

Reproductive Outcomes of Dual vs Single Triggers in ART Cycles

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IMPERIAL

Introduction

- In Assisted Reproductive Technology (ART), maximising egg retrieval + maturity is crucial for achieving **live births**.
- Three exogenous triggers** can be used to induce final oocyte maturation: human chorionic gonadotropin (**hCG**), gonadotropin-releasing hormone agonist (**GnRHa**) or combining both to form a ‘**dual**’ trigger.
- The **impact of dual trigger**, which theoretically combines the advantages of both single triggers (Fig. 1), on reproductive outcomes **remains debated**.
- Hypothesis: Dual trigger will lead to better reproductive outcomes than single trigger groups**

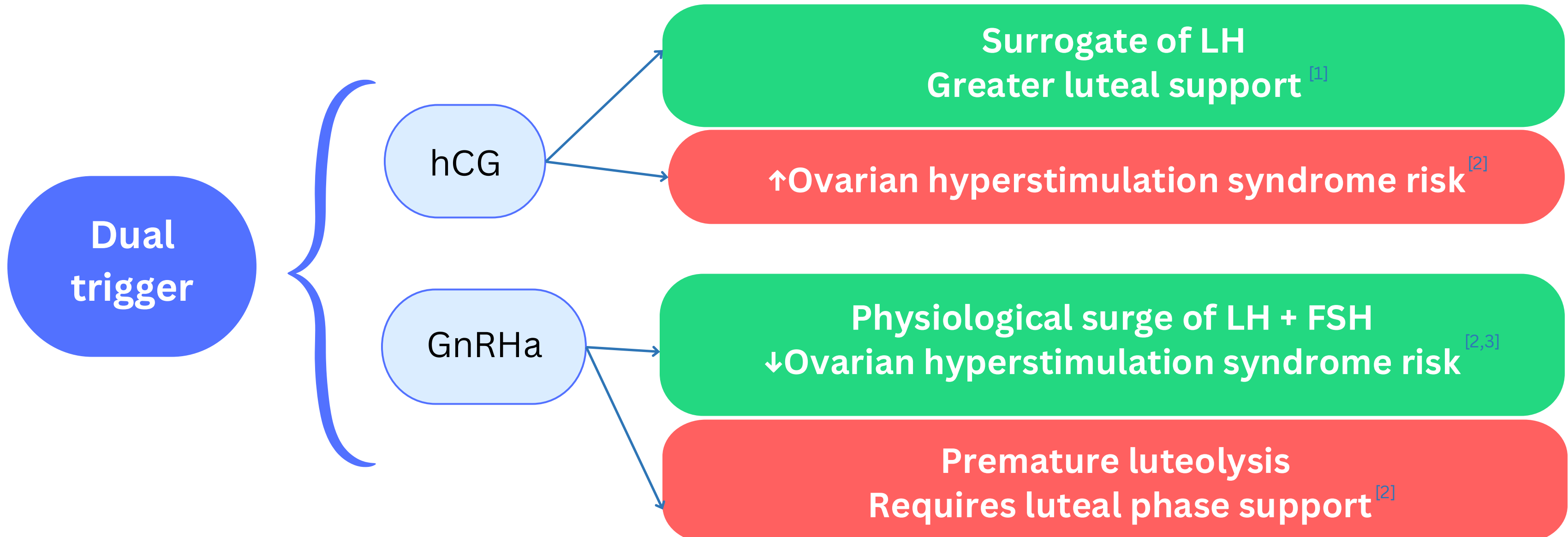


Figure 1. Advantages and disadvantages of single triggers

Methodology

- Retrospective, single-centre** study analysing **1,545 ART cycles** conducted at a private fertility clinic in London between **May 2023-March 2024**.
- Patients given either **hCG (n=854)**, **GnRHa (n=430)** or **dual trigger (n=261)**.
- Aims:** To compare baseline characteristics, stimulation cycle and pregnancy outcomes between triggers
 - 1° endpoint:** no. of retrieved oocytes, no. of mature oocytes, maturity rate, blastocyst quality, fertilisation rate
 - 2° endpoint:** Implantation/biochemical/clinical/ongoing pregnancy/live birth/miscarriage rates
- Inclusion criteria:** IVF, ICSI, and egg-freezing cycles using short or long protocol.
- Exclusion criteria:** IUI/donor cycles.

Results

Table 1. Comparison of ovulation stimulation cycle outcomes between trigger groups				
Variable	hCG group (n= 854)	GnRHa group (n= 430)	Dual trigger group (n= 261)	P value
No. of oocytes retrieved (n)	8.21 ± 5.68	18.41 ± 9.63	8.27 ± 5.88	< 0.001*
No. of mature (MII) oocytes (n)	5.80 ± 4.51	13.52 ± 7.86	5.79 ± 4.45	< 0.001*
Maturity rate (%)	69.58 ± 27.56	72.99 ± 19.35	68.73 ± 25.56	0.037*
No. of 2PN embryo	4.18 ± 3.73	10.86 ± 7.26	4.18 ± 3.40	< 0.001*
Fertilisation rate (%)	76.99 ± 28.62	84.69 ± 17.84	77.43 ± 29.11	< 0.001*
Blastulation rate	51.11 ± 34.04	44.14 ± 25.12	46.14 ± 33.26	0.014*
Blastocyst grade				0.003*
Good	40/138 (29.0)	31/54 (57.4)	17/44 (38.6)	
Average	50/138 (36.2)	8/54 (14.8)	10/44 (22.7)	
Poor	48/138 (34.8)	15/54 (27.8)	17/44 (38.6)	

Data presented as mean ± SD, *p<0.05

Table 2. Comparison of pregnancy outcomes between trigger groups in women who had a fresh embryo transfer				
Variable	hCG group (n= 282)	GnRHa group (n= 46)	Dual trigger group (n= 62)	P value
Implantation rate (%)	116/282 (41.1)	20/46 (43.5)	18/62 (29.0)	0.071
Biochemical pregnancy rate (%)	116/282 (41.1)	20/46 (43.5)	18/62 (29.0)	0.071
Clinical pregnancy rate (%)	88/282 (31.2)	15/46 (32.6)	15/62 (24.2)	0.517
Ongoing pregnancy rate (%)	76/282 (27.0)	14/46 (30.4)	12/62 (19.4)	0.365
Live birth rate (%)	76/282 (27.0)	14/46 (30.4)	12/62 (19.4)	0.365
Miscarriage rate (%)	12/282 (4.3)	1/46 (2.2)	3/62 (4.8)	0.765

Data presented in frequency and percentage; n (%) , *p<0.05

- hCG and dual groups had significantly higher maternal age** (hCG: 37.65 ± 4.45, dual: 38.50 ± 3.84 years, p<0.001) compared to the GnRHa group (35.75 ± 3.83 years, p<0.001).
- hCG and dual groups had similar ovarian responses**, but both were significantly **lower than the GnRHa group** (p<0.001).
- GnRHa group demonstrated significantly greater oocyte yield (GnRHa: 18.41, maturity rate and fertilisation rate** compared to the other two groups.
- All clinical pregnancy outcomes were comparable between the groups**, including live birth rate (GnRHa: 30.4%, hCG: 27.0%, dual: 19.4%, p=0.365), even after adjusting for age (p>0.05).

Limitations

- Retrospective, single-centre design limits external validity.
- Small dual trigger group size= ↑type II error risk.
- Patient selection bias + unmeasured confounders (e.g. co-morbidities) could influence results.
- Pregnancy outcomes were age-stratified, but stimulation cycle outcomes were not.

Conclusions

- Our study is the **first large-scale investigation comparing all three trigger groups**
- While **GnRHa improves oocyte maturity and fertilisation, hCG and dual triggers offset age-related ovarian decline, yielding similar pregnancy outcomes**.
- Although dual trigger was hypothesised to improve reproductive outcomes over single triggers, our findings suggest **no clear superiority**, likely due to **baseline age disparities**.
- Hence, trigger choice should be based on a combination of factors like **patient characteristics, financial considerations, and clinical judgement** to maintain outcomes.
- Further **multi-centre, age-matched, prospective, randomised control trials** are needed.

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