american society for emergency contraception

MECHANISM OF ACTION OF LEVONORGESTREL EMERGENCY CONTRACEPTIVE PILLS

BACKGROUND

Levonorgestrel emergency contraceptive pills (LNG ECPs), sold as Plan B One-Step and generic forms, are the most common and easily accessible form of emergency contraception in the United States because they are approved for over-the-counter sale. Ulipristal acetate ECPs and IUDs are more effective methods of EC, but are more difficult to get because they require the involvement of a healthcare provider and are not always available. The mechanism of action of LNG ECPs has been a subject of much confusion and public discussion; this factsheet describes what is known about how LNG ECPs work.

Levonorgestrel is a progestin (a synthetic form of the naturally occurring hormone progesterone). LNG ECPs work by interfering with the process of ovulation. LNG ECPs impede follicular development and maturation and/or the release of the egg from the ovary.[1–7] If there is no egg, fertilization cannot occur. The evidence does not support the theory that LNG ECPs can prevent implantation of a fertilized egg.[8,9]

HOW IT WORKS

Pregnancy: For pregnancy to occur, luteinizing hormone (LH) triggers ovulation (release of an egg from the ovary), then the egg must be fertilized by sperm and implanted in the uterine lining.

Ovulation: LNG can inhibit the LH surge, impeding follicular development and maturation, and/or ovulation, if taken before the LH surge has begun.[1–7,10,11] Two studies, conducted in 2007 and 2011, provide the most robust evidence that LNG ECPs disrupt ovulation but do not work after ovulation has occurred. Both studies found that 100% of expected pregnancies were prevented by LNG ECPs when taken before ovulation. Those who took LNG ECPs after ovulation got pregnant at the same rate as would be expected if they had not used ECPs at all. Therefore, they are likely ineffective when taken after ovulation and do not prevent implantation of a fertilized egg.[5,6]

Implantation: Several studies have investigated the effect of LNG ECPs on the endometrium (lining of the uterus) and biological markers of endometrial receptivity. As a whole, this body of literature does not demonstrate that LNG ECPs prevent implantation of a fertilized egg in the uterus.[1,2,8,12–15] Of note, two studies directly tested the effects of LNG on an in-vitro endometrial model. One found that LNG did not inhibit attachment of a blastocyst[13] and the other found that LNG has no direct effect on endometrial receptivity markers in this model.[12]

Sperm: Evidence is mixed about whether LNG ECPs affect sperm function by thickening cervical mucus (thereby inhibiting sperm motility) or interfering with sperm migration.[5,16–22] Some evidence indicates that progesterone activates the CatSper channel that controls sperm hyperactivity in the absence of an egg or causes sperm to disorient and move in the wrong direction. [23–27]

Existing pregnancy: If taken after implantation has occurred, LNG ECPs have no effect on an existing pregnancy and do not increase rates of miscarrumiage.[9,28,29]

REGULATORY HISTORY

Strong evidence indicating that LNG ECPs work before, and not after, ovulation has existed since 2011. Based on this evidence, the European Medicines Agency removed language suggesting an anti-implantation effect from the LNG label in 2013.[32] In December 2022 (nearly a decade later), the US Food and Drug Administration (FDA) approved an updated label that accurately describes the mechanism of action of LNG ECPs.[30] (Prior to the label update, the label suggested that it may prevent implantation of a fertilized egg in the uterus.[31])

IMPLICATIONS

Policy makers and courts in the United States and elsewhere (particularly Latin America) have used the hypothetical anti-implantation mechanism – in combination with a non-standard definition of pregnancy that equates a fertilized egg with a pregnancy - to restrict access to ECPs.[33,34] Following the Supreme Court decision in Dobbs v. Jackson Women's Health Organization, which will allows states to severely restrict or ban abortion, access to EC is a critical component of reproductive autonomy as the stakes for preventing pregnancy are higher than ever. This label change limits the ability of state legislatures to use ECP labels as a justification to limit access.

CONCLUSIONS

A large body of evidence indicates that levonorgestrel ECPs prevent or delay ovulation and do not prevent implantation. The FDA-approved LNG ECP labels now reflect this evidence, settling years of confusion about this issue.

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