Comparison of Gonadotropin-Releasing Hormone Agonist Doses for Triggering Oocyte Maturation

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Objective

Leuprolide acetate, a GnRH agonist, is commonly used to "trigger" meiosis resumption in oocytes during ovarian stimulation. Adequate response to Leuprolide acetate is determined by the luteinizing hormone (LH) level the morning following its injection. Commonly used Leuprolide acetate doses for ovulatory trigger include 40IU and 80IU. However, it is unknown whether a higher dose is associated with a difference in the post trigger LH level and oocyte maturity. The objective of this study was to assess the association between Leuprolide acetate trigger dose (40IU vs. 80IU) and risk of an inadequate LH response.

Design

Retrospective, multicenter cohort study

Materials & Methods

- Patients who underwent IVF or oocyte cryopreservation from 1/2017 to 12/2023 were included. All patients received a Leuprolide acetate trigger, with or without an hCG trigger.
- Patients with a baseline LH level <2 IU/L were excluded.
- Group 1 patients received a 40 IU dose of Leuprolide acetate and Group 2 patients received an 80 IU dose, per clinic protocol.
- The primary outcome was an inadequate LH response, defined as a post-trigger LH< 15 IU/L.
- Statistics were performed using Wilcoxon Rank-Sum Test and Poisson regression analysis adjusted for BMI and age.
- Sub-analyses of patients > 40 years and, separately, patients with BMI > 25 were performed.

Results

Leuprolide acetate dose	40 IU n = 8,350 cycles	80 IU n = 17,853 cycles
Mean day 3 LH IU/L (+/- SD)	7.0 +/- 3.2	6.0 +/- 3.2
Mean post-trigger LH IU/L (+/- SD)	70.3 +/- 34.5	55.0 +/- 32.7
Failed trigger rate (post-trigger LH < 15 IU/L)	0.6%	3.7%**

- The risk of an inadequate LH response was 0.6% (n= 51) for the 40 IU dose and 3.7% (n= 661) for the 80 IU group which was statistically significantly increased (aRR 5.50; 95% CI (4.11-7.37))**.
- In patients over 40, the 80 IU dose was associated with a significantly higher likelihood of an inadequate LH response (aRR 5.73; 95% CI (2.65-12.40)).
- In patients with BMI >25, the 80 IU dose was also associated with significantly higher likelihood of an inadequate LH response (aRR 4.05; 95% CI (2.75-5.99)).

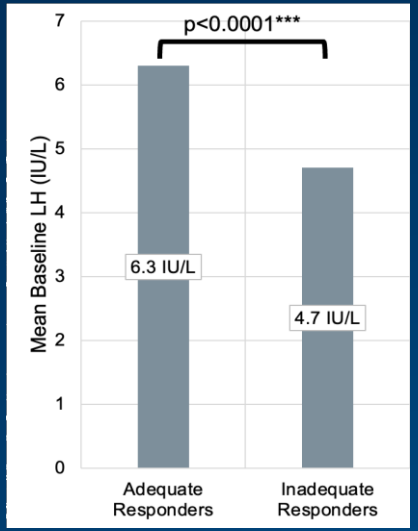

Figure 1. Mean baseline LH between adequate and inadequate responders

Conclusions

- An inadequate LH response to a Leuprolide acetate is uncommon in patients with low suspicion for hypothalamic dysfunction, occurring in **2.7%** of cycles in this cohort.
- Higher Leuprolide acetate trigger dose did not increase post trigger LH levels or reduce the likelihood of an inadequate LH response. Differences in lab assays, geographic distribution of patients, or variability in timing of blood draw may explain the higher LH levels associated with lower dose Leuprolide acetate trigger observed.
- While most patients with a low baseline LH level responded adequately to the trigger, caution should continue to be taken when using a Leuprolide acetate only trigger in this group.
- Patients and physicians can be reassured that using 40 IU dose of Leuprolide acetate is not associated with a greater likelihood of an inadequate response compared to the 80 IU dose.