

Assessment of the whole interceptive and post-fertilization effects of postcoital levonorgestrel



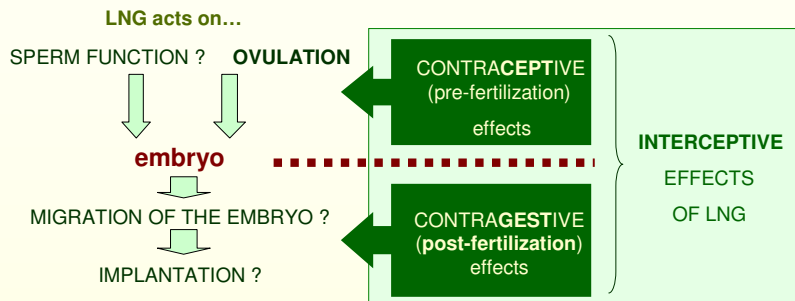
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1. BACKGROUND

- It is possible to assess what proportion of interceptive effects of levonorgestrel (LNG) takes place as **anovulatory action**, taking into account¹:
 - the magnitude of the **whole interceptive effect**,
 - anovulatory potency
 - timing of administration (with respect to intercourse and ovulation)
- However, **we don't know the actual interceptive effect**, because **clinical trials didn't use a placebo group**. They used an estimation method, and their assessment of interceptive effect could be over-estimated^{2,3,4,5}.



2. OBJECTIVE

- To know the **interceptive effect** after a dose of LNG, and then:
 - assess the proportion of its **anovulatory** and **post-fertilization** effects.

3. METHODS

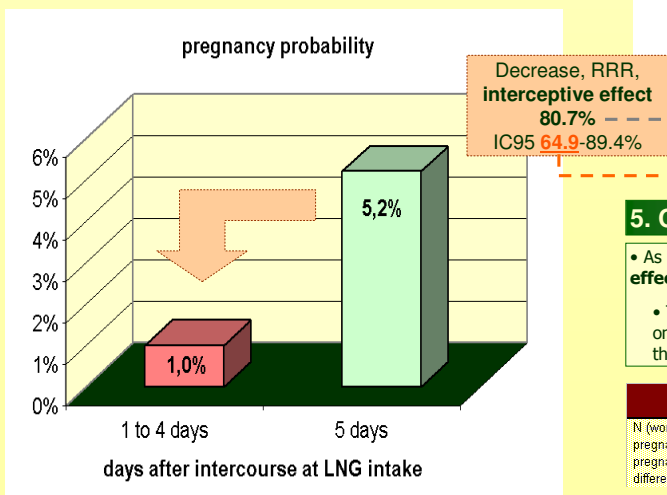
A recent systematic review (Piaggio et al.) pulled data from 6,794 women⁶. LNG administered in the fifth day after intercourse showed a pregnancy probability of 5,2%, slightly lower than 6-8%, calculated by an estimation method (6-8%).

- Using this cohort as a control group, we assessed the interceptive effect.
- We extrapolated it in **Mikolajczyk & Stanford's graph¹ (2007)** for knowing what proportion of the whole interceptive effect takes place as anovulatory or post-fertilization effects.

Table 1. Input data extracted from ref. 6.

group	A	B
days post-intercourse at intake	1 to 4 days	5 days
N (women)	6.564	230
pregnancies	66	12
days 2,3,4 vs. day 1	not significant	
day 5 vs. day 1	OR 5,81 (IC95% 2,87-11,76)	

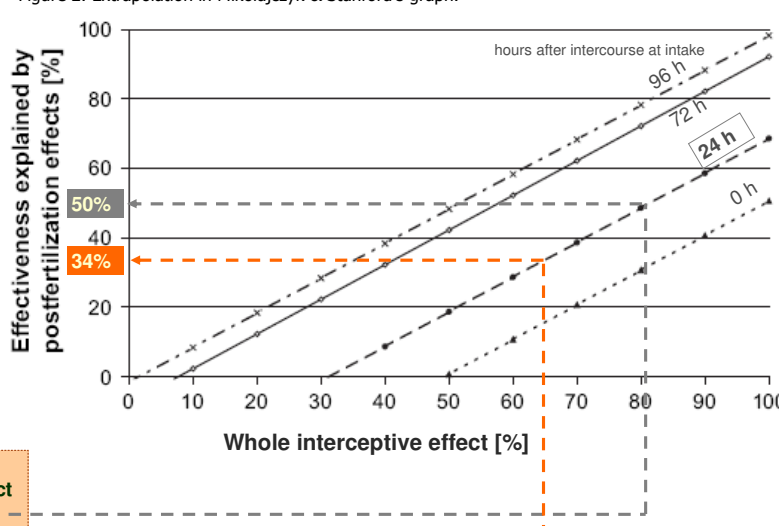
Figure 1. Pregnancy probability and assessment of interceptive effect



4. RESULTS

- The pregnancy rate was **1.0% taking the pill 1-4 days after intercourse** (66 pregnancies in 6,564 women), vs. **5.2% if it was taken in the fifth day** (12 in 230 women⁶ table 1 and fig.1).
- It shows a decrease on pregnancy probability (**interceptive effect**) of **80.7%** (IC95 64.9-89.4%; fig.1).
 - In a conservative approach (administration of the pill 24h after intercourse), we obtained an **anovulatory effect of 50%**. Fig.2.
- However, taking into account epidemiological data showing lack of effect on pregnancy rates at a population level⁷, we could assume an actual decrease that could be in the lower top of the confidence interval (**64.9%**).
- Extrapolating this effect, we obtained a **contribution of at least 34% for not-anovulatory mechanisms** and 66% for anovulatory effects (fig.2).

Figure 2. Extrapolation in Mikolajczyk & Stanford's graph.



5. CONCLUSIONS

- As an alternative pre-fertilization effect is unlikely⁸, we postulate at least **34% post-fertilization effects** for postcoital levonorgestrel.
- This is statistically compatible with previous contradictory Noe et al's data⁹, as they observed only 35 women. They refused the post-fertilization effect, and that was a reference for FIGO to adopt the same epidemiologically unfounded opinion in March 2011.

Table 2. Previous Noe et al. data⁹ statistically analyzed
Intake of LNG: day 0 (ovulation) or later

N (women)	35
pregnancies (observed)	6
pregnancies (expected)	7
difference (RRR, interceptive effect)	-14,5% (IC95 -59,5% to +63,5%)

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