American Journal of
Oral Medicine and Radiology

ISSN - 2394-7721

www.mcmed.us/journal/ajomr

Research Article

CRITICAL OF ENDOMETRIAL DYNAMIC OVULATORY EFFECTS IN EMERGENCY CONTRACEPTION WITH ULIPRISTAL ACETATE

Lakshmi

Assistant Professor, Department of Obstetrics & Gynecology, Sree Balaji Medical College and Hospital, Chrompet, Chennai – 600044.

ABSTRACT

When calculating the effectiveness of emergency contraception, the percent of observed and expected babies following risky sex is commonly employed (EC). Discrete hormone receptor modulators of the second generation are already developed and tested for use in the EC. Term of vocabulary acetate (UPA), like mifepristone, has been shown to have antiprogestin efficacy similar to contraceptives but to After risky sex, be useful for long to 120 hours. For preventing clinically evident pregnancies, UPA is much more effective than progestin (LNG).If taken at a later time, fertile phase, LNG has been shown to affect future luteal function. LNG loses its potency over time, and it is only effective after 72 hours of unprotected contact. The UPA is effective for five days following unprotected intercourse, regardless of which of the other five days it is utilised. As ovulation approaches, UPA's capacity to delay ovulation decreases, eventually reaching null just at peak of corpus luteum (LH): 1 to 2 hours before ovulation, UPA acts as a placebo. The drug's lengthy success is attributed to antiovulatory activity, as LH levels drop significantly as they reach their peak. The drug's success is most likely due to its strong uterine effects, which are always present regardless of the time of administration Because the threshold for changing uterine shape was lower than the limit for affecting folliculogenesis, these effects are everywhere.

Key words:- Ulipristal Acetate, Emergency Contraception, Ovulation Delay, Endometrial Effects, Unexpected Pregnancy.

Access this article online		
Home page: http://www.mcmed.us/journal/ajomr		Quick Response code
Received:25.07.15	**Revised**:12.08.15	**Accepted**:29.08.15

INTRODUCTION

Following sexual intercourse, contraception is use of any pill or technology with the goal of avoiding an undesired pregnancy (EC). Only during the fertile time of the period, which would be the 4 to 5 days years leading to conception or the day of ovulation, can unprotected intercourse result in pregnancy.

Corresponding Author
Dr. Lakshmi

Email: -

The fertile days are the preovulatory day, the implantation day, as well as the second day before ovulation, when intercourse is most common and the chance of pregnancy is greatest. Unprotected intercourse pregnancy is at an all-time high on these days. The following formula is widely used to calculate the efficiency of EC: The amount of actual pregnancies is compared to a number of estimated unprotected intercourse and 5th pregnancy These computations are difficult, and in some cases, the influence of EC may have been overstated.

Ovulation is supposed to be hampered by LNG. Ovulation is increased when EC is used early in the process, when chances for conception are minimal. usually lowered. When consumed during in the early ovulatory cycle, or the most viable weeks of the cycle, LNG had no effect on ovulation.

Preovulatory LNG injection led in a healthy ovulatory following a brief or insufficient luteal phase that can contribute to poor endometrial growth in the majority of the studies stated in the remarks. These activities could explain why LNG has such weak antiovulatory properties.

The availability of selective hormonal receptors stimulators (SPRMs), which were demonstrated to be highly efficient in terminating pregnancies, has prompted new attempts to incorporate them into EC Mifepristone, for example, has been found to work for up as 120 hours following intercourse. Mifepristone doses of 25 to 50 mg are the most effective for EC.

For EC applications, 2nd SPRMs have indeed been created and tested. UPA was discovered to have the same antiprogestin action as misoprostol and be After unprotected intercourse, the impact lasts up to 120 hours. Ella(One) (Laboratoire Hr Pharm, rue Beranger, Paris) is the European brand name for UPA, while Ella is the brand name in the United States.

We will look at studies looking at the impact of UPA at different stages of the menstrual cycle in this review. Our goal is to figure out which impacts are most important in determining UPA's efficacy in EC.

Methods

UPA's techniques of action were investigated using primary sources. Review papers were also used, but just to reflect upon their results on this particular subject. Only published papers between October 2010 and February 2013 were included in the search.

We also looked at phase Ii or Iii studies who compared UPA's efficacy to LNG's. Product labelling has been approved both by European Medicines Agency (Mec) and us Food and Drug (FDA).

Our search criteria were "Ulipristal Acetate" and "Preferential Hormone Receptors Modulators." The words "contraceptives," "unintended pregnancy," "ovulation," or "endometrium" were combined with these keywords. The references of retrieved articles were also checked to see whether any important publications were missed during the original search.

Results

In the primary literature, we found four papers that discussed the mode of action of Ppa in women, specifically its effects on dominant follicle or endometrium. HRA Pharma the FDA and indeed the EMA all utilise these experimental articles to back up their official conclusions. UPA's effects on follicles have been studied in two studies, while its effects just on endometrium have been studied in three studies. Both are looked into in a single study.

We'll get above some background material once we're in the articles. the UPA protein and its purported ability to prevent Following an unintended pregnancy, clinically apparent pregnancy occurs during the menstrual cycle's fertile period

Ulipristal Acetate Pharmacology And Pharmacodynamics

Ulipristal acetate is an orally administered progesterone-responsive tissue antagonist. It inhibits progesterone kinase DNA transcription and has a strong affinity for progesterone receptors

It binds to corticosteroids and androgen receptors as well as progesterone receptors, albeit with reduced affinities The doses required in vivo for such lowaffinity bound activities are around 50 times higher than for progestin receptor binding.UPA has similar antiprogestin efficacy to mifepristone, only well SPRM, while the latter has a higher antiglucocorticoid activity.

UPA was 94 percent linked to plasma components including high-density lipoprotein (HDL) or albumin. is excreted slowly after consumption. The active component monodemethyl- UPA is generated once the medication is metabolised. Monodemethyl-UPA in plasma has a half-life of around 33 hours in healthy women.

In humans, nonmicronized UPA serum concentrations peak 60 to 60 minutes after consumption. Increases in dosages approximately 50 mg result in proportionate increases in previous highs, but no additional fractional increases occur at 100 and 200 milligrammes, suggesting carrier site saturation.

When given fasting, microencapsulated UPA impacts extend serum concentrations at 60 minutes with such a Cmax & area under the curve that are twice as large as monodemethyl-UPA. Absorption rate has been reduced after an elevated meal, but The absorption time has been extended. As a consequence, the medication can be given. regardless of meal timing.

Ulipristal Acetate Efficacy In EC

A phase II study compared 775 UPA-treated women to 774 LNG users using nonmicronized 50 mg UPA. Within 72 hours of the intercourse, this therapy was started. Pregnancies were identified in seven cases (0.9%) and thirteen cases (1.7%), respectively. % and 69 percent of anticipated pregnancies were avoided, respectively, based on expected period days following risky sex.

In the second study, Ella(One) (844 women) was compared to LNG 1.5 mg in a multinational, solitary, non-inferiority experiment (852 women). EC was always administered within 24 hours of a sexual sex, regardless of the type of medication used. There were pregnancies

among women who had EC after 72 hours, with 15 (1.8 percent) (2.6%) in the UPA grouping and (2.6%) in the LNG grouping. Both groups had lower pregnancy rates than the general population (5.5 percent for UPA and 5.4 percent for LNG). In a group of 203 women, three babies were found 72 to 120 hours following unprotected intercourse (UPA and LNG). The LNG group was responsible for all of the babies.

Following that, these similar patients were combined or analysed alongside those in the phase II study owing to the equivalence of the UPA treatments. The UPA group used to have a lower fertility than the LNG group, with rates of 0.9 percent vs 2.5 percent at 24hrs, 1.4 percent against 2.2 percent at 72 h, and 1.3 percent versus 2.2 percent after 120 hours, respectively, relative to an expected rate of around 5.5 percent.

Finally, in a meta, women treated with Ella(One) in two phases received positive results. III trials were combined. There were pregnancies among the 2183 women. Obese women or women who had more sexual intercourses in the same cycle had greater pregnancy rates. The percentages varied from 1.3 percent in nonobese women and had no more sexual intercourses to 8.3 percent in obese women who had more unprotected intercourse.

Ulipristal Acetate Effects In Ec: Official Positions, Guidelines

UPA reduces or delays ovulation, according to the most prestigious international pharmacological institutes and scientific organisations.

Although the EMA's official study on UPA only says that "UPA, even when taken soon before ovulate, is able to cancel ovarian rupture in some women," the FDA argues that changes towards the endometrium, which may hamper implantation, can contribute to UPA's efficacy (p7) The sole information in the EMA package booklet for consumers is that "ellaOne® is thought to operate by stopping your ovaries from releasing eggs."

Finally, HRA Pharma dismisses the potential of UPA affecting with implantation, citing three studies on the effects on UPA in male sexual endometria : code codes 505, 506, and 503 inside its briefing materials.

Ulipristal Acetate Effects On Ovulation—Primary Literature

Only one study looked at how Ella(One) influences ovulation on various days during the fertile period. Even when administered right before ovulation, the authors claim inside the abstract and data that UPA can block or severely delay follicle rupture for even more than 5 days, which is highlighted in the title.

This shows that the effects of either placebo or UPA on ovulation were null when administered 1 to 2 days preceding ovulation, which contradicts the paper's results. Any claim that UPA can cause ovulation to be delayed for 24 to 48 hours even if it was given the day before the Rh maximum is ludicrous. In reality, both the placebo as well as the UPA are ineffective at that point as ovulation occurs about two days after the tablets are consumed

Ulipristal Acetate Effects On The Endometrium: Primary Literature

To begin, every study which has looked at UPA's stromal effects has discovered that threshold for changing endometrium shape are lower than the maximum for influencing folliculogenesis. Due to its trigger apoptosis link to progesterone receptors, UPA inhibits tissue fast, and this effect is visible with a single administration of the lowest dose.

In the mid-follicular phase, nonmicronized UPA (100 mg) decreased luteal-phase endometrial development in a comparable way. This effect lasted a long time. It began following the creation of a new leading ovary in late ovulation and lasted until menstruation. This means that any hazardous intercourse after taking UPA may result in conception but not successful embryogenesis.

Endometrial thickness decreased consistently regardless of dose If nonmicronized UPA (10, 50, or 100 mg) were given early in the luteal phase there was no effect on luteal phase hormones. Furthermore, the greatest doses of 50 mg (equivalent to Ella(One)) and 100 mg drastically decreased the risk of developing cancer. reduced uterine production by hormone luteal monocytes macrophages, as measured by immunohistochemistry using the allergens MECA . Endometrial epithelial cells' membranes contain important L-selectin ligands known as node addressins. They've been flipped. on during the insertion window to make the uterus less receptive to the blastula. By binding with endometrial ligands, L-selectin stimulates implantation in human blastocysts. Implant failure has been connected to their absence.

DISCUSSION

According to the most renowned international drug authorities and scientific organisations, UPA suppresses or delays ovulation. Except for the FDA no one believes Endometrial changes that impact implantation could jeopardise UPA's effectiveness. HRA Pharma is still at the same position three research on the determinants of UPA just on endometrium formally back it up.

All of the endometrial impacts outlined in these three articles in our opinion, are capable of interfering with the implantation process. As a reason, we believe Ella(Onegreatefficacysuccess)'s in preventing clinically obvious pregnancies is due to these effects rather than egg latency, which is undetectable on the cycle's most productive days. According to Passaro, half of the women who took Endometrial haemorrhage occurred after taking mg of nonmicronized UPA. ladies who have been treated at semi stage, when implantation occurs. She came to the conclusion that UPA had direct and comparable effects to mifepristone, implying that the two medicines are roughly equivalent in this regard.

UPA and mifepristone have a lot of the same side effects. According to a number of Chinese trials, mifepristone is highly helpful for Ep at dosages from 25 to 50 mg. 24 When administered Misoprostol 50 mg can cause a follicular delay when in the follicular phase maturity, which can cause conception to be delayed. When a major technology follicle is attracted, ovulation returns, a phenomenon that is more common at higher doses, including such 200 to 600 mg. These findings are equivalent to those obtained with significantly lower UPA dosages (10-100 mg) during the west midlands stage of the cycle.

Although DBA-lectin binding, an indicator of In five of the six people, endometrial secretory activity was reduced, and ppar reduced expression was mainly suppressed, a single light dose of medicines (10 mg) had no effect on endometrial shape.This demonstrates that endometrial size alone does not ensure ovarian responsiveness, as observed after UPA treatment.

Furthermore, both UPA and mifepristone have been shown to suppress fibroid growth using the same dosages and schedule Microencapsulated UPA has been shown to reduce fibroid size & uterine haemorrhage without the negative effects associated with other drugs. It is approved for fibroid elimination prior to surgery in West Europe.It comes in blister packs containing 28 5-mg tablets.

CONCLUSIONS

Our findings show that UPA inhibits clinical pregnancies primarily through its negative effects on endometriosis, a postfertilization pathway. Although this activity has only been confirmed when EC was missing before the end of the follicular phase fertile phase, the Ppa may function by delaying ovulation. UPA can only postpone ovulation until LH rises once the menstrual month begins. After that, the impact becomes inconsistent and eventually disappears during in the pre - ovulatory days.

We'd like to note out that 200 mg or nonmicronized Upc equals 120 mg of particles UPA, the amount in 4 Ella(One) tablets only or 24 of the -28 tablets with in uterine tumors multipacks. This should be considered while determining on prescription restrictions for any UPA-containing drug.

REFERENCES:

1. Gemzell Danielsson K. Mechanism of action of emergency contraception. Contraception. 2010;82(5):404-409.
2. Wilcox AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. N Engl J Med. 1995;333(23):1517-1521.
3. Wilcox AJ, Baird DD, Dunson DB, McConnaughey DR, Kesner JS, Weinberg CR. On the frequency of intercourse around ovulation: evidence for biological influences. Hum Reprod. 2004;19(7): 1539-1543.
4. Dunson DB, Baird DD, Wilcox AJ, Weinberg CR. Day-specific probabilities of clinical pregnancy based on two studies with imperfect measures of ovulation. Hum Reprod. 1999;14(7): 1835-1839.
5. Trussel J, Rodriguez G, Ellertson C. New estimates of the effectiveness of the Yuzpe regimen of emergency contraception. Contraception. 1998;57(6):363-369.
6. Fine P, Mathe´ H, Ginde S, Cullins V, Morfesis J, Gainer E. Ulipristal acetate taken 48-120 hours after intercourse for emergency contraception. Obstet Gynecol. 2010;115(2 pt 1):257-263.
7. Stirling A, Glasier A. Estimating the efficacy of emergency contraception— how reliable are the data? Contraception. 2002; 66(1):19-22.
8. Trussell J, Ellertson C, von Hertzen H, et al. Estimating the effectiveness of emergency contraceptive pills. Contraception. 2003; 67(4):259-265.
9. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. Lancet. 1998;352(9126):428-433.
10. Cheng L, Gu¨lmezoglu AM, Piaggio G, Ezcurra E, Van Look PF. Interventions for emergency contraception. Cochrane Database Syst Rev. 2008;(2):CD001324.
11. Mozzanega B, Cosmi E. How do levonorgestrel-only emergency contraceptive pills prevent pregnancy? Some considerations. Gynecol Endocrinol. 2011;27(6):439-442.
12. Croxatto HB, Brache V, Pavez M, et al. Pituitary–ovarian function following the standard levonorgestrel emergency contraceptive dose or a single 0.75-mg dose given on the days preceding ovulation. Contraception. 2004;70(6):442-450.
13. Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and metaanalysis. Lancet. 2010; 375(9714):555-562.
14. Brache V, Cochon L, Jesam C, et al. Immediate preovulatory administration of 30 mg ulipristal acetate significantly delays follicular rupture. Hum Reprod. 2010;25(9):2256-2263.
15. Noe´ G, Croxatto HB, Salvatierra AM, Reyes V, Villarroel C, Mun˜oz C, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. Contraception. 2010;81(5):414-420.
16. International Federation of Gynecology & Obstetrics (FIGO) and International Consortium for Emergency Contraception (ICEC). How do Levonorgestrel-only emergency contraceptive pills (LNG ECPs) work to prevent pregnancy March_2012.pdf. Accessed March 1, 2013.

17. The European Society of Contraception and Reproductive Health. ‘‘How do Levonorgestrelonly emergency contraceptive pills (LNG ECPs) work to prevent pregnancy?’’ about-esc/news/how-do-levonorgestrel. Accessed March 1, 2013.
18. Massai MR, Forcelledo ML, Brache V, et al. Does meloxicam increase the incidence of anovulation induced by single administration of levonorgestrel in emergency contraception? A pilot study. Hum Reprod. 2007;22(2):434-439.
19. Marions L, Hultenby K, Lindell I, Sun X, Sta°bi B, Gemzell Danielsson K. Emergency contraception with mifepristone and levonorgestrel: mechanism of action. Obstet Gynecol. 2002;100(1):65-71.
20. Durand M, del Carmen Cravioto M, Raymond EG, et al. On the mechanisms of action of short-term levonorgestrel administration in emergency contraception. Contraception. 2001;64(4):227-234.

Cite this article:
Lakshmi. Critical of Endometrial Dynamic Ovulatory Effects in Emergency Contraception with Ulipristal Acetate. *American Journal of Oral Medicine and Radiology*, 2015, 2(4), 265-269.