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Radaković, Branko; Šprem Goldštajn, Marina

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Case report

Ectopic Pregnancy as Contraceptive Failure in Patient with Epilepsy

Branko Radaković and Marina Šprem Goldštajn

University of Zagreb, School of Medicine, Department for Gynecology and Obstetrics, Zagreb, Croatia

A B S T R A C T

Epilepsy is a common neurologic condition which includes many women's health issues. Menstrual disorders, reproductive endocrinological disturbances, ovulatory dysfunction and infertility appear to be relatively frequent in women with epilepsy. Clinical decision making which contraceptive regimen is optimal for an individual woman with epilepsy is one of the most challenging tasks when taking care of women with epilepsy. A higher incidence of breakthrough bleeding and contraceptive failure was determined among women using antiepileptic drugs. There is the increased risk for contraceptive failure with the use of P450 3A4 enzyme-inducing antiepileptic drugs (AEDs) such as phenobarbital, carbamazepine, phenytoin, felbamate, topiramate and oxcarbazepine. Therefore, it is recommended to use noninducing AEDs, or for those who use inducing AEDs, the use of oral hormonal contraceptive pills which contained equal or more than 50 μg of estrogen, or intrauterine devices. The aim of the article is to present woman with epilepsy who was used combined low dose oral contraceptive pills containing 20 μg of ethinyl estradiol which in interaction with carbamazepine resulted with ectopic tubar pregnancy.

Key words: *tubar pregnancy, epilepsy, oral contraceptives, drug interaction*

Introduction

Epilepsy is a common neurologic condition which includes many women's health issues[1,2]. Menstrual disorders, reproductive endocrine disturbances, ovulatory dysfunction, and infertility appear to be relatively common in women with epilepsy[2]. Clinical decision making which contraceptive regimen is optimal for an individual woman with epilepsy is one of the most challenging tasks when taking care of women with epilepsy[3,4]. A higher incidence of breakthrough bleeding and contraceptive failure was determined among women using antiepileptic drugs. There is the increased risk for contraceptive failure with the use of P450 3A4 enzyme-inducing antiepileptic drugs (AEDs) such as phenobarbital, carbamazepine, phenytoin, felbamate, topiramate and oxcarbazepine[1,2]. The aim of the article is to present woman with epilepsy who used combined low dose oral contraceptive pills which interacted with carbamazepine, resulting with ectopic tubar pregnancy.

Case Report

A 26-year multiparous was submitted to the Department for Gynecology and Obstetrics Medical School University of Zagreb due to abdominal pain, amenorrhoea and vaginal bleeding. She has a decade history of epilepsy as a result of trauma injury. The patient is treated with carbamazepine in a daily dose of 800 mg. She was treated for seven months by her general practitioner with monophasic, combined, low-dose oral contraceptive pills which contained 20 μg of ethinylestradiol and 75 μg of gestoden. During the gynecological exam tha patient signalized extremely painful sensation in the projection of right fallopian tube. Ultrasound was performed, and suspect ectopic right tubar pregnancy was determined with empty endometral cavity. The level of β-human chorionic gonadotropin was 1368 IJ/L, and was significantly lower for expected eight weeks amenorrhoea duration. The patient underwent urge laparoscopic surgery. Intraoperatively, right fallopian tube was thicker, with haemorrhagic content and incipient expulsion of ectopic pregnancy through the abdominal tubar orifice, with 250 mL of coaguls and blood in the coul de sac. Right salpingectomia was performed. There was no immediate and late postoperative complications. Pathologist confirmed the diagnosis of ectopic tubar pregnancy. The patient was released from the Department after two days.

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Discussion and Conclusion

Pre-pregnancy councelling in women with epilepsy includes information on interactions of antiepileptic drugs and oral contraceptives in order to prevent contraceptive failure, and to decrease the risk of unplanned or ectopic pregnancy in women with epilepsy. An interaction between AEDs and combined oral contraceptive pills was first proposed when the dose of estradiol in the oral contraceptive pills was reduced from 100 to 50 micrograms[1,2]. Since then, interaction studies have been undertaken to look for possible interactions between AEDs and the combined oral contraceptive pills. AEDs that induce hepatic microsomal enzymes may interact with hormonal contraception resulting in high contraceptive failure[3]. They increased estrogen metabolism and progesteron protein binding, decreased the concentration of both hormones and thus reducing contraceptive efficacy[2,4]. If woman, who is received enzyme induce AEDs (phenobarbital, carbamazepine, phenytoin, felbamate, topiramate and oxcarbazepine), wanted to use oral hormonal contraception, it is recommended to take preparation containing at least 50 micrograms of ethinylestradiol[1,5]. Progestin only pills are likely to be ineffective if used in combination with enzyme induced AEDs. Subdermal progestogen implants are not recommended in patients with enzyme induced AEDs because of high contraceptive failures rates[1,2]. Although depo medroxyprogesterone acetate injections are effective, they are not recommended as the first contraceptive choice due to serious side effects such as delayed return to fertility, and impaired bone health[2,5,6]. The use of intrauterine devices appeared to be good alternative for contraception in patients receiving enzyme induced AEDs due to the lack of side effects. During the past decade, new antiepileptic drugs have been introduced[1–3]. They exhibit lower potential for drug interactions than classic AEDs, mostly because of their pharmacokinetic characteristics. For example, vigabatrin, levetiracetam and gabapentin, exhibit few or no interactions with other AEDs. Furthermore, there are no interactions between the combined oral contraceptive pill, progesteron only pill, medroxyprogesterone injections or levonorgestrel implants and the AEDs valproic acid, vigabatrin, tamotrigine, gabapentin, tiagabine, levetiracetam, zonisamide, ethosuximide and the benzodiazepines[1,7,8]. Therefore, physicians have a duty to offer appropriate and accurate counselling to epileptic patient concerning optimal choice for the use of oral contraceptives for those considering this method as contraception. Recommendations included possible use of a noninducing AEDs, or for those who use inducing AEDs--use of an oral contraceptive pills containing equal or more than 50 micrograms of estrogen[1–4].

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M. Šprem Goldštajn

University of Zagreb, School of Medicine, Department for Gynecology and Obstetrics, Petrova 13, 10 000 Zagreb, Croatia
e-mail: marina.sprem@zg.t-com.hr

EKTOPIČNA TRUDNOĆA – KONTRACEPCIJSKA GREŠKA U BOLESNICE S EPILEPSIJOM

SAŽETAK

Epilepsija je relativno čest neurološki poremećaj koji bitno utječe na različite aspekte zdravlja žene. Poremećaj menstruacijskog ciklusa, reprodukcijski endokrinološki poremećaji i neplodnost značajno utječu na kvalitetu života žene s epilepsijom. Klinička procjena i izbor optimalnog kontracepcijskog protokola u žena s epilepsijom je veliki izazov s obzirom na česta probojna krvarenja i kontracepcijski neuspjeh koji se javljaju u žena koje koriste antiepileptike i oralnu hormonsku kontracepciju. S obzirom na povećani rizik kontracepcijskog neuspjeha u žena koje koriste antiepileptike koji induciraju jetrene mikrosomalne enzime (phenobarbital, karbamazepin, fenitoin, felbamat, topiramat i okskarbazepin), preporuka je korištenje oralne hormonske kontracepcije koja sadrži 50 ili više mikrograma etinil estradiola, materničnog uloška ili promjena osnovne terapije epilepsije primjenom nove generacije antiepileptika koji ne induciraju jetrene mikrosomalne enzime. Cilj ovog rada je prikazati ženu s epilepsijom koja je koristila kombiniranu niskodozažnu oralnu hormonsku kontracepciju koja sadrži 20 μg etinil estradiola i antiepileptik karbamazepin, što je rezultiralo kontracepcijskim neuspjehom i ektopičnom tubarnom trudnoćom.