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Can women accurately assess the outcome of medical abortion based on self-assessment and low sensitivity urine pregnancy test ?

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Sous le sceau de l'Université Bretagne Loire

Thèse en vue du

DIPLÔME D'ÉTAT DE DOCTEUR EN MÉDECINE

Présentée par

Céline PIMENTEL

Née le 02 janvier 1986 à Gouvieux (60)

Test urinaire de faible sensibilité et auto-questionnaire: la patiente peut-elle apprécier seule l'efficacité de l'interruption volontaire de grossesse médicamenteuse?

Can women accurately assess the outcome of medical abortion based on self-assessment and low sensitivity urine pregnancy test?

Thèse soutenue à Rennes le 25 octobre 2017

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Table of Contents

List of university professors (2016-2017) **2-6**
List of university lecturers (2016-2017) **7-8**
Acknowledgements **9-10**
Table of contents **11**
List of appendices **12**
Introduction **13**
Matérials et méthods **14-16**
Study design and patients 14
Procedures 14-15
Interpretation of LSUP test 15
Self-performed survey 15
Statistical analysis 16
Résults **16-18**
Description flow chart 16
Characteristics of the women 17
MToP follow-up 17
Outcome of MToP 17
Primary objective 17-18
Secondary objective 18
Discussion **18-23**
Teratogenic effects of MToP 19
Ectopic pregnancies and MToP 19
Emergency post abortion consultations 19
What follow-up after abortion? 20
Choice of the LSUP test 20-21
Lost to follow-up problem 22
Highlights and limitations of our study 22-23
Conclusion **23**
Bibliography **24-26**
Glossary **27**
Appendices **28-34**

List of appendices

Figure 1: CheckTop® notice **28**
Figure 2: Flow chart **29**
Table 1: Characteristics of patients who have had an MToP **30**
Table 2: Comparison of patients according to the symptoms described **31**
Table 3: Tests performances **32**
Figure 3: Use and interpretation of Check Top® **33**
Table 4: Comparison between returners and no returners **34**

Introduction

Since 1990, there has been an average of 209 thousand annual abortions in France. The medication method was used for 57% of those terminations of pregnancy [1]. The medical termination of pregnancy (MToP) is simpler and requires fewer resources than surgical abortions. It also provides women with a choice of intervention.

Failures of MToP are rare within 63 days of gestation, with about 1% of ongoing pregnancies and 5% of incomplete abortions [2, 3]. Though exceptional, these failures can have extremely serious consequences, as continuing viable pregnancies after a failed medical abortion using misoprostol can result in congenital abnormalities in the infants [4]. Moreover, a pregnancy might remain unnoticed until the legal limit for induced abortion has passed. Because of those ongoing pregnancies, international guidelines persist in recommending follow-up care, either by a routine clinical follow-up or by a self-assessment of outcome at home [5-7].

In practice, the attendance at abortion follow-up visits is usually low, generally at about 60% [8]. Besides resulting in a poor assessment of abortion effectiveness, no-shows at scheduled appointments have a medical cost and complicate the organization of medical services. Some studies have indicated that medical abortion is associated with a more negative experience of care and lower acceptability than surgical abortion, which was partly attributed to the need for more follow-up visits [9]. In early medical abortions, a phone follow-up with a checklist of symptoms and with self-assessment by a low-sensitivity urine pregnancy (LSUP) test was proven as accurate and acceptable as a clinical follow-up [10-13]. In addition, prospective studies on remote post-abortion follow-ups lead to an improvement in compliance, with a loss to follow-up rate of between 13% and 30% [10, 12, 14].

Today, at Rennes University Hospital, patients are only offered conventional visits. To offer an alternative to post-abortion follow-up as well as to improve compliance and, hopefully, to decrease the rate of late ongoing pregnancies, we decided to test one of these urinary tests: the Check Top® test.

The primary objective is to analyze how the results of the test studied (self-performed questionnaire in association with a LSUP test) correlate with standard patient follow-up, consisting of a clinical examination, a blood hCG test and ultrasonography when needed. A secondary objective is to assess the benefit of LSUP tests in the follow-up of MToP by analyzing the concordance between qualitative results from the LSUP test and the blood human Chorionic Gonadotropin (hCG) test. Then we will describe the population of non-follow-up's patients.

Materials and methods

Study design and patients:

This prospective cohort study was performed between March 2017 and August 2017 at Rennes University Hospital. All the women who came for their post-abortion visit after an MToP were informed of this study. Eligible women were aged 18 years or older, able to understand the procedure and they gave written informed consent. Exclusion criteria were unscheduled consultation for an emergency post-abortion, inability to speak and understand French and being under guardianship or deprived of liberty.

This study was agreed to by the local ethical committee (IRB, France Avis n°: 16.103).

Procedures:

In our abortion unit, MToP are carried out until 63 days of gestation. All the women with an unwanted pregnancy were first seen by a nurse or a midwife to assess their eligibility for MToP in terms of gestational age and contraindications. The providers made a judgement regarding the place for misoprostol administration on the basis of the hospital's standard procedure and of the women's ability to reach a clinic within reasonable time in the event of a complication. The patients were free to choose to use misoprostol at the place of their convenience if there were no concerns. The providers followed their standard clinical procedures for MToP and no changes were made for the purpose of the study. Ultrasonography was routinely used to date pregnancy. After receiving mifepristone orally (600 mg), the women were given instructions on the use of misoprostol (400 µg to take orally 48 hours later, repeated not more than once, 4 hours apart in the absence of bleeding). The women were instructed to return for a clinical examination 14-21 days after intake of mifepristone. They were recommended to undergo a serum hCG test at the lab of their choice the day before the post-abortion appointment and to transmit the results.

The women included were those who came to the follow-up visit after taking mifepristone and outside such emergency contexts as bleeding, infectious or pelvic pain syndromes. They were asked to perform a LSUP test as well as to fill out a self-performed questionnaire to assess their opinion on the completion of the abortion and about the user-friendliness of the urinary test. Then, the standard follow-up was done by a doctor who concluded on whether the MToP failed or succeeded, basing themselves on hCG serum measurements, clinical examination and ultrasonography when needed.

A successful MToP is commonly defined as a complete uterine abortion, with no need for surgical intervention or for new abortive medication following administration of the regimen. The abortion was considered incomplete when a gestational sac, with or without an embryo, or a thick

heterogeneous mucosa, accompanied by clinical manifestations (bleeding, pelvic pain, etc.) persisted on ultrasound after the 14th day of taking mifepristone. Ongoing pregnancies were defined as the presence of an embryo with cardiac activity.

For all women who received an MToP between March and August 2017, we checked the hospital database to determine if they made an unscheduled visit because of a treatment complication within two months of MToP or if they went to the maternity service with an ongoing pregnancy.

Interpretation of LSUP test:

The Check Top® test has a detection threshold of 1000 mIU/mL. Women were given oral instructions and an illustrated leaflet (figure 1) on how to perform and read the LSUP test. The test was considered as negative if only one color band appeared in the control area and none in the test area. It was positive if color bands appeared clearly in the control area as well as in the test area. The test was considered as uninterpretable if no band was stained or if only the test area was stained, but not the control area. The patient interprets the urine test alone. The result was recorded in the self-administered questionnaire, but it was not revealed to the physician in charge of the post-abortion visit.

Self-performed survey:

The checklist questions were derived from previous studies [11, 15] and were adapted to the French population. We asked patients about their opinion on the user-friendliness and their interpretation of the test. Moreover, we collected their feelings after the abortion was done by asking three closed questions:

- "Did you feel any of the following things today: breast tenderness, nausea or morning sickness, need to urinate frequently, exhaustion or tiredness?"
- "How would you quantify the bleeding within 48 hours after taking Misoprostol?"
- "Do you feel that the abortion is complete?”

The last question summarizes the overall opinion of the patient following the results of the questionnaire and the urine test:

- "Given your feelings and the result of the urine test, do you think that a consultation with the doctor is necessary? Why?"

Statistical analysis:

The analysis was descriptive: we used Student's test for continuous variables, which were presented as mean, standard deviation, median and range. Fischer's exact test and Chi2 test were used for qualitative variables presented as frequency and percentage. A p-value <0.05 was considered as significant. Missing data were not integrated into the calculation of percentages. Regarding the outcome of MToP, a failed abortion was defined as:

- the presence of retained products of conception requiring surgery or medicinal treatment (sometimes expectative treatment is chosen, in which case the abortion is not considered failed);
- bleeding resulting in a secondary surgical procedure;
- the need for a renewed administration of misoprostol;
- any ongoing pregnancy.

We analyzed the qualitative data to correlate between the patients' opinion on the effectiveness of the drug method and the gold standard (GS), which associates clinical examination, plasmatic hCG and ultrasound if needed. We calculated the sensitivity, specificity, positive and negative predictive values (PPV, NPV) of the LSUP test as compared to the GS. We also sought to establish the Cohen's kappa coefficient of the urine test as compared to the plasma hCG assay. Finally, we compared the efficacy of screening for abortions failures between the GS and the realization of an LSUP test combined with a self-assessment. The manufacturer donated 150 urine tests for assessment during the first six months of inclusion. We anticipated that 10% of the tests may be lost during training or due to specimen errors. We also hypothesized that the urine tests associated with the women's opinion had a sensitivity of 95% to identify a failure of MToP [13] and that their specificity was 90% [12]. With an alpha risk of 5%, recruiting a sample size of 135 women resulte in 95% confidence intervals around the measurement of sensitivity of +/- 4.27 and around the measurement of specificity of +/- 0.59.

Results

Description flow chart (figure 2):

273 patients had an MToP between March and August 2017 and 206 (75.5%) went to a follow-up appointment.

135 patients agreed to take the LSUP test and the self-administered questionnaire. Two of them were excluded as their questionnaire was considered unexploitable.

Characteristics of the women:

The characteristics of the population at inclusion are presented in table 1. Each woman had an ultrasound scan to confirm the term of pregnancy before the MToP. The median term of pregnancy at the time of MToP was 6 weeks of gestation [min-max: 35-55 days of gestation], with a majority (94%, n=125) at less than 49 days of gestation.

MToP follow-up:

All the patients analyzed (n=133) took mifepristone on day zero and 400 to 800 µg of oral misoprostol on day two. The median time between the dating ultrasound and the administration of mifepristone was one day [min-max: 0-14]. Eleven patients took misoprostol at hospital (8.3%) and 122 patients at home (91.7%).

The follow-up visit took place 21 days [min-max: 14-31] after the administration of mifepristone. A serum hCG test was performed in 76.7% of cases (n=102), 20 days after the MToP [min-max: 11-28] and one day before the LSUP test [min-max: 0-11]. Serum hCG measurements show levels lower than 1000 mIU/mL for 89.2% of women who made the blood test (n=91).

Any bleeding occurring 48 hours after misoprostol intake was considered to be either very intense or rather intense in 23.3% and 51.9% of patients, respectively, and not very intense in 21.8% of cases or absent in 1.5% of cases. There was no correlation between the abundance of bleeding and the abortion result (table 2).

Eighteen patients reported persistent signs of pregnancy (13.5%): breast tension (8.3%), nausea-vomiting (4.5%), asthenia and malaise (10.5%), constipation (2.3%), urinary disorders (0.8%), and mood and sleep disorders (2.3%). There was no correlation between persistent signs of pregnancy and the failure of MToP (table 2).

Ultrasound scans were carried out 21 days after the MToP [min-max: 14-31] on 116 women (87.2%). Among successful MToP, the uterus was empty in 80.8% of these patients (n=101) and debris or clots were reported for 17.2% of the patients (n=15), requiring ultrasound monitoring after the next menstrual period in seven patients (5.6%).

Outcome of MToP:

The rate of successful MToP was 94.0% of women (n=125). Regarding failures (n=8; 6.0%), there were two ongoing pregnancies (1.5%), and three retained products of conception with bleeding (2.3%) required a surgical procedure. Three retained products of conception (2.3%) were treated with oral administration of 400 µg of misoprostol.

Primary objective (table 3):

Almost all women found the test easy (87.2%; 116/133) or rather easy (12.0%; 16/133) to perform (fig 3), and found it easy (82.0%; 109/133) or rather easy (17.3%; 23/133) to read (fig 3).

After completing the questionnaire and the LSUP test, nine patients thought the MToP procedure had failed (6.8%), 72 did not consider it necessary to see a doctor (54.1%), 42 wanted a consultation for reassurance (31.6%), nine for more information on abortion or contraception (6.8%), and none to request an analgesic treatment.

Among the patients persuaded to have totally expelled the pregnancy (n=122, 91.7%), none had an ongoing pregnancy, 2.3% had retained products of conception requiring a surgical aspiration (n=2) or complementary medication (n=1). Sensitivity, specificity, PPV and NPV of women's opinion about the success of MToP was respectively of 62.5%, 94.4%, 41.7% and 97.5%, with a Youden index of 0.57. However, all the patients who mistakenly thought they had totally expelled the pregnancy considered it necessary to see a doctor for reassurance because of a positive LSUP test. The sensitivity of the women's opinion combined to the LSUP test was 100%, specificity was 89.6%, PPV 38.1%, NPV 100%, with a Youden index of 0.89 and a kappa coefficient of 0.51.

Secondary objective:

There were eight cases of discrepancy: six women had a positive (n=1) or uninterpretable (n=5) LSUP test even though serum hCG levels were lower than 1000 mIU/mL, and two women had negative LSUP tests even though their blood levels were higher than 1000 mIU/mL. Thus, Cohen's coefficient kappa comparing to the blood test was 0.65. However, since the tests were not carried out on the same day, a correction factor should be used taking into account the half-life of hCG, which is 3.85 days within 14 days of an abortion [1] .With this correction, the overall concordance between urine and blood tests is 0.63. The characteristics of the "returners" versus the "non-returners" are compared table 4.

DISCUSSION

Given the extremely high efficacy of early medical abortion (94% in our study), most women do not need a clinical follow-up to confirm pregnancy termination. Our data show that Check Top® is effective and that most women can ascertain their abortion outcome using a simple self-administrated questionnaire and a LSUP test. This improvement in medical abortion service delivery could eliminate the need for standard follow-ups with ultrasound and serum hCG, both of which are costly to women and health care systems.

Reduced reliance on ultrasonography would also decrease the number of unnecessary interventions to which women are exposed, frequently owing to ultrasound examinations by inexperienced providers [17, 18].

Teratogenic effects of MToP:

However, continuing viable pregnancies after a failed MToP might remain unnoticed until the legal limit for induced abortion has passed. In cases where misoprostol failed to terminate pregnancy, congenital abnormalities in the fetuses have been reported, including scalp or skull defects, cranial-nerve palsies, and limb defects such as talipes equinovarus. The increase in uterine pressure related to uterine contractions or vascular spasm may be the cause of those teratogenic effects [4] [19]. Even if the absolute risk of malformations after exposure to misoprostol is relatively low, in the order of 1% among exposed fetuses [20], it is important to use a reliable method for excluding continuing pregnancy.

Ectopic pregnancies and MToP:

Ectopic pregnancy represents a special case of pregnancy continuing after an attempted abortion. It can be life-threatening if not detected and treated promptly. Studies of women seeking first-trimester abortion have shown proportions of ectopic pregnancy as low as 1.9 per 1000 procedures [21] and as high as 5.8 per 1000 among abortions performed at less than 6 weeks [22]. In our study, two ectopic pregnancies were detected after being suspected at the dating scan.

The United States Centers for Disease Control and Prevention [23] reported ten deaths from ectopic pregnancies after attempted abortions during the period 1973-1978. Although these data are old, it should be noted that the abortion-to-death intervals had a median of eleven days. This median interval is shorter than the standard two weeks recommended in follow-up protocols. Thus, the diagnosis will be guided not so much by a post-abortion visit, but by screening and clinically monitoring the patients at risk for extra-uterine pregnancy using the kinetics of the hCG. The women undergoing medical abortion who do not have vaginal bleeding within 24 hours after taking misoprostol should be instructed to contact their provider as they may be at a higher risk of ectopic pregnancy [24].

Emergency post abortion consultations:

Women with complications arising from an abortion generally seek healthcare, especially if they have received adequate counseling. In our study, three women were admitted to the emergency department for complications associated with abortion. Two of these patients were admitted for an abnormal bleeding two days after taking misoprostol, which required an emergency surgical aspiration. The third patient consulted for pelvic pain one month after an MToP; no complications were found.

Some health professionals have expressed concerns that women may be more likely to make unscheduled visits to the abortion service or to an emergency service if a clinical visit is not arranged. However, it has been shown that unscheduled visits are made by only a minority of women [25].

What follow-up after abortion?

Clarks and al. [11] conducted the largest study of alternative follow-up strategies after an MToP, with 3,054 women included at less than 63 days of gestation. The authors sought to determine whether the clinical assessment by the patient or physician associated with an LSUP test (performed by a lab technician) was as effective as an ultrasound follow-up. Separately, none was sensitive enough to identify all continuing pregnancies. However, a combination of either self-assessment or clinician assessment with a pregnancy test identified all 20 continuing pregnancies.

In our study, the LSUP test detected all the ongoing pregnancies and 75% (6/8) incomplete abortions, whereas the combination of the self-administered questionnaire and the urinary test revealed all ongoing pregnancies and all incomplete abortions.

With at-home follow-up, 61 patients (45.9%) in our study would have been reviewed in post-abortion consultation at our department: 17 patients (12.1%) with a positive (n=9) or uninterpretable (n=8) urine test, 4 (3.0%) with a feeling of not having expelled the whole pregnancy even though the LSUP test was negative, and 41 (30.1%) patients seeking medical consultation for another reason (for reassurance or to get information on abortion, contraception or an analgesic treatment).

The sensitivity of urine tests is improved by the use of any methods for monitoring post-abortion symptoms (medical examination, telemedicine by phone or SMS, etc.) [26], and must therefore be associated with them. Of course, the rate of patients for review will depend on the specificity of our test.

In 2012, Cameron et al. [10] showed that more than half of women preferred not to have a routine phone call, but rather simply contact the service themselves in case of an issue. Although this idea needs to be studied more in-depth, the main risk lies in the fact that some patients misinterpret their symptoms. For example, as it is important to start effective contraception immediately post-ToP to prevent another unintended pregnancy, some women with ongoing pregnancies might wrongly attribute the paucity of bleeding, amenorrhea or pregnancy symptoms to the hormonal effect of contraception.

Choice of the LSUP test:

In this study, we chose to use a low-sensitivity urine pregnancy test with a 1000 mIU/mL cutoff because it has been shown to be effective in previous studies [10, 25]. Moreover, it is a two-column sample test, which is likely to be interpreted by women better than a semi-quantitative pregnancy test. The difficulty in interpreting the test result was low, with only 0.8% of women reporting difficulties (n=1) and 6.0% of results described as uninterpretable (n=8). The tests with two or more hCG levels might be more discriminating to detect retained products of conception and ongoing pregnancies, but owing to these several thresholds of detection, those tests are more difficult to read and more

confusing for patients [13, 27, 28]. The use of high-sensitivity pregnancy tests at one month post-ToP delayed the detection of continuing pregnancies.

A 1000 mIU/mL sensitivity threshold was chosen based on the kinetics of β-hCG decline occurring after a ToP. In 2005, McCHESNEY et al. [29] showed that urinary concentrations of intact hCG are similar to serum concentrations during early pregnancy. Other teams have demonstrated that after misoprostol intake, hCG levels dropped by > 99% by 14 days [30, 31]. Between seven and nine weeks of gestation, the average rate of hCG is estimated at 100,000 mIU/mL [30]. Following the decrease described above, the expected rate of hCG should be less than 1000 mIU/mL after 14 days and more of the abortion.

The main sources of false-positive urine tests are human errors of qualitative interpretation if the test is taken too soon or if the urine contains blood or proteins [32]. More problematic are the false-negative urine test results that can occur with markedly elevated hCG levels, as observed in patients with molar pregnancy or in those with choriocarcinoma. The excess of intact hCG variants (free beta–submit hCG or core fragment of β-hCG) might interfere with assays by oversaturating the assay system, which is widely known as the "hook" effect [32]. If there is no evidence of diurnal variation in the excretion of urinary chorionic gonadotrophin [33], urine hCG tests may yield a false-negative result in very dilute urine [34]. It is recommended that patients should not drink large amounts of fluids before collecting a urine sample for pregnancy testing.

In our study, eight patients yielded an uninterpretable test. Among them, only one had a hCG level > 1000 mUI/mL (1826 mUI/mL) on the day of the LSUP test. One of these uninterpretable LSUP tests had a hCG level of 1053 mUI/mL the day before the LSUP test. Consequently, given the decrease of hCG, the rate should be less than 1000 mUI/mL on the day of the LSUP test. The other uninterpretable LSUP tests had a hCG level < 250 mUI/mL.

Comparing to serum hCG, the rate of false positives (FP) with the LSUP test was 5.9% (6/102). Among those FP, five tests were considered uninterpretable, with a hCG blood level of less than 250 mIU/mL. One patient who felt that her abortion was incomplete interpreted her test as positive. Her hCG level was 128 mIU/mL and the clinical and ultrasound examinations were perfectly normal.

There were only two false negatives (FN) with the LSUP test. One of them occurred because the blood test for hCG (hCG at 1098 mUI/mL) was taken 2 days before the LSUP test, leading to level of hCG less than 1000 mUI/mL on the day of the follow-up visit. The other FN result occurred in a woman with a hCG level of 1658 mUI/mL one day before the LSUP test. She believed that the abortion was complete and the ultrasound showed only a slight retention requiring only simple monitoring.

These false-negatives reinforce the need to remind women that no test is perfect and that scant bleeding, pregnancy symptoms or missed periods after treatment should prompt contact with the provider.

Lost to follow-up problem:

The loss of sight rate at the follow-up visit at our center is 24.5% (n=67), which is less than what is reported elsewhere in the literature [12]. Little is known about the women who decline follow-up. A Canadian study found several factors associated with a failure to attend the abortion follow-up visit, including young age, smoking, previous induced abortion, and advanced gestational age at the time of the procedure [35].

In our study, we found that "non-returners" were younger ($p<0.001$), less educated ($p=0.04$) and had more previous induced abortions ($p=0.007$) than "returners". There were no different findings regarding smoking habits. Moreover, as MToP were not routinely performed beyond eight weeks of gestation, there was no difference of gestational age at the time of the procedure. We believe that the follow-up on these patients with risky behaviors would probably be improved if they were given a choice on how to be followed up, in particular by limiting the trips to the healthcare provider and by respecting patient autonomy. For instance, at the Royal infirmary of Edinburgh, where the standard follow-up of ToP offers remote monitoring, the loss-to-follow-up rate dropped from 40% to 25% [12]. Even though this is an improvement, this rate is likely to decrease further with the development of telemedicine and of connected technologies.

Highlights and limitations of our study:

Although it was small in number of participants, our prospective study confirms the adequate sensitivity of LSUP tests, and more particularly of Check Top® to detect ongoing pregnancies. Even though the study was not carried out in real-life conditions, it has internal validity owing to the fact that the patient alone interpreted the urine test and the questionnaire. Moreover, our results are perfectly consistent with the literature data. In spite of the insistent recommendations to assay hCG plasma prior to the post-abortion consultation, we observed a missing data rate of 23.3% (31/133). Moreover, when the assay was performed, in 18.6% of cases (n=19), it was done 3 days or more before the visit, making its interpretation hazardous. This reinforces our feeling that to improve patient follow-up by making it less restrictive, it is necessary to resort to ambulatory follow-up providing point-of-care testing.

Of course, patient access to the results of plasma hCG assays could influence the reading and interpretation of urinary self-tests and responses to the self-report, but this test use and interpretation is considered as easy or rather easy by 99% of patients.

We emphasized the high rate of uninterpretable tests (6.0%), which were considered as positive tests and therefore decreased their specificity. If follow-up occurs at home, this would lead to an increased number of patients coming for consultation. We did not find any particular characteristic in the patients with an uninterpretable LSUP test: all had the same level of schooling, BMI, smoking status than the rest of the population studied, and the time of day when the LSUP test was taken did not vary among them.

The number of women enrolled who were at 49 days of gestation or more was small (6.0 %), therefore reducing our ability to draw any conclusions about the use of the test in the 8th week of gestation.

Conclusion:

The evidence now clearly shows that the pathway for women requesting an early medical termination of pregnancy (< 49 days of gestation) and who are certain of their decision could consist of a single clinic visit. At this single visit, all of the following could reasonably take place [36]:

- pregnancy dating,
- counseling on pregnancy termination,
- administration of mifepristone with a supply of misoprostol for home use,
- instructions on when and how to conduct a pregnancy test,
- advice and contact numbers in case of an emergency or if the patient wants to contact the ToP service,
- provision of supplies of effective ongoing contraception.

Moreover, all women having an abortion should be able to return for routine follow-up if they so wish.

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Glossary

FN: False negative

FP: False positive

hCG: human Chorionic Gonadotropin

LSUP: Low Sensitivity Urine Pregnancy

MToP: Medical Termination of Pregnancy

NPV: Negative Predictive Value

PVV: Positive Predictive Value

Se: Sensibility

Sp: Specificity

ToP: Termination of Pregnancy

Appendices

Fig. 1: Check Top® notice

checkToP® 1000 mUI/mL

Test d'autodiagnostic à utiliser pour confirmer l'interruption Volontaire de Grossesse (IVG) jusqu'à 9 semaines d'aménorrhée ou pour confirmer une fausse couche spontanée.

Mesure le taux d'hCG au-dessus de 1000 mUI/mL

INTRODUCTION

checkToP® n'est pas un test de grossesse classique. **checkToP®** est un test urinaire rapide de basse sensibilité à réaliser à domicile. Il détecte la présence d'hCG (hormone gonadotrophine chorionique humaine) dans les urines. Il confirme les interruptions de grossesse intra-utérines jusqu'à 9 semaines d'aménorrhée (9 SA) ainsi que la fausse couche spontanée.

Votre médecin vous expliquera si et comment utiliser ce test.

CONTENU

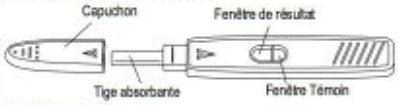
***Réf.* 3066-1000AI:** Chaque boîte comprend une (1) notice et un (1) test **checkToP®** emballé dans un sachet en aluminium scellé contenant 1 sachet dessiccant.

***Réf.* 3067-1000AI:** Chaque boîte comprend vingt (20) notices et vingt (20) tests **checkToP®** emballés individuellement dans un sachet en aluminium scellé contenant 1 sachet dessiccant.

FONCTIONNEMENT

checkToP® est un test qualitatif de détection rapide de présence d'hCG dans les urines. Le test détecte la présence d'un taux d'hCG de 1000 mUI/ mL ou plus. Le résultat apparaît entre 5 et 10 minutes.

Si le taux d'hCG est en dessous de 1000 mUI/mL, un seul trait de couleur apparaît dans la fenêtre témoin. Si le taux d'hCG est au-dessus de 1000 mUI/mL, deux traits de couleur apparaissent, un dans la fenêtre témoin et un dans la fenêtre de résultat.



PRECAUTIONS

1. Ce test est uniquement destiné à un usage externe (Il s'agit d'un dispositif médical de diagnostic *in vitro*). Ne pas avaler.
2. Lisez attentivement les instructions d'utilisation avant d'effectuer le test. Le test n'est pas fiable si les instructions ne sont pas suivies à la lettre.
3. A conserver entre +4°C et +30°C. **Ne pas congeler.**
4. Ne pas utiliser après la date d'expiration. La date d'expiration est imprimée sur chaque sachet aluminium ainsi que sur l'emballage extérieur. Ne pas utiliser si le sachet aluminium est endommagé.
5. Ne pas réutiliser **checkToP®**.
6. Conserver hors de la portée des enfants.
7. Après usage, jeter tous les composants du kit avec les déchets ménagers habituels.

MODE D'UTILISATION

Le test doit être effectué après l'interruption de grossesse au moment indiqué par votre gynécologue. Généralement entre 10 et 20 jours après :

- la prise du premier comprimé dans le cadre de la procédure d'interruption médicamenteuse de grossesse jusqu'à 9 semaines d'aménorrhée.
- une fausse couche spontanée

1. Retirer le test **checkToP®** du sachet aluminium et jeter le sachet.
2. Retirer le capuchon. Effectuer le test soit :

- en tenant la tige absorbante directement sous le flux d'urine pendant 5 à 10 secondes.

  Prendre soin de ne pas uriner sur la fenêtre de résultat.
- soit en recueillant l'urine dans un récipient propre et sec. Plonger la tige absorbante dans l'urine recueillie pendant au moins 5 à 10 secondes afin qu'elle soit complètement imprégnée.

3. **Remettre le capuchon** sur le test.
4. Poser le test sur une surface plane et sèche, les deux fenêtres vers le haut. Le résultat s'affichera dans les fenêtres et pourra être lu entre 5 à 10 minutes. Ne pas lire le test après 10 minutes.

LECTURE DU RESULTAT

Attendre entre 5 à 10 minutes avant de lire le résultat du test. Dans les 5 à 10 minutes une ligne apparaît dans la fenêtre témoin (la plus petite fenêtre).

5-10 min

Important : Ne pas lire avant 5 minutes ou après 10 minutes.

Résultat positif :

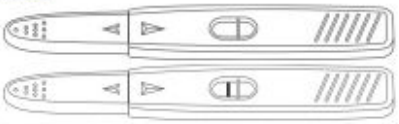
Si 2 traits roses sont apparus durant les 10 minutes : un trait dans la fenêtre témoin et un autre dans la fenêtre de résultat, le test est positif. Votre taux d'hCG peut être au-dessus de 1000 mUI/mL. Cela pourrait signifier l'échec de la procédure d'interruption de grossesse ou que celle-ci n'est pas complète, ou que la fausse couche spontanée n'a pas eu lieu. **Dans tous les cas, vous devez consulter votre gynécologue.**

Remarque: Un trait peut être plus sombre que l'autre. Les deux traits peuvent avoir des nuances rose-violet. Le trait de résultat peut être plus clair ou plus sombre que le trait témoin. Toutefois, vous devriez voir clairement deux traits parallèles.

Résultat négatif :

Si un seul trait coloré apparaît dans la fenêtre témoin (la plus petite fenêtre) et qu'il n'apparaît pas de trait dans la fenêtre de résultat (la plus grande fenêtre), le test est négatif. L'interruption de grossesse ou la fausse couche spontanée est confirmée.

Invalide :



Le test ne peut être lu si aucun trait de couleur n'apparaît dans la fenêtre témoin du test. Même si un trait de couleur apparaît dans la fenêtre de résultat, il est recommandé de refaire le test avec un nouveau test **checkToP®** sur un échantillon d'urine fraîche obtenu 24 heures après le test invalide.

QUESTIONS / REPONSES

Comment fonctionne le test checkToP®?

Lorsqu'une femme est enceinte, son corps commence à produire l'hormone gonadotrophine chorionique humaine (hCG), qui est excrétée dans les urines où sa concentration augmente au fil du temps. Le test **checkToP®** détecte l'hormone hCG dans les urines si le taux d'hormones est de 1000 mUI/mL ou plus. Si l'interruption de grossesse est effective ou si une fausse couche spontanée s'est produite alors le niveau d'hCG devrait tomber en dessous de 1000 mUI/mL dans les 10 à 20 jours. **checkToP®** ne détecte pas les niveaux d'hCG inférieurs à 1000 mUI/mL alors que les tests de grossesse classiques seront positifs.

Dois-je faire le test à un certain moment de la journée ?

Oui, nous recommandons d'utiliser **checkToP®** sur les premières urines du matin qui sont plus concentrées.

La trop grande consommation d'eau ou de boisson peut-elle affecter le résultat ?

Oui, une trop grande consommation de liquide peut diluer l'urine et rendre la détection d'hCG plus difficile. Un apport anormal de liquide n'est donc pas recommandé.

Que faire si je ne suis pas sûre du résultat du test ?

Si vous ne pouvez pas déterminer si oui ou non une ligne apparaît dans la fenêtre ovale, refaire le test 1 jour après avec un nouveau test **checkToP®**. Si vous suivez les instructions, vous devriez obtenir des résultats exacts. Certains médicaments contenant de l'hCG ou utilisés en association avec de l'hCG (tels que Pregnyl, Profasi, Pergonal) et certains cas médicaux rares peuvent donner un faux résultat positif. L'alcool, les analgésiques, les antibiotiques, les pilules contraceptives, les traitements hormonaux contenant du citrate de clomifène (tels que Clomid, Serophen) ou les antalgiques ne devraient pas affecter le résultat du test.

J'ai laissé la tige absorbante dans mon urine pendant plus de 10 secondes. Vais-je obtenir un résultat valide ?

Oui. Quelques secondes en plus n'affecteront pas le résultat du test.

J'ai laissé la tige absorbante dans mon urine moins de 5 secondes. Vais-je obtenir un résultat valide ?

Non, car le volume de l'échantillon d'urine peut être insuffisant.

Que se passe t-il si la ligne de la fenêtre de résultat est plus foncée que la ligne de la fenêtre témoin ou si la ligne dans la fenêtre de résultat est plus claire que la ligne de la fenêtre résultat ?

Tant que vous voyez une ligne dans chaque fenêtre, le résultat du test est positif.

Une fois le résultat obtenu, que dois-je faire ?

Vous devez suivre les recommandations qui vous ont été données par le personnel médical.

Si je n'attends pas les 5 minutes avant de lire le résultat ?

Si vous lisez le test avant les 5 minutes, vous ne donnez pas au test assez de temps pour fonctionner, et le résultat du test peut ne pas être exact. NE PAS INTERPRETER LES RESULTATS si 10 minutes se sont écoulées après avoir amené la tige absorbante en contact avec de l'urine.

Quelle est la fiabilité du test ?

checkToP® est très fiable et a été utilisé par des professionnels de santé pour confirmer le succès de l'interruption médicamenteuse de grossesse jusqu'à 9 SA (hôpitaux et laboratoires).

Les rapports d'évaluation montrent que **checkToP®** peut détecter l'hCG au-dessus de 1000 mUI/mL dans plus de 99% des cas. Aucun test n'étant parfait et même si le test est négatif, vous devez contacter votre médecin si vous ressentez des symptômes de grossesse tels que des saignements peu abondants, absence de règles à la date prévue, sensibilité des seins, nausées et si votre ventre s'arrondit.

Puis-je utiliser checkToP® pour diagnostiquer une grossesse ?

Oui, cependant **checkToP®** n'est pas en mesure de détecter les grossesses précoces et ne sera positif que si le taux d'hCG est supérieur à 1000 mUI/ mL. D'autres tests de grossesse sont plus sensibles et donnent un résultat positif à partir de 5 à 25 mUI/mL.

MISES EN GARDE

- **checkToP®** ne peut pas être utilisé pour les grossesses dont le taux d'hCG initial est inférieur à 1000 mUI/mL.
- Utiliser **checkToP®** uniquement dans le cadre d'un traitement médical prescrit par votre médecin traitant. L'interprétation clinique du test doit être faite avec ou conformément aux consignes du personnel médical.

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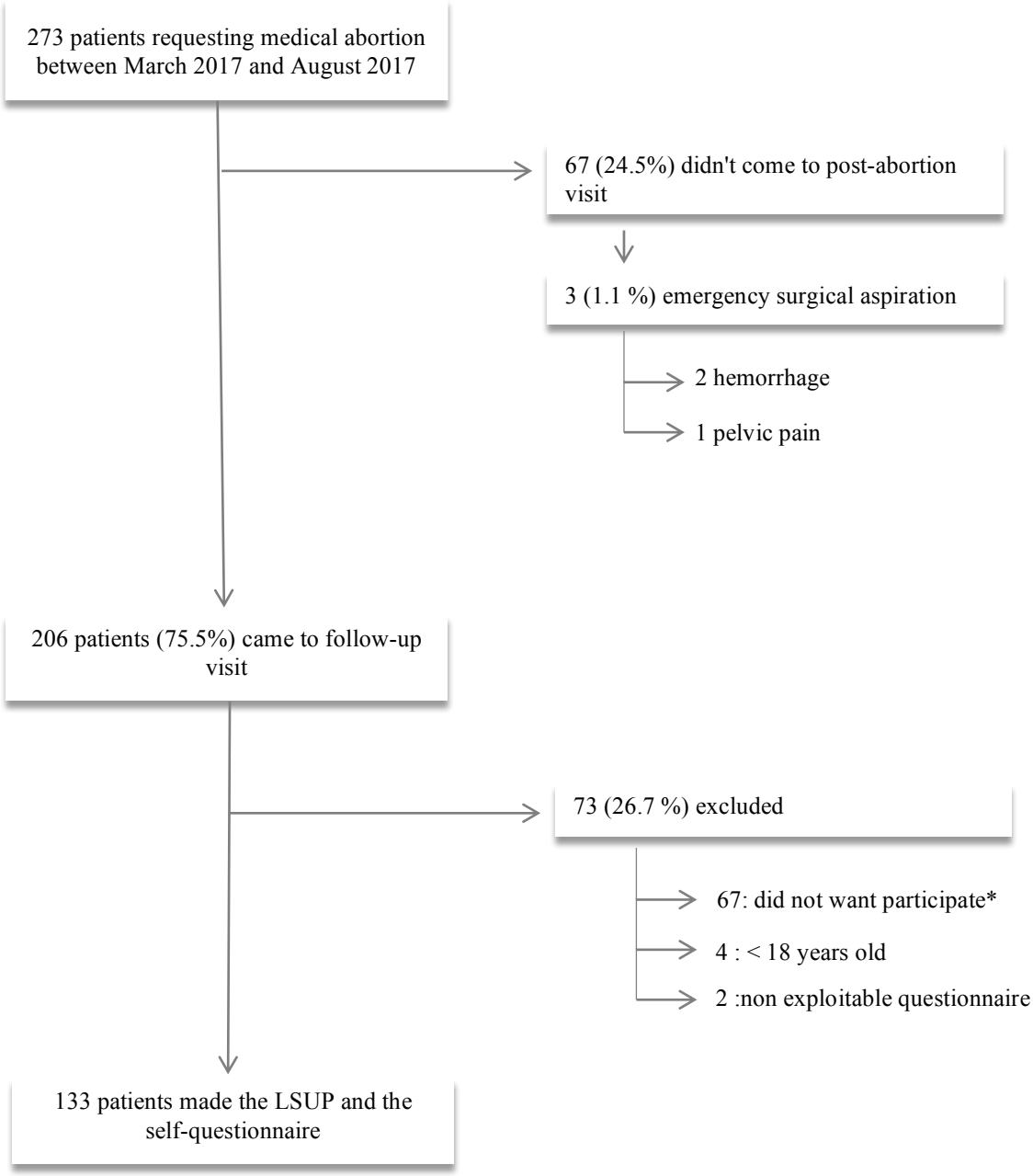
Fig. 2: Flow chart



*Reasons for non-participation were not collected

Table 1: Characteristics of patients who have had an MToP

Women's characteristics	n=133
Age (years): mean (+/- SD)	30.7 (+/- 7)
BMI	23.2 (5.1)
Smoking	62 (46.6%)
Education level	
(French secondary school diploma)	
No optained	31 (23.3%)
Optained	33 (24.8%)
Two-year university degree	26 (19.5%)
Three-year university degree	25 (18.8%)
Five-year university degree	16 (12%)
Eight-year university degree	2 (1.5%)
Previous pregnancy	
Gestity	3 [1-8]
Parity	1 [0-5]
Prior abortion	0 [0-3]
At least one prior abortion	43 (32.3%)
Term of abortion (day)	42 [35-55]
Interval between:	
Pregnancy dating and MToP (day)	1 [0-14]
MToP and follow-up visit (day)	21 [14-31]

Results expressed as median (min-max), mean (+/- SD) or sample size (%)

Table 2: Comparison of patients according to the symptoms described

	Success of MToP (n=125)	Failure of MToP (n=8)	p
Abundance of bleeding:			
None	1 (0.8%)	0 (0.0%)	1
Not intense	25 (20.0%)	1 (12.5%)	0.17
Rather intense	71 (56.8%)	5 (62.5%)	1
Very intense	28 (22.4%)	2 (25%)	0.73
Persistence of pregnancy symptoms	17 (13.6%)	1 (12.5%)	0.83

Results expressed as sample size (%)

Table 3: Tests performances

LSUP test + self-assessment compared to clinical conclusion

	MToP failure	MToP success	Total	
T+	8	13	21	Se= 100 Sp= 89.6 VPP= 38.1 VPN= 100 Youden index= 0.90 Kappa coefficient = 0.51
T–	0	112	112	
Total	8	125	133	

LSUP test compared to clinical conclusion

	MToP failure	MToP success	Total	
LSUP t +	7	10	17	Se= 87.5 Sp= 92.0 VPP= 41.2 VPN= 99.1 Youden index= 0.80
LSUP t –	1	115	116	
Total	8	125	133	

Self-assessment compared to clinical conclusion

	MToP failure	MToP success	Total	
Self-assessment +	5	7	12	Se= 62.5 Sp= 94.4 VPP= 41.7 VPN= 97.5 Youden index= 0.57
Self-assessment –	3	118	121	
Total	8	125	133	

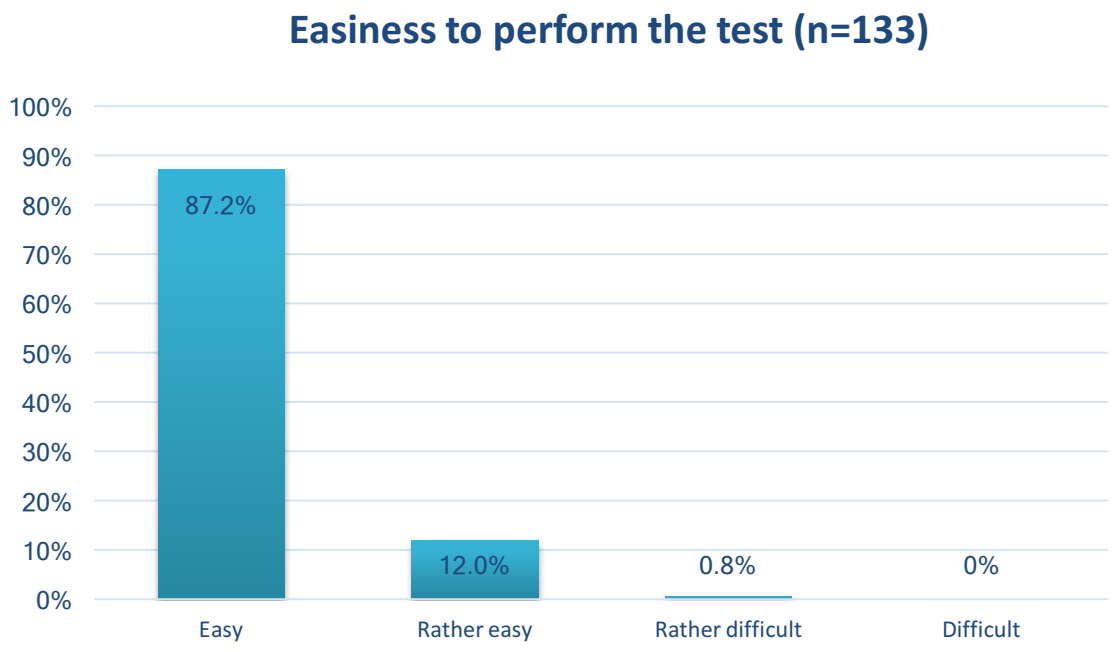
LSUP test compared to blood hCG

	MToP failure	MToP success	Total	
LSUP t +	9	6	15	Kappa coefficient = 0.69
LSUP t –	2	85	87	
Total	11	91	102	

LSUP test and self-assessment = T
LSUP t + = LSUP test positive or uninterpretable
LSUP t – = LSUP test negative
Self-assessment + = patient's opinion of failure of MToP
Self-assessment – = patient's opinion of success of MToP

LSUP test + and self-assessment + = T+
LSUP test + and self-assessment – = T+
LSUP test – and self-assessment + = T+
LSUP test – and self-assessment – = T–

Fig 3: Use and interpretation of Check Top®



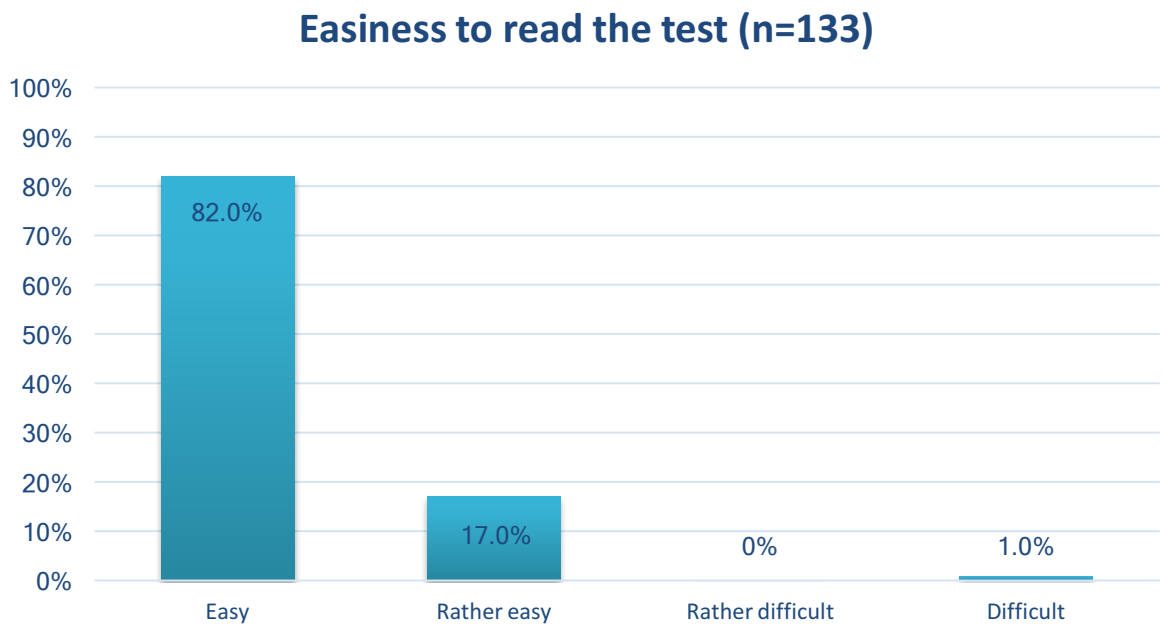


Table 4: Comparison between returners and no returners

Women's characteristics	Returners n=133	No returners n=67	p
Age (years)	30.7 (+/- 7)	27 (+/-6.9)	**<0.001**
Smoking	62 (46.6%)	38 (56.7%)	0.20
Education level			
(French secondary school diploma)			
No optained	31 (23.3%)	25 (37.3%)	**0.04**
Optained	33 (24.8%)	25 (37.3%)	0.09
Two-year university degree	26 (19.5%)	11 (16.4%)	0.58
Three-year university degree	25 (18.8%)	5 (7.5%)	**0.04**
Five-year university degree	16 (12%)	1 (1.5%)	**0.01**
Eight-year university degree	2 (1.5%)	0 (0%)	0.50
Previous pregnancy			
Gestity	3 [1-8]	3 [1-12]	0.28
Parity	1 [0-5]	1 [0-7]	0.42
Prior abortion	0 [0-3]	0 [0-5]	**0.01**

Results expressed as median (min-max), mean (+/- SD) or sample size (%)

U.F.R DE **MEDECINE** DE RENNES

N°

PIMENTEL Céline

Test urinaire de faible sensibilité et auto-questionnaire : la patiente peut-elle apprécier seule l'efficacité de l'interruption volontaire de grossesse médicamenteuse?

Can women accurately assess the outcome of medical abortion based on self-assessment and low sensitivity urine pregnancy test?

34 feuilles, 1 illustration, 3 graphiques, 4 tableaux, 30 cm - Thèse : Médecine ; Rennes 1 ; 2017 ; N°

Résumé français

Introduction: L'échec de l'interruption volontaire de grossesse médicamenteuse (IVGm) peut avoir de lourdes conséquences telles que le dépassement du terme légal d'avortement et la survenue de malformations congénitales chez le fœtus liées à l'effet tératogène du misoprostol. **Objectif :** Etudier, dans le cadre du suivi post-IVGm, la corrélation entre un test de grossesse urinaire de faible sensibilité (hCG urinaire) associé à un auto-questionnaire et le suivi standard reposant sur un examen clinique, un dosage sanguin d'hCG et la réalisation d'une échographie si besoin. **Méthodes :** Etude prospective incluant les patientes venues à la visite post-IVGm entre Avril et Septembre 2017. Avant la consultation médicale, elles ont réalisé un test d'hCG urinaire, répondu à un auto-questionnaire et donné leur opinion sur le succès de l'IVGm. Ce dernier est défini par une évacuation complète du produit de conception sans recours à une aspiration chirurgicale ou à une nouvelle prise de médicaments abortifs. **Résultats :** Inclusion de 133 patientes. Le taux de succès de l'IVGm était de 94,0%. Concernant les échecs, on compte deux grossesses évolutives (1,5%) et six rétentions (4,5%) traitées soit par aspiration chirurgicale soit par une nouvelle prise de misoprostol. La sensibilité du test de Bhcg urinaire associée à l'opinion de la patiente est de 100%, la spécificité de 89,6%, la valeur prédictive positive de 38,1% et la valeur prédictive négative de 100% avec un index de Youden de 0,89 et un coefficient kappa de 0,51.

Conclusion : Etant donné la grande efficacité de l'IVGm, la plupart des patientes ne nécessitent pas de suivi médical pour établir son succès. Notre étude montre que les patientes sont capables avec un test de hCG urinaire et un auto-questionnaire d'évaluer l'efficacité de l'IVGm.

Résumé anglais

Background: Failed medical terminations of pregnancy (MToP) can have serious consequences such as exceeding the legal age of abortion and the occurrence of fetal malformations related to the teratogenic action of misoprostol. **Objective:** To study the correlation between a low-sensitivity urine pregnancy (LSUP) test associated to a self-performed questionnaire and the standard patient follow-up after an MToP, consisting of a clinical examination, a blood test for hCG and ultrasonography when needed. **Methods:** Prospective cohort study including women who came to their post-abortion visit after an MToP from April to September 2017. They performed an LSUP test and a self-performed questionnaire to assess their opinion on the completion of the abortion. Then a standard follow-up was done by a doctor. A successful MToP was defined as a complete uterine abortion, with no need for surgical intervention or for new abortive medication. **Results:** 133 women were included in this study. The rate of successful MToP was 94.0%. Regarding failures, there were two ongoing pregnancies (1.5%) and six retained products of conception (4.5%) treated either by a surgical procedure or with a renewed oral administration of misoprostol. Sensitivity of the LSUP test associated with the women's opinion was 100%, specificity was 89.6%, positive predictive value 38.1%, negative predictive value 100%, with a Youden index of 0.89 and a kappa coefficient of 0.51. **Conclusion:** Given the extremely high efficacy of MToP, most women do not need a clinical follow-up to confirm pregnancy termination. Our data show that most women can ascertain their abortion outcome using a simple self-administrated questionnaire associated with a LSUP test.

Rubrique de classement : Gynécologie-Obstétrique

Mots clés : interruption médicamenteuse de grossesse, avortement volontaire, test urinaire de grossesse, visite du post-abortum

Mots-clés anglais: Medical termination of pregnancy, low sensitivity urinary test, follow-up visit

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