LETTER

EMERGENCY CONTRACEPTION AND ECTOPIC PREGNANCY: REPORT OF 2 CASES

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The incidence of ectopic pregnancy has been increasing over the last few years, reaching a value of 1 case in 80 pregnancies, and it continues to be the main cause of maternal death during the first trimester in the United States.[1] The main causes of tubal ectopic pregnancy, which generally results from damage to or dysfunction of the fallopian tubes, are salpingitis, previous tubal surgeries, and alteration in tubal motility mainly due to the use of certain contraceptive methods.[2]

Emergency contraceptive methods have been developed to prevent undesired pregnancies after unprotected sexual intercourse and have been used for more than 20 years.[3-6] The most commonly employed methods are (a) the Yuzpe regimen, which recommends the administration of 2 doses of 100 µg ethinyl estradiol and 500 µg levonorgestrel at 12-hour intervals,[7] and (b) the exclusive use of 750 µg levonorgestrel in 2 doses separated by a 12-hour interval. The latter method has been applied in some countries since 1979, but only in 1994 did a coordinated study by the WHO show that its efficacy was superior to that of other emergency contraceptive methods available at the time.[8, 9]

Pulkkinen and Talo[10] described the physiology of tubal ciliary and myoelectrical activity. The static force of the cilia results in fluid flow toward the uterus; the spermatozoa overcome this, and cilia are not obligatory for normal implantation, since patients with congenital inactivity of all cilia (Kartagener´s syndrome) are able to have intrauterine pregnancies. It is the myoelectrical activity that plays a vital role in tubal propulsion. In general, estrogens stimulate tubal myoelectrical activity and progesterone inhibits it.[11]

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The mechanisms of the contraceptive action of levonorgestrel are believed to be multifactorial. Among these mechanisms, alteration in tubal motility may contribute to a delayed arrival of the egg in the endometrial cavity, a fact leading to the occurrence of ectopic pregnancy. Moreover, pharmacologic levels of progesterone may relax tubal myoelectrical activity to such an extent that transport through the isthmus does not occur.[12,13]

We report here 2 cases of ectopic pregnancy that occurred after the use of emergency contraceptive pills containing 0.75 mg levonorgestrel (Postinor 2®) by women without apparent risk factors for ectopic pregnancy.

CASE 1

A 36-year-old woman sought the Emergency Obstetric Service of a University Hospital in São Paulo due to menstrual delay and a small amount of vaginal bleeding of a 1-week duration. The patient reported an episode of unprotected sexual intercourse 17 days after the last menstrual period, which was followed by the correct use of Postinor 2.

Seventeen days after the use of the drug, the patient noted a small amount of vaginal bleeding that persisted until the time of the visit. The patient was a secundigravida and primipara (one previous spontaneous abortion) and reported regular menstrual cycles (bleeding for 5 days and a 30-day interval between cycles).

Examination of the patient at admission showed good general health, normal color and hydration, normotension, and a normal heart rate. The abdomen was soft and not tender upon deep palpation and sudden decompression. There was a small amount of blood discharged into the posterior vaginal fornix, with discrete bleeding through the external orifice of the cervix. The vaginal exam revealed an

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anteverted uterus of normal size and a left adnexal pouch that was tender upon combined palpation.

The urinary hCG test was positive. Transvaginal ultrasonography showed a uterus with parenchyma and normal dimensions, a 6-mm thick centered endometrium and an empty cavity. The right and left ovaries were normal. An oval and heterogenous image measuring 19 x 17 x 13 mm was visualized close to the left ovary in addition to a minimum amount of free fluid in the Douglas' cul-de-sac. Serum ß-hCG was 3,188 mU/mL upon initial determination.

In view of the stable initial clinical condition, serum hCG was again determined after 48 hours and was found to be 3,921 mU/mL. Based on the established diagnosis of evolving ectopic pregnancy, the patient was informed about the therapeutic possibilities and opted for pharmaceutical treatment, which consisted of the intramuscular injection of a single dose of methotrexate (50 mg/kg^2). The patient remained asymptomatic and was followed up on an outpatient basis until complete regression of serum ß-hCG values.

CASE 2

A 25-year-old woman was seen at the Emergency Obstetric Service of a University Hospital in São Paulo with complaints of strong hypogastric pain irradiating to the right iliac fossae and a small amount of genital bleeding of a 1-month duration. The patient reported that she had unprotected sexual intercourse 1 month before the onset of the clinical symptoms, and had used Postinor 2 correctly. The picture of progressive pelvic pain started 3 days after use of the drug, and the patient sought medical care. A condom was used as the contraceptive method. The patient was nulliparous, reported a previous spontaneous abortion, and had no pelvic infections.

Physical examination at admission showed that the patient was in good general health and hemodynamically stable. The abdomen was soft and discretely tender upon deep palpation of the hypogastrium and iliac fossae, with painless sudden decompression. Gynecologic examination showed a small amount of bleeding in the posterior vaginal fornix and the absence of bleeding through the external orifice of the cervix. The vaginal exam revealed a uterus of normal size and slightly tender adnexal pouches upon combined palpation. The adnexa were not palpable, but an irregular mass was detected that led to bulging of the posterior vaginal fornix. Laboratory exams and transvaginal ultrasonography were requested.

The urinary hCG test was positive. Transvaginal ultrasonography showed a uterus of normal dimensions, with no topical gestational sac or ovaries being visualized. A heterogenous nodular mass measuring approximately 6 cm in diameter surrounded by a hyperechoic halo was observed in the retrouterine region, suggesting an ectopic pregnancy. Serum ß-hCG was 2,354 mU/mL upon initial determination.

After establishment of the diagnostic hypothesis of ectopic pregnancy, the patient underwent exploratory laparotomy, which was performed without complications. During surgery, a ruptured right uterine tube, a small amount of free blood in the pelvis, and a saccular formation in the retrouterine excavation were observed. The latter was removed and sent for anatomopathologic examination. The exam showed normal embryologic tissue with necrosis and hemorrhagic areas. Right salpingectomy was also performed.

The patient had a good clinical evolution.

DISCUSSION

Several studies demonstrate that oral emergency contraceptives may be considered as safe methods for preventing undesired pregnancy after unprotected sexual intercourse. In 2000, Wellbery[14] reported a 75% reduction in the number of undesired pregnancies with the use of this emergency contraceptive method. In 2003, Trussell et al[6] published a clinical study on patients correctly using emergency contraception (2 doses of 0.75 mg levonorgestrel at a 12-hour interval, a maximum of 72 hours after unprotected sexual intercourse) and reported a pregnancy rate of 5.2%.

On the other hand, some authors have warned of the possibility of undesired effects after the use of this method. Sheffer-Mimouni et al[3] reported 3 cases of ectopic pregnancies after the use of levonorgestrel close to the ovulatory period, and warned that attention should be paid to the risk of tubal pregnancy in patients complaining of abdominal pain and genital bleeding after emergency contraception. Farkas[15] considered the method to be unsafe because of the observation of a 6.4% ectopic pregnancy rate in users of levonorgestrel, in addition to the high frequency of irregular genital bleeding.

The mechanism whereby levonorgestrel impairs conception after unprotected sexual intercourse is still controversial.[3] Levonorgestrel is an exogenous progestin that antagonizes the effect of gonadotropin release mediated by estrogens, which is vital for ovulation. Use of the drug during the periovulatory period is believed to delay or even inhibit follicular rupture or to interfere with the formation and function of the corpus luteum.[16-19]

When emergency contraception is performed during a period close to ovulation, the chance of modifying ovulatory function is lower, a fact that may explain the higher rates of failure observed after use during this period.[20] Administration of levonorgestrel during the preovulatory phase

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acts by altering the fertilization capacity of sperm and by increasing cervical mucus viscosity, which impairs the ascension of male gametes.[16] In addition, the drug is able to interfere with the preparation of the endometrium by modifying integrin molecules and steroidal receptors, events that decrease the nidation capacity of the blastocyst.[16,21,22] It should be emphasized that treatment efficacy is maximal (close to 100%) when the drug is taken up to 24 hours after unprotected intercourse. This observation, together with the reduced efficacy of the method with increasing time interval between coitus and the beginning of treatment, suggests that the mechanism of contraceptive action occurs mainly during fertilization and not during the period of blastocyst implantation.[20]

Another action frequently attributed to levonorgestrel is alteration of tubal motility. Inversion of tubal peristalsis and reduced fimbrial beating may contribute to a delayed arrival of the egg in the endometrial cavity.[3,23,24,25] Moreover, Paltieli et al[25] believe that reduced fimbrial beating by progesterone is dose-dependent. The same modification in tubal function could be a possible explanation for the occurrence of ectopic pregnancy after emergency contraception.[3]

We believe that the ectopic pregnancy in case report 2 was due to levonorgestrel, because unfertilized and fertilized ova remain in the ampulla for approximately 3 days.[26] During this period, depending on different causes, implantation may occur in the tubal mucosa, and clinical signs can be found shortly after this period.

The small number of cases reported in the literature, as well as the multifactorial etiologic character of ectopic pregnancy, impairs the establishment of an unquestionable causal relationship between emergency contraception with levonorgestrel and ectopic pregnancy. We report here 2 cases of patients who used emergency contraception with levonorgestrel and who did not show any other identifiable risk factor for ectopic pregnancy. We warn that special attention should be paid to patients who use emergency contraceptive methods and complain of genital bleeding and/or abdominal pain, in an attempt to anticipate the diagnosis of ectopic pregnancy and thus improve therapeutic outcome.

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