Coll. Antropol. **38** (2014) 1: 379–384
Review

Ulipristal Acetate in Emergency Contraception

Marina Šprem Goldštajn, Dinka Pavičić Baldani, Lana Škrgatić, Branko Radaković, Hrvoje Vrčić and Tomislav Čanić

University of Zagreb, School of Medicine, University Hospital Center Zagreb, Department of Obstetrics and Gynecology, Division of Human Reproduction, Zagreb, Croatia

A B S T R A C T

Despite the widespread availability of highly effective methods of contraception, unintended pregnancy is common. Unplanned pregnancies have been linked to a range of health, social and economic consequences. Emergency contraception reduces risk of pregnancy after unprotected intercourse, and represents an opportunity to decrease number of unplanned pregnancies and abortions. Emergency contraception pills (ECP) prevent pregnancy by delaying or inhibiting ovulation, without interfering with post fertilization events. If pregnancy has already occurred, ECPs will not be effective, therefore ECPs are not abortificants. Ulipristal acetate (17α-acetoxy-11β-(4N-N,N-dymethilaminophenyl)-19-norpregna--4,9-diene-3,20-dione) is the first drug that was specifically developed and licensed for use as an emergency contraceptive. It is an orally active, synthetic, selective progesterone modulator that acts by binding with high affinity to the human progesterone receptor where it has both antagonist and partial agonist effects. It is a new molecular entity and the first compound in a new pharmacological class defined by the pristal stem. Up on the superior clinical efficacy evidence, UPA has been quickly recognized as the most effective emergency contraceptive pill, and recently recommended as the first prescription choice for all women regardless of the age and timing after intercourse. This article provides literature review of UPA and its role in emergency contraception.

Key words: *emergency contraception, ulipristal acetate*

Introduction

Despite the widespread availability of highly effective methods of contraception, unintended pregnancy is common. In both US and EU it is estimated that about half of all pregnancies are unplanned[1,2]. Situation in Croatia is estimated to be similarly unsatisfactory[3]. More than half of unwanted pregnancies – an estimated 45.5. million worldwide – are resolved by induced abortion each year[4]. Unplanned pregnancies have been linked to a range of health, social and economic consequences[1].

Emergency contraception (EC) is defined as the use of any drug or device used after an unprotected sexual intercourse or contraceptive method failure to prevent an unwanted pregnancy[5]. It is an occasional contraception method and should not replace regular contraception. EC significantly reduces the risk of unintended pregnancy after the sexual intercourse[6–8.] It has been estimated that millions of unintended pregnancies could be avoided if effective EC were widely accessible[9]. While interventions to make EC available have clearly failed in reducing abortion rates[10], it has been well recognized that EC is underused worldwide. In order to benefit from lessons learned and to secure positive population impacts from introducing dedicated ECPs in Croatia, EC methods and policies have been recently evaluated and four actionable points were recognized[11].

Methods used postcoitally included estrogen only regimen, combination of estrogen and levonorgestrel (LNG), LNG only, mifepristone and insertion of a copper intrauterine device (IUD)[6]. Recently, a new class of progesterone receptor modulator ulipristal acetate has been introduced[6]. Up on the superior clinical efficacy evidence, UPA has been quickly recognized as the most effective ECP[6,7] and recently recommended as the first choice ECP[12] for all women regardless of the age and timing after intercourse. UPA is considered to be a pluripotent molecule, already confirmed to be effective in preoperative treatment of uterine fibroids[13,14] and intensively investigated in various different indications[15].

Objective of this paper is to provide overview on UPA and its role in EC.

Received for publication June 8, 2013

Emergency Contraception

Following unprotected sexual intercourse, pregnancy is likely to result only during the fertile period that extends from 5 days before ovulation to the day of ovulation[16]. Once released, oocyte deteriorates rapidly to a point where fertilization is unlikely. During this fertile period probability of conception varies. In estimating the need for emergency contraception after the unprotected intercourse, it is important to consider variability of the ovulation, and major discrepancy observed between women's self-report of stage of a menstrual cycle and the dating calculation based on endocrine data[17]. As it is difficult to accurately predict the exact stage of the menstrual cycle at which unprotected intercourse occured, emergency contraception is generally indicated at any time of the cycle[6–8].

Yuzpe method was introduced in late 1970s, and consisted of 200 mcg ethinyl estradiol and 1000 mcg levonorgestrel divided in two doses, and given within 72 h after the intercourse[18]. It has remained the standard hormonal EC method until the introduction of LNG only and mifepistrone regimens[19,20]. LNG only regimen is more effective and causes fewer side effects compared to the Yuzpe regimen[19]. It is to be given in a single 1.500 mcg dose within 72 hours after the intercourse. Its key limitation is decrease in efficacy over the time after the intercourse, as well as inability to prevent ovulation once the LH surge has started[19–23]. Mifepistrone is effective and well tolerated in EC, but for social and political reasons it is available for EC only in Russia and China[16,24]. UPA is the first drug that was specifically developed and licensed for use as an emergency contraceptive. It is to be given in a single 30 mg dose, within 120 h after the intercourse.

A major barrier to the widespread acceptability and use of EC is concern regarding mechanisms of action of EC methods. The best available evidence indicates that emergency contraception pills (ECP) prevent pregnancy by delaying or inhibiting ovulation[6–8,16,23] therefore ECPS do not seem to interfere with postfertilization events. Endometrial effects of ECP do not contribute to their efficacy in EC. If pregnancy has already occurred, ECPs will not be effective, therefore ECPs are not abortificants[6–8,12]. When IUD is used as a regular or emergency method of contraception, it acts primarily to prevent fertilization. EC insertion of a copper IUD is significantly more effective than use of ECPs, reducing the risk of pregnancy by more than 99.9%[8,25]. Such a high level of effectiveness implies that emergency insertion of a copper IUD might prevent some pregnancies after fertilization[6].

The EC should be taken as early as possible but no later than 120 hours for IUD and UPA, and no later than 72 hours for LNG. Inserting IUD for emergency contraception has the advantage of providing further contraception, while all ECP users need to use additional barrier methods till end of the cycle during which they took ECP[6].

UPA – Structure

The development of molecules with specific steroid antagonist properties holds great promise for a variety of therapeutic applications. Ulipristal acetate (17α-acetoxy-11β-(4N-N,N-dymethilaminophenyl)-19-norpregna-4,9-diene-3,20-dione) was first synthesized by Research Triangle Institute under a contract with the National Institute of Child Health and Human Development (NICHD) for the development of new compounds that exhibit selective inhibition of the progesterone receptor with minimal effect on other steroid receptors. It is therefore a new molecular entity and the first compound in a new pharmacological class defined by the pristal stem. Its hormonal and antihormonal activity, selectivity and potency of its proximal metabolites were thoroughly evaluated[26,27].

UPA – Pharmacodynamics

UPA is an orally active, synthetic, selective progesterone modulator that acts by binding with high affinity to the human progesterone receptor[28,29], where it has both antagonist and partial agonist effects[21]. The drug has minimal affinity for the androgen receptor and no affinity for the human estrogen or mineralocortocoid receptors[29]. Although UPA has demonstrated some affinity for gluccocorticoid receptor in animals, no antiglucocorticoid effects have been observed in humans. Moreover, its glucocorticoid receptor antagonist activity is much reduced compared to that of mifepistrone[27] indicating that ulipristal acetate belongs to a new class of progesterone receptor modulators with dissociated glucocorticoid activity.

The key UPA mechanism of action in emergency contraception is to inhibit or to delay ovulation, although it is not fully clear by which mechanism this occurs[23,26–29]. A series of clinical pharmacodnynamics studies found that when administered at a point in the menstrual cycle prior to the onset of the LH surge, or before the peak in LH level had been reached, UPA significantly delays the LH peak by at least five days. When administered prior to the LH peak, UPA significantly delayed follicular rupture[31]. In a placebo controlled study in women with normal menstrual cycles, single doses of UPA 10, 50, 100 mg administered at the mid follicular stage with the follicle diameter of 14–16 mm significantly suppressed lead follicle growth, which lead to a dose dependent delay in folliculogenesis and plasma estradiol levels suppression[31]. Double blind crossover randomized placebo controlled study demonstrated that a single UPA dose of 30 mg given immediately prior ovulation significantly delayed follicular rupture even in women in whom LH surge has already commenced[23]. This indicates that UPA is effective during a longer period compared to LNG, which needs to be administered before the onset of LH surge in order to effectively prevent pregnancy[22]. However it is important to recognize that if UPA is administered after the LH peak being reached, follicular rupture

is not delayed[23]. Animal studies indicate that UPA may have a direct inhibitory effect on follicular rupture[30].

Endometrial effects of UPA were shown to be dose dependent. Following a single UPA dose of 10, 50 and 100 mg given in the early luteal phase and within 2 days of LH surge, endometrial thickness was reduced in a dose dependent manner with statistic difference, for all doses combined and *vs*. placebo[32]. The decrease between 10 and 50 mg appeared to be minimal. In addition to this, alterations in progesterone dependent markers of implantation also were observed in endometrial glandular epithelium[32].

UPA had a dose dependent effect on menses when administered in mid luteal phase. Higher doses (100–200 mg) were associated with earlier menses (33 ADIS 20) Clinical trials have showed that a cycle length was increases by a mean of 2.5 days. There was no indicator of cycle lenght being influenced by the time of the menstrual cycle in which UPA was given (34 ADIS 21).

UPA – Pharmacokinetics

In a study of 20 women under fasting conditions following the administration of a single 30 mg oral dose, UPA was demonstrated to be rapidly absorbed. It reached mean peak plasma concentrations (Cmax) of the drug and its major active metabolite mono-demethylated ulipristal acetate of 176 ng/mL and 69 ng/mL respectively at 0.9 and 1.0 hours[28,29]. Corresponding values for the area under the plasma concentration-time curve from time zero to infinity AUC were 556 and 246 ng h/mL.

A high fat meal reduces mean Cmax by –45%, and delays tmax from a median of 0.75 hours to 3 hours, and mean AUC is increased by 24% compared with the administration in the fasting state[28,29]. Similar was observed with the main metabolite. In despite of this finding, phase III trials have not demonstrated any effects of concomitant food intake and UPA efficacy[35].

UPA is highly bound to plasma proteins (>94%) albumin, alpha-1-acid-glycoprotein and high density lipoprotein[28,29]. Following ingestion, UPA is intensively metabolized in the liver to mono-demethylated metabolites of which only the mono-demethylated metabolite is pharmacologically active. In vitro studies show that metabolism is predominantly mediated by cytochrome P450 (CYP)3A4 enzymes, and to a lesser extent by CYP1A2 and CYP2D6[28,29].

Excretion of UPA is primarily via the feces. After a single dose of 30 mg micronized UPA, 32 hours is the estimated terminal elimination plasma half-life for UPA, and 27 for mono-demethylated-ulipristal acetate[28,29].

No differences have been observed between women of different ethnic groups in clinical studies[25,26]. Pharmacokinetic studies in women with renal impairment or in women aged <16 years have not been performed. Repeated UPA doses in animal studies resulted in some embryo-fetal loss, but at doses low enough to maintain gestation, no indication of any teratogenic potential has been detected[28,29]. As for any new molecular entity, the sum of information on the impact of exposure to UPA in early pregnancy remains limited, however currently raising no concern. An online registry has been established in order to facilitate the collection of information on pregnancies that were exposed to UPA in the early stages of pregnancy.

Drug interaction studies have not been performed with UPA. Having in mind major CYP3A4 metabolism pathway, interactions are possible when co-administered with agents that induce or inhibit CYP3A4[28,29]. Therefore, co-administration of CYP3A4 inducers (rifampicin, phenitoin, phenobarbital, long tem use of ritonavir, ECP containing levonorgestrel) or agents that increase gastric pH is not recommended as plasma concentrations of UPA may be decreased leading to a loss of efficacy.

Having in mind UPA's affinity for progesterone receptor, it could interfere with progesterone actions. Although the use of UPA is not contraindicated to the continued use of regular hormonal contraception, it is possible that the contraceptive action of combined hormonal contraceptives (CHC) and progesterone only contraceptives (POC) may be reduced[29].

UPA – Efficacy

The effectiveness of a preventive therapy is best measured by comparing probability that the condition will occur if the therapy is used to the probability that it will occur without treatment. For majority of preventive therapies effectiveness is determined by randomized clinical trials comparing treatment to placebo. In the case of emergency contraception placebo controlled trials are considered to be non ethical. Inital EC efficacy was demonstrated in noncomparative observational trials. Therefore, the chance that pregnancy would occur in the absence of EC is estimated indirectly using published data on probability of pregnancy on the each day of the menstrual cycle[38,39]. The estimate is compared with the actual number of pregnancies observed after treatment in observational treatment trials. EC effectiveness calculation obviously involves many assumptions that are hard to validate.

The efficacy of UPA has been evaluated during phase II and III clinical research: one phase II trial[34] and two phase III[38,39] multicentre trials in women requesting emergency contraception following unprotected sexual intercourse. Two trials were randomized, single[35] or double[34] blind non-inferiority trials that compared pregnancy rates between UPA and LNG. The third open label study[39] compared pregnancy rates between UPA and those estimated in the absence of EC. Two randomized trials compared the efficacy of UPA and LNG, one up to 72 hours after sexual intercourse[34], and the other up to 120 hours after the intercourse[38]. When these two studies of a similar design were combined in a meta-analysis, UPA was found to have 42% lower pregnancy rate than LNG within 72 hours after the intercourse: in the LNG treatment group (N=1625) there were 35 pregnancies,

while in UPA tretment group (N= 1617) there were 22 pregnancies[38]. Even more important, within 24 hours after the intercourse, during the day of the best LNG efficacy, UPA was found to have 65% lower pregnancy rate than LNG: in LNG treatment group (N=600) there were 15 pregnancies, while in UPA group (N=584) there were 5 pregnancies[38]. In the open label trial, the pregnancy rate in patients receiving UPA within 48–120 hours from unprotected sexual intercourse was significantly lower than that of expected pregnancy rate in the absence of emergency contraception[39]. This study delivered another important learning, that unlike LNG, UPA has demonstrates sustained efficacy when administered at any time between 48–120 hours from unprotected intercourse[39].

Rational behind significantly lower pregnancy rates on UPA when compared to LNG seems to be higher UPA efficacy in postponing imminent ovulation as LNG is no more effective than placebo in preventing ovulation after the onset of the LH surge, and after the follicular diameter has reached 15–17 mm. On the contrary, UPA can effectively delay ovulation even after the onset of the LH surge (till it reaches its peak concetration), and follicular diametar reached 18–20 mm. Additional efficacy related advantage of UPA is sustained efficacy through 120 hours from unprotected sexual intercourse.

UPA – Tolerability and Safety

In all trials UPA was generally well tolerated, with majority of side effects being mild to moderate in severity and resolving spontaneously in 89–94%. Tolerability of UPA seems to be comparable to LNG[34,38,39].

The most frequently reported UPA treatment related adverse effects were headache, nausea, dymenorrhea and abdominal pain, a profile similar to that reported in LNG comparative groups.

In an open lable phase II study the most frequently reported treatment related adverse effects (AE) of UPA were headache (9.3%), nausea (9.2%) and abdominal pain (6.8%)[39]. Other AE reported in this study were dysmenorrhoea (4.15%), dizziness (3.5%) and fatigue (3.4%).

In another phase III study UPA was demonstrated to be as well tolerated as LNG[35]. The most common adverse events in UPA and LNG treatment groups were headache (19% *vs.* 18.5%) nausea (13% *vs.* 11.5%), dysmenorrhoea (13% *vs.* 14.5%), fatigue (5.5.% *vs.* 4%) and abdominal pain (5% *vs.* 6.5%)[38].

UPA was generally associated with delayed onset of menses[31,35,36]. Mean menstrual cycle length increased by 2.1[38], 2.6[31] and 2.8[39] days in UPA groups, while the onset of menses was a mean of 1.2[38] and 2.1[34] days earlier in LNG groups.

UPA has not affected the duration of bleeding[38].

Intermenstrual bleedings with UPA in most cases were described as spotting and were reported by 8.7% of women compared of 3.3% before enrolment[39].

There were no changes of clinical significance in complete blood count, hepatic and renal function, lipids and random glucose analysis in 100 women monitored before and after UPA treatment[36].

There are no medical contraindications to the use of combined or progestin only ECPs with the exception of pregnancy[6–8,12]. UPA is a novel chemical entity and is contraindicated in existing or suspected pregnancy[29]. As for any new molecular entity, the sum of information on the impact of exposure to UPA in early pregnancy remains limited and currently raising no concern[6–8,12,29]. Although no teratogenic potential was observed, animal data are insufficient with regard to reproduction toxicity[29]. Therefore, a pregnancy registry has been established in order to facilitate the collection of information on pregnancies in EU that were exposed to UPA in early stages of pregnancy, allowing further investigation[29]. The key reason ECP should not be used in pregnancy is not because they are harmful but because they are ineffective[6].

UPA is lipophilic compound and therefore excreted in the human milk. Risk to the breast-fed child cannot be excluded. After the intake of UPA, brestfeed should be discontinued for a week. During this time it is recommended to express and discard the milk in order to stimulate lactation[29].

A rapid return of fertility is likely following UPA treatment, therefore continuing or initiating regular contraception is recommended as soon as possible[29].

Conclusion

UPA is the first of a new class selective progesterone receptor modulators that acts by binding with high affinity to the human progesterone receptor where it has both antagonist and partial agonist effects. It is the first entity specifically developed for EC, but it is also intensively investigated in other indications. UPA provides effective, sustained and well tolerated emergency contraception when taken within 120 hours after unprotected intercourse or contraceptive failure. Before prescribing UPA and all other ECPs pregnancy must be excluded, usually by reviewing dates and the nature of the last period. Unlike LNG, UPA is able to prevent follicular rupture and to potentially prevent pregnancy even when given in advanced follicular stage of the menstrual cycle and thus provides a longer treatment window than LNG. Because of superior efficacy within 24 hours, 72 hours and 120 hours from unprotected intercourse when compared to LNG, UPA is recognized as the most effective ECP, and recently recommended as the first prescription choice for all women regardless of the age and timing after intercourse.

REFERENCES

1. GOLD RB, SONFIELD A, RICHARDS CL, Next steps for America's family planning program, Guttmacher Institute, accessed 23.04.2013. Available from: URL: http://www.guttmacher.org/pubs/NextSteps.pdf — 2. KSIHEN M, BELFIELD T, J Fam Plann Reprod Health Care, 32 (2006) 211. — 3. ŠPREM GOLDŠTAJN M, PAVIČIĆ BALDANI D, ŠIMUNIĆ V, Gynaecol Perinatol, 21 (2013) 133. — 4. HENSHAW SK, SINGH S, HAAS T, Int Fam Plan Perspect, 25 (1999) 30. DOI: 10.2307/2991869. — 5. INTERNATIONAL CONSORTIUM FOR EMERGENCY CONTRACEPTION, What is emergency contraception, accessed 23.04.2013. Available from: URL: http://www.cecinfo.org. — 6. TRUSSEL J, BIMLA SCHWARZ MD. Emergency contraception. In: HATCHER RA, TRUSSEL J, NELSON AL, CATES W, KOWAL D, POLICAR M (Eds) Contraceptive Technology (Ardent Media, New York 2011). — 7. FIGO, Emergency contraceptive pills, Medical services and delivery guidelines, International consortium for emergency contraception 2012, accessed 23.04.2013. Available from: URL: http://www.cecinfo.org/custom-content/uploads/2013/03/Medical-and-Service-Delivery-Guidelines-English-2012.pdf — 8. CHENG L, CHE Y, GULMEZOGLU AM, Methods of emergency contraception, Cochrane Summaries 2012, accessed 23.04.2013. Available from: URL: http://summaries.cochrane.org/CD001324/methods-of-emergency-contraception — 9. Consensus statement on emergennncy contraception. Consortium for emergency contraception. Contraception, 52 (1995) 211. — 10. RUSSELL J, ELLERTSON C, VON HERTZEN H, BIGRIGG A, WEBB A, EVANS M, FERDEN S, LEADBETTER C, Contraception, 67 (2003) 259. DOI: 10.1016/S0010-7824(02)00535-8. — 11. ŠPREM GOLDŠTAJN M, PAVIČIĆ BALDANI D, VRČIĆ H, OREŠKOVIĆ S, Coll Antropol, 36 (2012) 345. — 12. RABE T, ALBRING C, AHREND HJ, MUECK A, MERKLES E, KONIG K, MERKI G, Joint statement by the German Society for Gynecologic Endocrinology (DGGEF) and the Professional Association of Gynaecologists (BVF), Emergency contraception: an update, accessed 23.04.2013. Available from: URL: http://www.bvf.de/fach_info.php?r=1&m=0&s=0&artid=421. — 13. DONNEZ J, TATARCHUK TF, BOUCHARD P, PUSCASIU L, ZAKHARENKO NF, IVANOVA T, UGOCSAI G, MARA M, JILLA MP, BESTEL E, TERRILL P, OSTERLOH I, LOUMAYE E; PEARL I STUDY GROUP, N Engl J Med, 366 (2012) 409. DOI: 10.1056/NEJMoa1103182. — 14. DONNEZ J, TOMASZEWSKI J, VÁZQUEZ F, BOUCHARD P, LEMIESZCZUK B, BARÓ F, NOURI K, SELVAGGI L, SODOWSKI K, BESTEL E, TERRILL P, OSTERLOH I, LOUMAYE E; PEARL II STUDY GROUP, N Engl J Med, 366 (2012) 421. DOI: 10.1056/NEJMoa1103180. — 15. HRA PHARMA, accessed 23.04.2013. Available from: URL: http://www.hra-pharma.com/rd-pipeline.php. — 16. GEMZEL L,DANIELSSON K, Contraception, 82 (2010) 404. DOI: 10.1016/j.contraception.2010.05.004. — 17. NOVIKOVA N, WEISBERG E, STANCZYK FZ, CROXATTO HB, FRASER IS, Contraception, 75 (2007) 112. DOI: 10.1016/j.contraception.2006.08.015. — 18. YUZPE AA, LANCE WJ, Fertil Steril, 28 (1977) 932. — 19. WORLD HEALTH ORGANIZATION, TASK FORCE ON POSTOVULATORY METHODS FOR FERTILITY REGULATION, Lancet, 352 (1998) 428. — 20. WORLD HEALTH ORGANIZATION, TASK FORCE ON POSTOVULATORY METHODS FOR FERTILITY REGULATION, Lancet, 353 (1999) 697. — 21. PIAGGIO G, VON HERTZEN H, GRIMES DA, VAN LOOK PF, Lancet, 353 (1999) 721. DOI: 10.1016/S0140-6736(98)05718-3. — 22. CROXATTO HB, BRACHE V, PAVEZ M, COCHON L, FORCELLEDO ML, ALVAREZ F, MASSAI R, FAUNDES A, SALVATIERRA AM, Contraception, 70 (2004) 442. — 23. BRACHE V, COCHON L, JESAM C, MALDONADO R, SALVATIERRA AM, LEVY DP, GAINER E, CROXATTO HB, Hum Reprod, 158 (2010) 2256. DOI: 10.1093/humrep/deq157. — 24. CREMER M, MASCH R, Minerva Ginecol, 62 (2010) 361. — 25. TRUSSEL J, ELLERTSON C, Fertility Control Reviews, 4 (1995) 8. — 26. GAINER EE, ULMANN A, Steroids, 68 (2003) 1005. DOI: 10.1016/S0039-128X(03)00130-2. — 27. ATTARDI BJ, BURGENSON J, HILD SA, REEL JR, J Steroid Biochem Mol Biol, 88 (2004) 277. DOI: 10.1016/j.jsbmb.2003.12.004. — 28. MCKEAGE K, CROXTALL JD, Drugs, 71 (2011) 935. DOI: 10.2165/11207410-000000000-00000. — 29. EUROPEAN MEDICINES AGENCY, Ulipristal acetate 30mg: summary of product characteristics, accessed 23.04.2013. Available from: URL: http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001027/WC500023670.pdf. — 30. PALANISAMY GS, CHEON YP, KIM J, KANNAN A, LI Q, SATO M, MANTENA SR, SITRUK-WARE RL, BAGCHI MK, BAGCHI IC, Mol Endocrinol, 20 (2006) 2784. DOI: 10.1210/me.2006-0093. — 31. STRATTON P, HARTOG B, HAJIZADEH N, PIQUION J, SUTHERLAND D, MERINO M, LEE YJ, NIEMAN LK, Hum Reprod, 15 (2000) 1092. DOI: 10.1093/humrep/15.5.1092. — 32. STRATTON P, LEVENS ED, HARTOG B, PIQUION J, WEI Q, MERINO M, NIEMAN LK, Fertil Steril, 93 (2010) 2035. DOI: 10.1016/j.fertnstert.2008.12.057. — 33. PASSARO MD, PIQUION J, MULLEN N, SUTHERLAND D, ZHAI S, FIGG WD, BLYE R, NIEMAN LK, Hum Reprod, 18 (2003) 1820. — 34. CREININ MD, SCHLAFF W, ARCHER DF, WAN L, FREZIERES R, THOMAS M, ROSENBERG M, HIGGINS J, Obstet Gynecol, 108 (2006) 1089. DOI: 10.1097/01.AOG.0000239440.02284.45. — 35. US FDA, CENTER FOR DRUG REGULATION AND RESEARCH, Clinical pharmacology and biopharmaceutics reviews, accessed 23.04.2013. Available from: URL: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022474s000ClinPharmR.pdf — 36. DIXON GW, SCHLESSELMAN JJ, ORY HW, BLYE RP, JAMA, 244 (1980) 1336. — 37. WILCOX AJ, WINBERG CD, BAIRD DD, N Engl J Med, 333 (1995) 1517. DOI: 10.1056/NEJM199512073332301. — 38. GLASIER AF, CAMERON ST, FINE PM, LOGAN SJ, CASALE W, VAN HORN J, SOGOR L, BLITHE DL, SCHERRER B, MATHE H, JASPART A, ULMANN A, GAINER E, Lancet, 375 (2010) 555. DOI: 10.1016/S0140-6736(10)60101-8. — 39. FINE P, MATHÉ H, GINDE S, CULLINS V, MORFESIS J, GAINER E, Obstet Gynecol, 115 (2010) 257. DOI: 10.1097/AOG.0b013e3181c8e2aa.

M. Šprem-Goldštajn

University of Zagreb, School of Medicine, University Hospital Center Zagreb, Department of Obstetrics and Gynecology, Division of Human Reproduction, Petrova 13, 10000 Zagreb, Croatia
e-mail: marina.goldstajn@gmail.com

ULIPRISTAT ACETAT U HITNOJ KONTRACEPCIJI

SAŽETAK

Unatoč dostupnosti vrlo učinkovitih metoda kontracepcije, učestalost neželjenih trudnoća vrlo je visoka. Neplanirane trudnoće dovode do niza zdravstvenih rizika, te nose socijalne i ekonomske posljedice. Hitna kontracepcija umanjuje rizik od trudnoće nakon nezaštićenog spolnog odnosa, i predstavlja mogućnost za smanjenje broja neplaniranih trudnoća i pobačaja. Pilule za hitnu kontracepciju (eng. emergency contraceptive pill, ECP) spriječavaju trudnoću odgađajući ili inhibirajući ovulaciju, bez interferencije sa postfertilizacijskim procesom. Ukoliko je do trudnoće već došlo, ECP neće biti učinkovita. Stoga se ECP ne smatraju abortivnim sredstvima. Ulipristal acetat (UPA) (17α-acetoksi-

-11β-(4N-N, N-dymethilaminophenyl)-19-norpregna-4,9-dien-3,20-dion) je prvi lijek koji je posebno razvijen i licenciran za upotrebu kao hitni kontraceptiv. Ulipristal acetat je oralno aktivni, sintetički, selektivni modulator progesteronskih receptora koji djeluje vežući se s visokim afinitetom za humani receptor za progesteron. Posjeduje i antagonističke i parcijalno agonističke učinke. Ulipristal acetat se smatra novim molekularnim entitetom i prvom komponentom farmakološke klase definirane kao pristalna osnova. S obzirom na dokazan klinički superioran učinak, UPA je brzo prepoznat kao najučinkovitije sredstvo za hitnu kontracepcijsu, te je nedavno preporučen kao lijek prvog izbora za sve žene bez obzira na dob. Ovaj članak daje pregled literature o UPA i njegovoj ulozi u hitnoj kontracepciji.