A Scientific Argument against the Use of Plan B in Catholic Hospitals

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The mechanism of action of levonorgestrel emergency contraception (hereafter as LNG EC), sold as Plan B, given to prevent pregnancy after an act of intercourse (or rape) is a politically charged but morally important question.

The question of mechanism of action is fundamentally a scientific one.

In the discussion on mechanism of action of LNG EC, there is a lot of confusion concerning terms that are used and how particular studies support or refute a postfertilization effect of LNG EC. This brief article is meant to provide a clear, concise summary of the scientific literature pertaining to the mechanism of action of LNG EC, *with special emphasis on the best quality evidence.*

Effectiveness of LNG EC to prevent pregnancy depends on when it is given, before or after ovulation.

When given after ovulation, there is good evidence that LNG EC is not effective in preventing pregnancy.[1] There is also convincing support that LNG EC given after ovulation (actually after the LH surge which occurs the day before ovulation) neither prevents implantation, nor disrupts an embryo that already implanted.[3]

Many focus their attention on this scientific literature that indicates LNG EC does not prevent or disrupt implantation when administered after ovulation (or the LH surge) to support the claim that LNG EC is not abortifacient whenever given. The period of time that is concerning, however, is when LNG EC is given *before* ovulation in the fertile window. Consider the following:

First, when given before ovulation (in the fertile window), there is good evidence that LNG EC is very effective in preventing pregnancy.

A study by Noe et al. in 2010 is the largest (n=337) and most robust to date looking at the effectiveness of LNG EC based on when the drug was administered.[2] The day of ovulation was determined by the gold standard of serial ultrasounds to determine follicular rupture (which implies an egg is released). The effectiveness of LNG EC was evaluated based on whether it was given before or after ovulation and whether or not LNG EC was effective was based on the difference between expected and actual pregnancies.

As expected, the effectiveness of LNG EC - given on the day of ovulation or later - was basically non-existent (7 expected and 6 actual pregnancies). **In stark contrast, the effectiveness of LNG EC - given in the fertile window** (-5 to -1 days before ovulation) – **to prevent of pregnancy was complete** (13 expected but 0 actual pregnancies).

Second, when given in the fertile window (before ovulation), the predominant mechanism of action is not to prevent ovulation.

Again, the study of Noe et al. addresses the question of mechanism of action with this observation: *when LNG EC was given in the fertile window, breakthrough ovulations occurred 62 out of 87 times (71%).*[3] This led the authors to conclude "FR (follicular rupture or ovulation) occurred in some two-thirds of women taking LNG-EC preovulatory; this suggests that other mechanism than suppression of ovulation prevents pregnancy in these women."

Note: This study provides robust evidence that is contrary to the presumption that prevention of ovulation is the predominant mechanism of action for LNG EC given in the fertile window. There is now little scientific support for the presumption that prefertilization effects alone account for the efficacy of LNG EC given in the fertile window.

Key Points:

- Given that LNG-EC administered in the fertile window does not prevent ovulation the majority of the time, the presumption should be that fertilization is likely to occur at a significant rate.

- Given that LNG-EC administered in the fertile window is almost completely effective to prevent pregnancy, **the presumption should be that postfertilization effects occur at a significant rate.**

In other words, it is precisely the effectiveness of LNG EC given in the fertile window to prevent pregnancy, together with predominant rates of breakthrough ovulations, that lead many critical minds to conclude that LNG EC likely acts with postfertilization effects - often referred to as abortifacient effects – in a significant amount of time.

The burden of proof, therefore, lies in finding convincing evidence that LNG EC given in the fertile window lead to postfertilization effects.

Policy Note: Rape protocols that try to pinpoint impending ovulation, by detecting the LH surge, either cannot do so accurately or simply identify the fertile window, which is *precisely* when LNG EC would be potentially abortifacient.

The mechanism(s) of action that account(s) for the very high effectiveness LNG EC given in the fertile window may be both by prefertilization and postfertilization effects - though the scientific support for prefertilization effects is tenuous, and there is scientific support for postfertilization effects linked directly to preovulatory LNG EC.

- Some proposed prefertilization effects of LNG EC *given in the fertile window* include prevention of ovulation, (so that no egg is released), causing 'unfertilizable eggs' to be released (so that the eggs, though released are unable to

be fertilized), increasing cervical mucus viscosity (so the sperm cannot reach the egg) and sperm incapacitation (so that sperm cannot penetrate the egg).

- *The scientific literature supporting prefertilization effects of LNG EC given in the fertile window - is tenuous at best.* There is mounting, robust evidence demonstrating that preventing ovulation or follicular rupture is NOT the predominant mechanism for LNG EC in the fertile window.[4] The mechanism of 'unfertilizable eggs' has never been linked to LNG EC.[5] The thickening of cervical mucus is an unlikely mechanism if LNG EC is given several hours after intercourse and there is evidence to suggest that LNG EC does not affect sperm capacitation.[6]

- Some proposed postfertilization effects of LNG EC *given in the fertile window* include luteal phase insufficiency (so that implantation of or support for embryos is inhibited), and toxic pH environments (which would be embryocidal).

- *There is scientific literature supporting postfertilization effects of LNG EC given in the fertile window.* Studies have shown that LNG EC given in the fertile window leads to lower luteal phase hormone levels,[7] decreased endometrial receptivity (as evidenced by glycodelin-A levels),[8] shorter luteal phase[9] or earlier bleeding,[10] and very high intrauterine pH levels to as high as 9[11] (which is a 10-fold increase above the normal intrauterine pH). All of these effects have been linked to preovulatory LNG EC.

The scope of this brief article is not to provide a systematic review of the scientific evidence for and against each of these possible mechanisms of action. These mechanisms of action for LNG EC given in the fertile window are only proposed mechanisms, or theories, *none* of which have been proven.

The scientific support for prefertilization effects of LNG EC given in the fertile window is tenuous or not linked to LNG EC, whereas there is scientific support for postfertilization effects of LNG EC given in the fertile window that is biologically plausible and linked to LNG EC.

Summary Point: *It is scientifically untenable to state that postfertilization effects of LNG EC - given in the fertile window - never (or even rarely) occurs.*

Dr. Trussell and Dr. Raymond (both world-renowned, staunch supporters of contraception) admit in their review of LNG, "to make an informed choice, women must know that [emergency contraceptive pills]… may at times inhibit implantation of a fertilized egg in the endometrium."[12]

Conclusion

Given that breakthrough ovulations occur the majority of the time when LNG EC is given in the fertile window, together with the scientific support in favor of postfertilization

effects that follow, leads to the conclusion that postfertilization effects of LNG EC have NOT been ruled out, but rather, likely occur at a significant rate. To state otherwise is statistically improbable and scientifically untenable.

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[1] Noe G, Croxatto HB, Salvatierra AM, et al, "Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation," *Contraception* 81 (2010):414-20; Novikova N, Weisberg E, Stanczyk FZ, Croxatto HB, Fraser IS, "Effectiveness of levonorgestrel emergency contraception given before or after ovulation--a pilot study," *Contraception* 75 (2007):112-8.

[2] Noe G, Croxatto HB, Salvatierra AM, et al, "Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation," *Contraception* 81 (2010):414-20.

[3] Ibid.

[4] Ibid.

[5] Verpoest WM, Cahill DJ, Harlow CR, Hull MG, "Relationship between midcycle luteinizing hormone surge quality and oocyte fertilization," *Fertil Steril* 73 (2000):75-7.

[6] do Nascimento JA, Seppala M, Perdigao A, et al, "In vivo assessment of the human sperm acrosome reaction and the expression of glycodelin-A in human endometrium after levonorgestrel-emergency contraceptive pill administration," *Hum Reprod* 22 (2007): 2190-5.

[7] Durand M, Seppala M, Cravioto Mdel C, et al., "Late follicular phase administration of levonorgestrel as an emergency contraceptive changes the secretory pattern of glycodelin in serum and endometrium during the luteal phase of the menstrual cycle," *Contraception* 71 (2005):451-7; Durand M, del Carmen Cravioto M, Raymond EG, et al., "On the mechanisms of action of short-term levonorgestrel administration in emergency contraception," *Contraception* 64 (2001): 227-34.

[8] Durand M, Seppala M, Cravioto Mdel C, et al., "Late follicular phase administration of levonorgestrel as an emergency contraceptive changes the secretory pattern of glycodelin in serum and endometrium during the luteal phase of the menstrual cycle," *Contraception* 71 (2005):451-7.

[9] Durand M, Koistinen R, Chirinos M, et al., "Hormonal evaluation and midcycle detection of intrauterine glycodelin in women treated with levonorgestrel as in emergency contraception," *Contraception* 82 (2010): 526-33.

[10] Tirelli A, Cagnacci A, Volpe A, "Levonorgestrel administration in emergency contraception: bleeding pattern and pituitary-ovarian function," *Contraception* 77 (2008):328-32; Gainer E, Kenfack B, Mboudou E, Doh AS, Bouyer J. "Menstrual bleeding patterns following levonorgestrel emergency contraception," *Contraception* 74 (2006):118-24.

[11] Kesseru E, Garmendia F, Westphal N, Parada J. "The hormonal and peripheral effects of d-norgestrel in postcoital contraception," *Contraception* 10 (1974): 411-24.

[12] Trussell J., Raymond E, *Emergency Contraception: A Last Chance to Prevent Unintended Pregnancy.* Office of Population Research at Princeton University. June 2010.