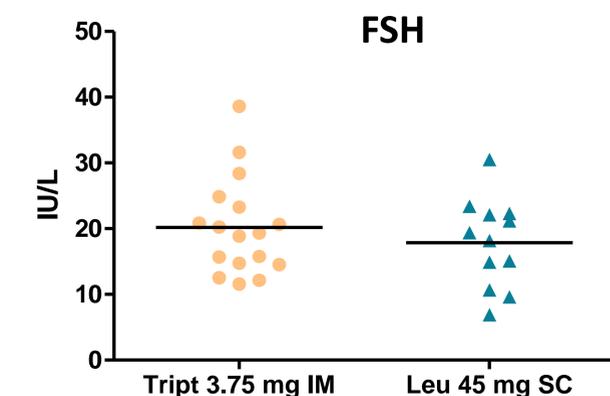
LH flare: median (range)

Tript 3.75 group : 15.5 (7.8 - 46.8) IU/L
Leu 45 group : 26.4 (14.4 - 62.9) IU/L
(p=NS)



FSH flare: median (range)

Tript 3.75 group : 19.3 (11.6 - 38.6) IU/L
Leu 45 group : 18 (6.9 - 30.5) IU/L
(p=NS)



Data were analysed by Mann Whitney U test.
Horizontal lines in graphs represent mean values.

CONCLUSIONS

Similar LH-FSH flare at first dose of depot aGnRH was observed in patients that received Triptorelin 3.75 mg IM and Leuprolide 45 mg SC. Leuprolide 45 mg, long-acting, biannual administration did not induce a significant higher gonadotropin flare as compared to the monthly Triptorelin 3.75 mg. This result suggests that there should be no concerns regarding flare when using Leuprolide 45 mg to initiate treatment for CPP in girls.

REFERENCES

- 1- Freire A.V. et al Assessment of Estradiol Response after Depot Triptorelin Administration in Girls with Central Precocious Puberty. *Horm Res Paediatr* 2016; 85:58-64.
- 2- Klein K.O. et al Phase 3 Trial of a Small-volume Subcutaneous 6-Month Duration Leuprolide Acetate Treatment for Central Precocious Puberty. *J Clin Endocrinol Metab* 2020; 105 (10):1-12.

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