Medical Abortion: An overview and management of Mifepristone related side effects and complications

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Summary

Mifepristone, first developed in France in 1980 also known as RU-486, blocks the actions of progesterone. After undergoing clinical trials it was licensed for medical termination of pregnancies.

Mifepristone is a safe, effective and economical alternative among abortion methods used in many of the developed countries.

Although safe and effective, the method has side effects and carries risks.

Side effects are an expected part of medical abortion. Some arise from the abortion process itself and some from the medications used.

Abdominal cramps and bleeding are normal consequences of the abortion process, but may exceed the woman's expectations due to previous experiences.

As with surgical abortions, a small percentage of incomplete terminations can be experienced.

Nausea and vomiting, which are common nuisances at the early stages of pregnancy, although usually self-limiting can

Medikal düşük: Mifepristona bağlı yan etki ve komplikasyonların gözden geçirilmesi ve yönetimi

Özet

Mifepriston, RU-486 adıyla da bilinen, ilk kez 1980 yılından beri Fransa'da başlamak üzere giderek yaygınlaşan, medikal düşükler için Dünya Sağlık Örgütü tarafından önerilen progesteron antagonistidir.

Özellikle misoprostol ile birlikte kullanıldığında güvenli, etkin ve ekonomik bir düşük seçeneği olması, evde gerçekleşmesi nedeniyle kadının mahremiyetinin korunmasına olanak sağlaması, girişimsel bir yöntem olmaması ve oluşan yan etkilerin genellikle kendi kendini sınırlaması nedeniyle kadınlar arasında tercih edilmesine neden olmuştur.

Kramplar, ağrı, bulantı, kusma, diyare ve vajinal kanama gibi yan etkiler düşük eyleminin bir parçası olup, kullanılan ilaçlara bağlı olarak da gelişebilir.

Bulantı ve kramplar mifepristona ait yan etkilerken, ateş, üşüme-titreme ve yine kramplar misoprostole bağlı olarak görülebilir.

be increased.

Headache and dizziness are usually mild and self-limiting.

Hot flushes and sensations of warmth or fever are also fairly common side effects of medical abortion which are usually short-lived and resolve spontaneously.

Endometritis, especially in patients screened and treated for STI's, is a rare complication of medical abortion.

Previous allergic reaction to one of the drugs involved, documented history of familial porphyria, adrenal insufficiency, known or suspected ectopic pregnancy, clotting disorders or anticoagulant therapy, are absolute contraindications to medical abortion.

Caution is also required in long-term corticosteroid therapy, an IUD in place and severe anemia.

Key words: mifepristone, misoprostol, medical abortion, side effects

Ağrı en çok gebelik materyalinin uterin kaviteden atılması sırasında görülür ve kadının yaşı, gebelik haftası, gebelik öyküsü, korku, endişe ve alınan destek gibi ölçütlerle değişkenlik gösterir. Ağrı basit ağrı kesicilerle kontrol altına alınabilir. Siddetli ve sürekli ağrı ileri tetkik gerektirir.

Kanama ortalama olarak 9-17 gün kadar sürer.

Geçmişte kullanılan ilaçlara karşı allerjik reaksiyon gelişmiş olması, ailesel porfiri öyküsü, adrenal yetmezlik, ektopik gebelik, kanama bozuklukları, antikoagulan kullanımı kesin kontrendikasyonları oluştururken, aşırı anemi, rahim içi araç varlığı ve uzun süreli kortikosteroid kullanımı dikkatli olunması gereken durumlardır.

Anahtar kelimeler: mifepriston, misoprostol, medikal düşük, yan etkiler.

Mifepristone, a synthetic steroid also known as RU-486, which antagonizes the actions of progesterone, was developed in France in 1980. After undergoing clinical trials it was licensed for the use of medical termination of pregnancies in France in 1988, the UK in 1991, and the US in 2000.1,2

Mifepristone, recommended in the list of essential medicines by the World Health Organisation, is a safe, effective and economical alternative among abortion methods. It has approval in many of the developed countries and underway of legal procedures and trials in many of the developing countries. 1-3

Literature reveals information about the administration, effectiveness as well as side effects and risks of mifepristone.4,5

Mifepristone is recommended to be administered with a prostaglandin analogue, commonly misoprostol, to facilitate the expulsion of the gestational material. This combination, used for medical termination of pregnancy lessens the necessity for surgical intervention in most of the cases.^{1,6,7}

The possibility for privacy, since women can safely self-administer misoprostol at home, the mild nature of the side effects and the non-invasive treatment regimen resulted in high degrees of satisfaction with the method.6-9

Pregnancy always has its own potential risks for any woman, but when compared with continuing the pregnancy, mifepristone is reported to carry thirteen times less risk of mortality.5,10

Mifepristone can be administered as soon as an intrauterine pregnancy is confirmed, preferably by the help of a transvaginal ultrasound, by confirming the double decidual sac sign and the presence of the yolk sac at about 5 weeks.3, 11, 12

A positive pregnancy test without the ultrasonographic confirmation of an intrauterine sac is a dilemma for the practitioners which needs to be resolved. In this case, the pregnancy may be a very early one, a missed abortion, or an ectopic pregnancy; hence it is crucial to confirm that the pregnancy was intrauterine at the follow-up visit in case the provider decides to carry out the medical termination rather then to wait and confirm before the procedure starts.¹³

Side effects such as cramping, nausea, vomiting, diarrhea, and vaginal bleeding are a predictable part of medical abortion. They are resulted either from the abortion process itself or from the medications used in combination or alone and are increased directly with gestational age.14,15

While the most common mifepristone-related side effects present as nausea and cramping; misoprostolrelated side effects are usually cramping, fever, and chills. These side effects are reported to be well accepted by 85% of the women and pain, affecting 90% of women, is stated as a tolerable side effect by 74%.16

Pain intensity and request for relief are modified by factors such as age and background of the woman, gestational age, previous history of pregnancy, fear, anxiety and out coming support during the procedure. Pain is related both to the expulsion of the gestational sac and embryo from the uterine cavity and to prostaglandin side effect.

Health-care providers are obliged to give adequate support and counseling before the procedure and analgesics such as NSAIDs which are sufficient to control the pain in most cases should be readily available for all women beforehand.^{17,18}

Severe, persisting pain should raise suspicion and important causes such as ectopic pregnancy should be ruled out.14, 16

Varying results of studies from France and the United States and the original label for 200 mg mifepristone tablets report the duration of vaginal bleeding after using mifepristone for medical abortion, which is referred to a very heavy period or early miscarriage, as 9-17 days with a maximum of 69 days. Overall, it has been shown that the mean bleeding or spotting duration was 24 days.^{17, 19, 20}

It is reported that 2% to 10% of women require surgical intervention due to incomplete termination, continuing pregnancy or merely to take control of bleeding. In a minority of women, heavy vaginal bleeding may call for hospital admissions and studies done with large series have revealed transfusion rates of less than 0.1%. In case of retained products, infections may occur, and antibiotherapy may be needed.1,6,7 14,21

Bleeding is heaviest usually at the time of passing of tissues and is commonly more prolonged compared to the surgical procedure. Although expected this may contradict with the woman's previous experiences of bleeding. On-call evaluations of bleeding and informing the patient in advance of what to expect are sometimes needed with medical abortion cases in the presence of symptoms such as dizziness, weakness or fatigue.17

Surgical intervention is required in less than 1% of first trimester medical abortions in case of excessive bleeding.^{22, 23}

Subjective symptoms caused by continuing heavy bleeding resistant to medical treatment, presence of orthostatic instability, a low Hb level, and the patient's preference for surgical aspiration are indications for surgical evacuation. 14, 15, 17

The clinical state of the patient determines the plans of monitoring or any type of intervention.^{24, 25}

More frequently than surgical abortions, 2% to 5% of medical abortion cases, result in incomplete termination of pregnancy which may require vacuum aspiration.

Inspite of the fact that incomplete rates are higher than the surgical methods, large studies have shown high rates of acceptability and satisfaction even with women who experienced an incomplete abortion of which more than two thirds reported that they would use the method again. Overall, more than 85% of women stated that they would both recommend and choose the method again. 9, 26

Nausea and vomiting, which are also natural and common nuisances at the early stages of pregnancy, can be increased and sometimes accompanied by diarrhea after misoprostol administration, are shown to be usually self-limiting.27

Headache and dizziness are among mild and self-limiting side effects

Dizziness may be caused by any of the medications or as a result of the abortion process. Usually bed rest, hydration, slow position changes and assistance with ambulation unless associated with high volume loss are sufficient precautions to take.14

Both mifepristone and misoprostol, may cause drug reactions which may result in hot flushes, sensations of warmth or fever. These are side effects of medical abortion which are encountered frequently, usually short-lived and resolving spontaneously. High temperatures exceeding 38°C, persisting more than 24 hours calls for careful evaluation for infection.17

Routine administration of prophylactic antibiotics is not recommended for medical abortion. Endometritis, is rarely seen, since patients get a chance to be screened and treated for genitourinary tract infections at the time of administration. Persistent pelvic pain accompanied or not by irregular bleeding, fever following the days after the expulsion of the gestational material should alert physicians for endometritis or incomplete abortion. 13, 14

Mifepristone, only effective in treating intrauterine pregnancy may yield one of the most life threatening complications of a gestational state in case of an undiagnosed ectopic pregnancy. Every effort must be made before the medical abortion process in order not to miss an ectopic pregnancy. A pseudogestational sac, which may mimic an early intrauterine gestational sac, should always be kept in mind until the presence of a yolk sac or a fetal pole is depicted by ultrasound. 12, 17

Previous allergic reaction to one of the drugs involved, documented history of familial porphyria, adrenal insufficiency, known or suspected ectopic pregnancy, clotting disorders or anticoagulant therapy, are the few absolute contraindications to medical abortion.

Moreover caution is also required in a range of circumstances such as long-term corticosteroid therapy, an IUD in place and severe anemia.

There is no evidence that age, anemia, breastfeeding, insulin-dependent diabetes or thyroid disease, multiple pregnancy, obesity, previous caesarean section, smoking, uterine malformations, previous cervical surgery represent any contraindications.²⁸

Unwanted pregnancies will continue to occur as a consequence of human sexuality and the topic of abortion will always be a controversial one but women will continue to seek safe, legal abortion methods.

Kaynaklar

- 1. Dickerson V, American College of Obstetricians and Gynecologists. ACOG letter on safety of RU-486, 7 December 2004[news release]. Accessed from http://www.acog.org/from_home/publications/press_releases/nr12-07-04.cfm on March 2010).
- 2. Baulieu EE. Contraception by the progesterone antagonist RU 486: a novel approach to human fertility control. Res Reprod 1987; 19: 3-4.
- 3. Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion. Evidence-based Clinical Guideline Number 7, September 2004. Accessed from www.rcog.org.uk On September 2010).
- 4. Ingham R, Lee E. Evaluation of Early Medical Abortion (EMA) Pilot Sites, Final Report. Accessed from http://www.bpas.org/js/filemanager/files/evaluation_of_early_medical_abortion_pilot_sites.pdf On August 2010.
- 5. Association of Reproductive Health Professionals What You Need to Know Mifepristone Safety Overview (Updated April 2008) Accessed from http://www.arhp.org/uploadDocs/mifepristonefactsheet.pdf on September 2010.
- 6. Schreiber CA, Creinin MD, Harwood B, Murthy AS. A pilot study of mifepristone and misoprostol administered at the same time for abortion in women with gestation from 50 to 63 days. Contraception 2005; 71: 447-450.
- 7. Faucher B, Baunot N, Madelenat P. The efficacy and acceptability of mifepristone medical abortion with home administration misoprostol provided by private providers linked to the hospital: a prospective study of 433 patients. Gynecol Obstet Fertil 2005; 33: 220-227.
- 8. Y. Li, F. Chen, T. Chen, S. Li, M. Chen, T. Kuo. Concurrent Use of Mifepristone and Misoprostol for Early Medical Abortion. Taiwanese Journal of Obstetrics and Gynecology2006; 45(4):325-8.
- 9. Ibis Reproductive Health Mifepristone and misoprostol regimen. Accessed from http://medicationabortion.com/mifepristone/index.html on September 2010.
- 10. Bartlett L, Berg C, Shulman H, Zane S, Green C, Whitebread S, et al. Risk factors for legal induced abortion-related mortality in the United States. Obstet Gynecol 2004; 103: 729-37.
- 11. World Health Organization. Safe abortion: technical and policy guidance for health systems. Geneva 2003.
- 12. Deborah Levine. Ectopic Pregnancy. Radiology 2007, 245, 385-97. Accessed from http://radiology.rsna.org/content/245/2/385. on September 2010.
- 13. Suzanne R. Trupin, MD, FACOG, Carey Moreno, BS. Medical Abortion: Overview and Management. 03/08/2002; Medscape General Medicine. 2002;4(1) © 2002 Medscape. Accessed frrom http://www.medscape.com/viewarticle/429755 on March 2010.
- 14. Kruse B, Poppema S, Creinin MD, Paul M. Management of side effects and complications in medical abortion. Am J Obstet Gynecol 2000; 183(2

Suppl): 65-75.

- 15. Spitz IM, Bardin CW, Benton L, Robbin A.Early Pregnancy termination with mifepristone and misoprostol in the United States. N Engl J Med 1998; 338(18): 1241-7.
- 16. Schaff EA, Eisinger SH, Stadalius LS, Franks P, Gore BZ, Poppema S. Low-dosemifepristone 200 mg and vaginal misoprostol for abortion. Contraception 1999; 59 (1): 1-6.
- 17. Management of the side effects and complications of early medical abortion. (Gestations <49 days). Accessed from http://www. amac.org.nz/Managing_Side_Effects. doc On March 2010.
- 18. World Health Organization, Frequently asked clinical questions about medical abortion, WHO Library Cataloguing-in-Publication Data 2006.
- 19. Grimes DA, Creinin MD. Induced Abortion: An Overview for Internists. Annals of internal medicine2004;140(8) 620-6
- 20. Medication Guide Mifeprex. Accessed from
- www.fda.gov/downloads/Drugs/DrugSafety/ucm088643.pdf . On September 2010).
- 21. Kahn JG, Becker BJ, MacIsaac L, et al. The efficacy of medical abortion: a meta-analysis. Contraception. 2000; 61:29-40.
- 22. Harper C, Winikoff B, Ellertson C, Coyaji, K. Blood loss with mifepristone-misoprostol abortion: measures from a trial in China, Cuba and India. Int J Gynaecol Obstet 1998; 63(1): 39-49.
- 23. Ashok PW, Penney GC, Flett GM, Templeton A. An effective regimen for early medical abortion: a report of 2000 consecutive cases. Hum Reprod 1998; 13(1O): 2965-5.
- 24. Wolman I, Jaffa AJ, Pauzner D, Hartoov J, David MP, Amit A. Transvaginal sonohysterography: a new aid in the diagnosis of residual trophoblastic tissue. J Clin Ultrasound 1996;24(5): 257-61
- 25. Dillon EH, Case CQ, Ramos IM, Holland CK, Taylor. KJ. Endovaginal US and Doppler findings after first-trimester abortion. Radiology 1993; 186(1): 87-91
- 26. Rachel K. Jones, Stanley K. Henshaw. Mifepristone for Early Medical Abortion: Experiences in France, Great Britain and Sweden. Perspectives on Sexual and Reproductive Health 2002;34(3) Special report.
- 27. El-Rafaey, H., D. Rajasekar, D, Abdalia M, Calder L, Templeton A. Induction of abortion with mifepristone (RU486) and oral or vaginal misoprostol. N Engl J Med 1995; 332(15): 983-7.
- 28. The ICMA Information Package on Medical Abortion. Information for health care providers. Accessed from http://www.medicalabortionconsortium.org/articles/for-health-care-providers/ on March 2010).

