Management of Medical Termination of Pregnancy (MToP) up until the 7th week of gestation in the Czech Republic

Slunska P.[1], Hanacek J.[2], Fanta M.[3], Sehnal B.[4], Gerychova R.[5], Hola A.[2], Zdenkova A.[3], Neumannova H.[4], Dziakova M.[5], Lubusky M.[1]

[1]Department of Obstetrics and Gynecology, Palacky University Olomouc, Faculty of Medicine and Dentistry, University Hospital Olomouc, Czech Republic
[2]The Institute for the Care of Mother and Child, Charles University in Prague, Third faculty of Medicine, Czech Republic
[3]Department of Gynecology and Obstetrics, Charles University in Prague, First faculty of Medicine, General University Hospital in Prague, Czech Republic
[4]Department of Gynecology and Obstetrics, Charles University in Prague, First faculty of Medicine, Hospital Na Bulovce, Prague, Czech Republic
[5]Department of Gynecology and Obstetrics, Masaryk University, Faculty of Medicine, University Hospital Brno, Czech Republic

ABSTRACT

Objective: In the Czech Republic (CR), it is possible, to carry out Medical Termination of Pregnancy (MToP) in the 1st trimester since June 2014, in case a woman submits a written request for it and in case the ultrasound examination confirms an intrauterine singleton prosperous pregnancy, between day 42 and 49 of gestation, crown-rump length (CRL) of the embryo 2–9 mm. The aim of the study is to analyze the management of MToP up until the 7th week of gestation in five centres in the CR.
Design: Multicenter cohort (prospective) study.
Setting: Department of Obstetrics and Gynecology, Palacky University Olomouc, Faculty of Medicine and Dentistry, University Hospital Olomouc; The Institute for the Care of Mother and Child, Charles University in Prague, Third faculty of Medicine; Department of Gynecology and Obstetrics, Charles University in Prague, First faculty of Medicine, General University Hospital in Prague; Department of Gynecology and Obstetrics, Charles University in Prague, First faculty of Medicine, Hospital Na Bulovce, Prague; Department of Gynecology and Obstetrics, Masaryk University, Faculty of Medicine, University Hospital Brno.
Methods: In 2014–2016, a total of 1820 pregnant women requested MToP. The diagnosis of an intrauterine singleton prosperous pregnancy was set by transvaginal ultrasound, CRL 2–9 mm. MToP was carried out by combination of mifepristone (600 mg orally) and misoprostol (400 mcg orally) within 48 hours. MToP follow up (exclusion of ongoing pregnancy) after 2–3 weeks was carried out by transvaginal ultrasound as well.
Results: In 11.0% of women (201/1820) who requested MToP, CRL > 9 mm, unprosperous, multiple or ectopic pregnancy was diagnosed. In the remaining 1619 women MToP was carried out, but in 221 cases (13.7%) at least one additional pre-first visit was needed before the diagnosis of intrauterine singleton prosperous pregnancy CRL 2–9 mm could be established, in 19 cases (1.2%) two pre-first visits and in 5 cases (0.3%) even three. Gestational age was 42–49 days (average 47.1, median 47), the women were 14–47 years of age (average 30.7, median 30). In 20.8% of women (336/1619) MToP follow up was missed and of the remaining 1283 women, ongoing pregnancy (MToP failure) was diagnosed in 1.6% (21/1283), incomplete abortion in 6.5% (83/1283) and complete abortion in 91.9% (1179/1283). A subsequent surgical intervention was carried out in 7.4 % of women (95/1283).
Conclusion: A medical facility performing MToP in the 1st trimester should develop its own methodology in accordance with the legislation in force, Summaries of Product Characteristics, and recommendations of professional associations. The methodology should also include a method of evaluation of the result and management. The subsequent surgical intervention should only be performed in indicated cases. The main goal of MToP follow up is to exclude ongoing pregnancy (MToP failure), and the patient should be informed in detail about the risks involved and possibilities of their solution, it is necessary to obtain an informed consent.

KEYWORDS

medical termination of pregnancy, first trimester

Corresponding author: Professor Marek Lubusky, MD, PhD, MHA,
e-mail: marek@lubusky.com
Ces Gynek, 2017, 82, 5, p. I–VIII

INTRODUCTION

In the Czech Republic (CR), it is possible to carry out Termination of Pregnancy (ToP) in the 1st trimester in case a woman submits a written request for it and in accordance with the specific legislation [1, 2]. The procedure can be done by a pharmacological or a surgical method. At the moment, medicinal products for two pharmacological methods that can be used to terminate pregnancy in the 1st trimester (until 49th, or 63th day of the secondary amenorrhea) are authorized for use in the CR [15, 16, 17, 18], however, authorized medicinal products for the second method (until 63th day) [17] are not currently available in the CR. Medical products for the first method (until 49th day) are available in the CR since June 2014 [5, 6, 11, 14, 15, 16].

The aim of the study is to analyze the management of Medical Termination of Pregnancy (MToP) up until the 7th week of gestation in five centres in the CR.

MATERIALS AND METHODS

The multicenter cohort (prospective) study was carried out in five centres in the Czech Republic (University Hospital Olomouc, The Institute for the Care of Mother and Child in Prague, General University Hospital in Prague, Hospital na Bulovce in Prague, University Hospital Brno).

In 2014–2016, a total of 1820 pregnant women requested MToP up until the 7th week of gestation (Table 1).

The diagnosis of an intrauterine singleton prosperous pregnancy was set by transvaginal ultrasound, and the dating of pregnancy was carried out according to the crown-rump length (CRL) of the embryo. At CRL = 2 mm it is possible to prove a prosperous pregnancy (presence of blood circulation pulsation), and CRL = 9 mm corresponds to the 49th day of secondary amenorrhea (Scheme 1).

MToP was carried out by administering the first medicinal product containing the active substance mifepristone 600 mg (Mifegyne® 3 tablets of 200 mg each) in a single oral dose followed 36 to 48 hours later by the administration of the second medicinal product containing the active substance misoprostol 400 mcg (Mispregnol® 1 tablet of 400 mcg) orally. After 14 to 21 days following the administration of the medicinal product with the active substance mifepristone (Mifegyne®), a follow up transvaginal ultrasound examination was carried out to exclude ongoing pregnancy (Scheme 2).

Evaluation of the result

1) „Ongoing pregnancy“ – a medical abortion has failed, if the pregnancy continues,

2) „Incomplete abortion“ – presence of a non-vital embryo / fetus in the uterine cavity; another abnormal ultrasound finding in the area of uterine cavity or cervical canal, and simultaneously presence of clinical symtoms; persistent value of human chorionic gonadotropin (hCG) in serum of more than 1000 IU/l (positive low sensitivity urine hCG test),

3) „Complete abortion“ – a medical abortion is successful when the expulsion has occured without the need of any other observation (Expectant management) or additional treatment (misoprostol alone or Surgery).

Management

1) „Ongoing pregnancy“ – repetition of the pharmacological method – MToP (up until the 9th week of gestation, CRL ≤ 25 mm), or surgical method – SToP (up until the 12th week of gestation, CRL ≤ 55 mm); continuing the pregnancy – Prenatal care,

2) „Incomplete abortion“ – Expectant management or additional misoprostol or Surgery.

RESULTS

Out of the total of 1820 pregnant women who requested MToP up until the 7th week of gestation, 8 women (0.4%) were diagnosed with a biochemical pregnancy of unknown location unprosperous, 147 women (8.1%) were diagnosed with a clinical intrauterine singleton prosperous pregnancy, but with CRL > 9 mm, 27 women (1.5%) were diagnosed with a clinical intrauterine singleton unprosperous pregnancy, 10 women (0.5%) with a clinical intrauterine multiple prosperous pregnancy, and 9 (0.5%) women with a clinical ectopic pregnancy (unprosperous). Therefore, in a total of 11.0% women (201/1820), it was not possible to carry out the procedure, and they were excluded from the study (Table 1).

In 1619 women a clinical intrauterine singleton prosperous pregnancy, CRL 2–9 mm, was diagnosed, and MToP was carried out, but in 221 cases (13.7%) at least one additional pre-first visit was needed before the diagnosis could be established, in 19 cases (1.2%) two pre-first visits and in 5 cases (0.3%) even free. Gestational age was 42–49 days (average 47.1, median 47), the women were 14–47 years of age (average 30.7, median 30), of them, 171 women were at an age of 40 and more (10.6%) (Table 1).

A total of 20.8% of women (336/1619) did not attend the follow up ultrasound examination to exclude ongoing pregnancy, and the result thus could be evaluated in 1283 women only. Ongoing pregnancy (MToP failure) was diagnosed in 1.6% (21/1283), Incomplete abortion in 6.5% (83/1283) and Complete abortion in 91.9% (1179/1283). A subsequent surgical intervention was carried out in 7.4% of women (95/1283) (Table 1).

Table 1 Medical Termination of Pregnancy (MToP) up until the 7th week of gestation – material, methods and results in five centres in the Czech Republic.

1 – University Hospital Olomouc, 2 – Hospital Na Bulovce in Prague, 3 – The Institute for the Care of Mother and Child in Prague, 4 – General University Hospital in Prague, 5 – University Hospital Brno; the crown-rump length (CRL) of the embryo

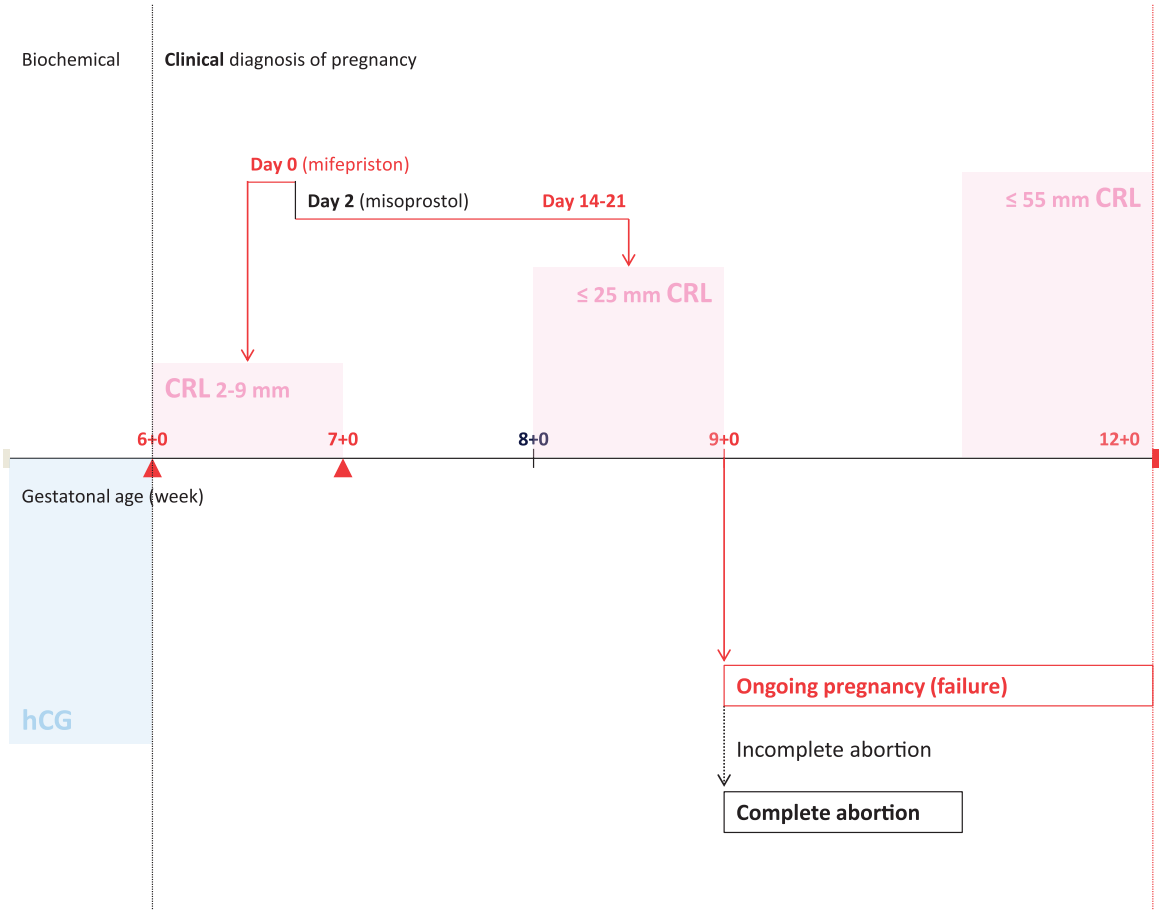
	2014-2016											
	Centre 1		Centre 2		Centre 3		Centre 4		Centre 5		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Request for "Medical Termination of Pregnancy"	**223**		**385**		**481**		**435**		**296**		**1820**	
PregnancyPregnancy												
biochemical												
of unknown location												
of unknown count												
unprosperous	0	0.0%	2	0.5%	3	0.6%	2	0.5%	1	0.3%	8	0.4%
clinical												
intrauterineintrauterine												
singletonsingleton												
prosperous												
CRL 2-9 mm	**208**	**93.3%**	**346**	**89.9%**	**415**	**86.3%**	**381**	**87.6%**	**269**	**90.9%**	**1619**	**89.0%**
CRL > 9 mm	10	4.5%	27	7.0%	51	10.6%	42	9.7%	17	5.7%	147	8.1%
unprosperous	5	2.2%	6	1.6%	6	1.2%	6	1.4%	4	1.4%	27	1.5%
multiplemultiple												
prosperous	0	0.0%	2	0.5%	3	0.6%	2	0.5%	3	1.0%	10	0.5%
unprosperous	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
ectopic (unprosperous)	0	0.0%	2	0.5%	3	0.6%	2	0.5%	2	0.7%	9	0.5%
1st visit	**208**		**346**		**415**		**381**		**269**		**1619**	
Pre-first visit 1x	59	28.4%	36	10.4%	45	10.8%	42	11.0%	39	14.5%	221	13.7%
2x	4	1.9%	1	0.3%	3	0.7%	2	0.5%	9	3.3%	19	1.2%
3x	1	0.5%	1	0.3%	1	0.2%	1	0.3%	1	0.4%	5	0.3%
Gestational age (days)												
Minimum	42		42		42		42		42		42	
Maximum	49		49		49		49		49		49	
Average	45.6		48.1		47.2		47.3		46.4		47.1	
Median	45		48		47		47		46		47	
Age of woman (years)												
Minimum	16		14		16		16		14		14	
Maximum	44		41		46		47		45		47	
Average	29.4		28.5		33.5		30.6		30.2		30.72	
Median	29		28		33		30		29		30	
Mifepristone - 3 tablets (600 mg)												
2nd visit (36-48 hours after mifepristone)	**206**	99.0%	**342**	98.8%	**410**	98.8%	**376**	98.7%	**266**	98.9%	**1600**	98.8%
Misoprostol - 1 tablet (400 mcg)												
3rd visit (follow-up 2-3 weeks later)	**193**	92.8%	**271**	78.3%	**307**	74.0%	**282**	74.0%	**230**	85.5%	**1283**	79.2%
Ongoing pregnancy	**6**	3.1%	**4**	1.5%	**4**	1.3%	**3**	1.1%	**4**	1.7%	**21**	1.6%
repeated Medical abortion	1		0		0		0		0		1	
Surgery	6		4		3		3		4		20	
Prenatal care	0		0		1		0		0		1	
Incomplete abortion	**4**	2.1%	**16**	5.9%	**35**	11.4%	**14**	5.0%	**14**	6.1%	**83**	6.5%
Expectant management	0		6		0		0		0		6	
additional misoprostol	2		0		0		0		0		2	
Surgery	2		10		35		14		14		75	
Complete abortion	**183**	94.8%	**251**	92.6%	**268**	87.3%	**265**	94.0%	**212**	92.2%	**1179**	91.9%

DISCUSSION

„Unwanted Pregnancy" – diagnosis

In 11% of pregnant women who requested MToP, it was not possible to carry out the procedure: 8% of women were diagnosed with an intrauterine singleton prosperous pregnancy, but according to the dating, the pregnancy corresponded to more than 49th day of secondary amenorrhea, and it was not possible to carry out the procedure by pharmacological method anymore (the available medicinal products are authorized for administration until the 49th day of secondary amenorrhea – the so-called „on-label use", afterwards, the intervention can only be performed by a surgical method) [15, 16]; 2% of women were diagnosed with an unprosperous pregnancy, and the procedure should therefore be reimbursed from the public health insurance funds (medical reasons are present – the so-called „medical indication", however, there is no reimbursement mechanism determined for the pharmacological method) [3, 4]; 1% of women were diagnosed with an intrauterine multiple prosperous pregnancy (medicinal products are not authorized for use in multiple pregnancy – the so-called „off-label use") [15, 16]. From the medical point of view, the pharmacological method can be used in all the above mentioned cases with the exception of ectopic pregnancy, however, organizational, legal and economic aspects pose a problem [1, 2, 3, 4, 5, 7, 8, 9, 10, 14, 18, 19, 20, 21].

An intrauterine singleton prosperous pregnancy can only be diagnosed by ultrasound, and at the earliest, from the 42nd day of the secondary amenorrhea (presence of blood circulation pulsation in the embryo, CRL = 2 mm). The pharmacological method can therefore be offered to a



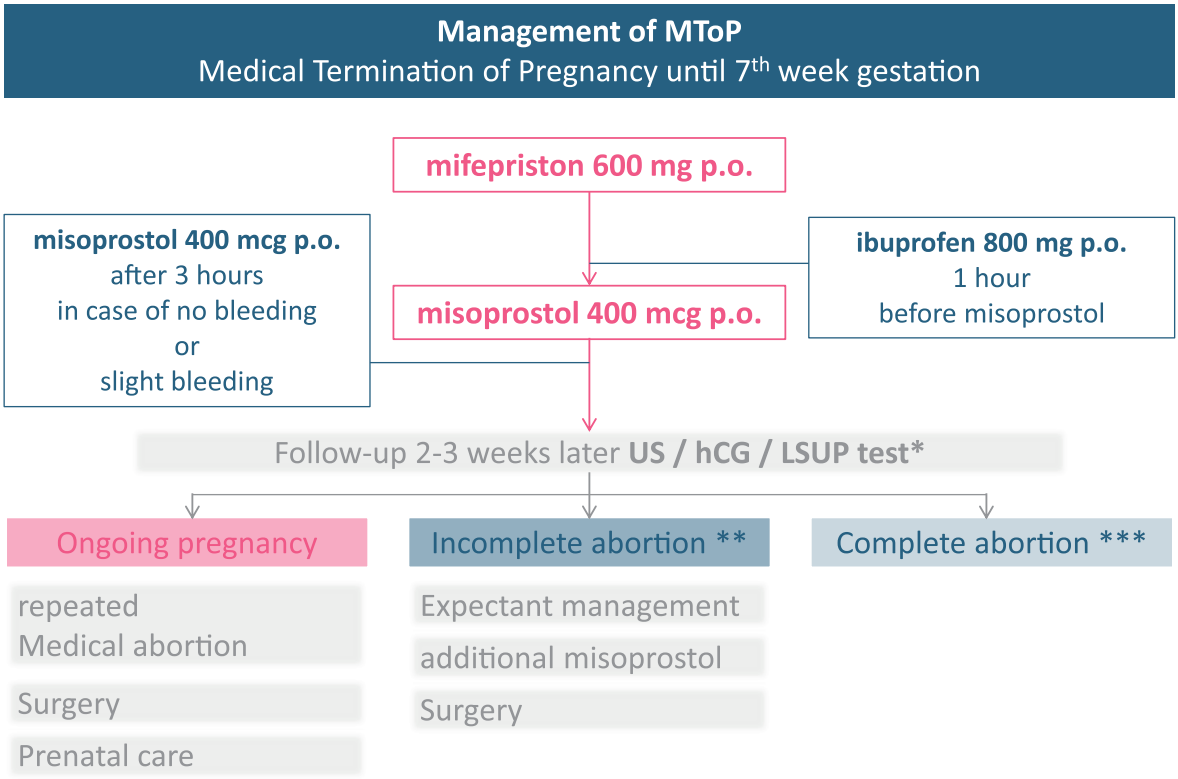
Scheme 1 **Medical Termination of Pregnancy (MToP) up until the 7th week of gestation – diagnosis of pregnancy and management of the procedure according to gestational age**

Setting the diagnosis of an intrauterine singleton prosperous pregnancy by ultrasound examination, and the dating of pregnancy according to the crown-rump length (CRL) of the embryo. At CRL = 2 mm, it is possible to prove a prosperous pregnancy (presence of blood circulation pulsation), CRL = 9 mm corresponds to the 49th day of secondary amenorrhea, CRL = 25 mm, to the 63th day, and CRL = 55 mm, to the 84th day.

The main goal of the follow up ultrasound examination is to exclude ongoing pregnancy, because in case the pregnancy continues, it is possible to proceed, depending on the actual gestational age and the patient's wish, in the following way:

- repetition of the pharmacological method - MToP (up until the 9th week of gestation, CRL ≤ 25 mm),
- surgical method - SToP (up until the 12th week of gestation, CRL ≤ 55 mm),
- in case the patient decides to continue the pregnancy, it is necessary to inform the patient in detail about the potential risk of abnormal fetus development (approx. 1% of cases, damage to central nervous system and/or extremities have been reported), it is necessary to obtain the **INFORMED CONSENT** from the patient, it is recommended to make detailed fetal anomaly scan by ultrasound.

pregnant woman only from the 42nd to 49th day of secondary amenorrhea (CRL 2–9 mm). From the organizational point of view, if the patent comes earlier, at least one more clinical visit is necessary (10–28% of cases in the individual centres), on the other hand, if she comes later, the pharmacological method cannot be carried out (5–11% of cases in the individual centres). In the case of an „unwanted pregnancy" it is thus very important for a woman to come to the health facility carrying out the pharmacological method as soon as she finds out that she is pregnant. From the medical point of view however, it is not necessary to confirm a prosperous pregnancy, and the pregnancy can also be terminated by the pharmacological method in the 1st trimester even after the 49th day of secondary amenorrhea. However, this means using the authorized medicinal product in a manner that is not in accordance with the Summary of Product Characteristics, i.e. the so-called „off-label use", and in case there are no medical reasons for it, this procedure means an unnecessary risk for the doctor from the legal point of view. On the other hand, in case there are medical reasons – the so-called



Scheme 2 Medical Termination of Pregnancy (MToP) up until the 7th week of gestation - evaluation of the result and management

EVALUATION OF THE RESULT

- „Ongoing pregnancy" – a medical abortion has failed, if the pregnancy continues
- „Incomplete abortion" – presence of a non-vital embryo/fetus in the uterine cavity; another abnormal ultrasound finding in the area of uterine cavity or cervical canal, and simultaneously presence of clinical symtoms; persistent value of human chorionic gonadotropin (hCG) in serum of more than 1000 IU/l (positive low sensitivity urine hCG test)
- „Complete abortion" – a medical abortion is successful when the expulsion has occured without the need of any other observation (Expectant management) or additional treatment (misoprostol alone or Surgery)

MANAGEMENT

- „Ongoing pregnancy" – repetition of the pharmacological method – MToP (up until the 9th week of gestation, CRL ≤ 25 mm), or surgical method – SToP (up until the 12th week of gestation, CRL ≤ 55 mm); continuing the pregnancy – Prenatal care
- „Incomplete abortion" – Expectant management or additional misoprostol or Surgery

„medical indication" and the intervention should be reimbursed from the public health insurance funds, there is no reimbursement mechanism determined for the pharmacological method. The gynecologic and obstetric „medical indications" for the ToP at a request of the patient in case the pregnancy does not exceed 12 weeks include e.g. a conception after the 40th year of age (6–13% of cases in the individual centres), a conception after two previous cesarean deliveries, or a failure of intrauterine contraception [1, 2].

MToP follow up examination after 2–3 weeks – evaluation of the result and management

A total of 21% of women (7–26% in individual centres) did not attend the follow up ultrasound examination, and the result thus could not be evaluated.

An ultrasound examination can reliably diagnose/exclude ongoing pregnancy or presence of a non-vital embryo/fetus in the uterine cavity. What poses a danger, however, is the high false positivity rate in the evaluation of abnormal ultrasound

finding in the area of uterine cavity or cervical canal. The surgical intervention should only be indicated if clinical symptoms are present (mainly heavy or persisting bleeding), not on the basis of an abnormal ultrasound finding.

The value of serum hCG of more than 1000 IU/l (positive low sensitivity urine hCG test) cannot reliably diagnose/exclude ongoing pregnancy, or presence of a non-vital embryo/fetus in the uterine cavity, and consequently it is always necessary to perform an ultrasound examination. Moreover, the serum hCG value of more than 1000 IU/l can be expected in MToP follow up in approximately 10% of women even in the case of a „Complete abortion". However, the value of serum hCG of less than 1000 IU/l (negative low sensitivity urine hCG test) can reliably exclude the ongoing pregnancy [Slunska et al., unpublished results].

The low sensitivity urine hCG test thus seems to be the most effective for the purposes of MToP follow up, because it is positive only at the serum hCG value of more than 1000 IU/l. A woman can perform the test herself, it is cheap and the negative result reliably excludes ongoing pregnancy. In the case of a positive result (approx. 10% of cases), or presence of clinical symptoms, it is possible to perform an ultrasound examination.

Moreover, it is apparent from our results that although it is always recommended to women to undergo the follow up ultrasound examination, many of them do not come for it at all. It is therefore very important that a woman is informed in detail about the importance of MToP follow up, and her informed consent is necessary.

MToP failure „Ongoing pregnancy" – informed consent and management

The main goal of MToP follow up is to exclude ongoing pregnancy, because in case the pregnancy continues, it is possible to proceed, depending on the actual gestational age and the patient's wish, in the following way: 1) repetition of the pharmacological method – MToP (up until the 9th week of gestation, CRL ≤ 25 mm), 2) surgical method – SToP (up until the 12th week of gestation, CRL ≤ 55 mm), [13], 3) in case the patient decides to continue the pregnancy, it is necessary to inform the patient in detail about the potential risk of abnormal fetus development (approx. 1% of cases, damage to central nervous system and/or extremities have been reported) [12], it is necessary to obtain the informed consent from the patient, it is recommended to make a detailed fetal anomaly scan by ultrasound [15, 16] (Scheme 1).

MToP failure „Ongoing pregnancy" was diagnosed in 2% of women (1–3% in the individual centres). In one case the pharmacological method was repeated, however, without success, and the pregnancy was subsequently terminated by the surgical method. In one case the patient decided to continue the pregnancy and gave birth to a healthy child. In the other cases, the pregnancy was terminated by the surgical method. The Summary of Product Characteristics (SmPC) reports a total of approximately 1–2% of cases, and subsequently, the surgical method should be preferred, because the pharmacological method probably fails due to an individual non–responsiveness to the active substances [15, 16].

„Incomplete abortion" – diagnosis and management

„Incomplete abortion" was diagnosed in a total of 7% of women (2–11% in the individual centres). SmPC reports a total of approximately 2–3% of cases [15, 16]. This includes the following subunits: 1) presence of a non-vital embryo/fetus in the uterine cavity was diagnosed in 2% of women (1–3% in the individual centres) and in most cases, a subsequent surgical intervention was performed, SmPC reports approximately 1–2% of cases, and the Expectant management or administration of additional misoprostol should be preferred (according to the recommendations of WHO and/or FIGO, however, this is the use of a medicinal product that is not in accordance with the SPmC, the so-called „off-label use") [7, 8, 9, 16, 19, 20, 21], 2) another abnormal ultrasound finding in the area of uterine cavity or cervical canal, and simultaneously presence of clinical symptoms were diagnosed in 5% of women (1–10% in the individual centres), and in most cases, a subsequent surgical intervention was performed, which however was indicated only on the basis of an abnormal ultrasound finding without presence of clinical symptoms, SmPC reports approximately 1–2% of cases and the surgical intervention should be indicated only if clinical symptoms are present (mainly heavy or persisting bleeding) [15, 16], 3) persistent value of serum hCG of more than 1000 IU/l (positive low sensitivity urine hCG test) were not evaluated in the study in the MToP follow up.

Subsequent surgical intervention

After MToP up until the 7th week of gestation, the subsequent surgical intervention was performed in a total of 7% of women (4–12% in the individual centres). SmPC reports a total of approximately 5% of cases [15, 16].

Medical Termination of Pregnancy (MToP) up until the 7th week of gestation

METHODOLOGY

1. Confirmation of an intrauterine singleton prosperous pregnancy and the dating of pregnancy by ultrasound examination, between day 42 and 49 of gestation, crown-rump length (CRL) of the embryo 2–9 mm
2. Informing the patient about the MToP including the related risks and potential adverse effects
3. Supplementing a written request for "termination of pregnancy"
4. Supplementing the "Informed content of the patient with MToP up until the 7th week of gestation"
5. Direct payment by the patient before performing the procedure
6. Verification or assessment of the RhD blood group of the patient (it is not necessary to wait for the result of the assessment to begin the procedure)
7. The patient obtains a safety card, which is part of the package of the medicinal product (it contains data about the reference contact and prescribing centre that the patient could use in the case of problems after the procedure)
8. Day 0 – administration of the medicinal product containing the active substance mifepristone 600 mg (Mifegyne® 3 tablets of 200 mg each) in a single oral dose, after which the patient remains in the proximity of the medical facility for 1 hour due to a potential adverse effect
9. In the case of administration of a product containing the active substance mifepristone (Mifegyne®), supplementing the "abortion report"
10. The protocol contains the administration of analgetics, all patients should be offered an analgetic treatment during the first part of the procedure, the group most often recommended is the non-steroidal antiphlogistics, approximately 1 hour before administration of the medicinal product containing the active substance misoprostol (Mispregnol®), it is convenient to administer a prophylactic medicinal product containing the active substance ibuprofen 800 mg in a single oral dose
11. Day 2 – after 36 to 48 hours, oral administration of the medicinal product containing the active substance misoprostol 400 mcg (Mispregnol® 1 tablet of 400 mcg), after which the patient again remains in the proximity of the medical facility for 1 hour due to a potential adverse effect or a possibility of fast expulsion of pregnancy tissue (vomiting within 30 minutes after using the tablet could lead to decreased efficacy, i.e. it is recommended to take a new tablet orally)
12. In the case of administration of the medicinal product containing the active substance of misoprostol (Mispregnol®), it is possible to consider using hormonal or other method of contraception
13. In the case of an RhD negative blood group of the patient it is necessary to administer, for a prevention of RhD alloimmunization, immunoglobulin (Ig) G anti-D at a dose of at least 100 mcg intramuscularly (administration of a higher dose is not a mistake), IgG anti-D shoud be administered 72 hours after the beginning of the procedure at the latest
14. After 3 hours, in case of no bleeding or slight bleeding, it is convenient to repeat the administration of the medicinal product containing the active substance misoprostol 400 mcg (Mispregnol® 1 tablet of 400 mcg) orally, after which the patient remains again in the proximity of the medical facility for 1 hour due to a potential adverse effect or a possibility of fast expulsion of pregnancy tissue (vomiting within 30 minutes after using the tablet could lead to a decrease in efficacy, i.e. it is recommended to use a new tablet orally)
15. After administration, writing a report on using an authorized medicinal product in a manner that is not in accordance with the Summary of Product Characteristics, the so-called "off-label use" (medicinal product with the active substance mifepristone is authorized for use in the Czech Republic but it is not approved for use in this indication) http://www.sukl.cz/modules/unregistered/?rewrite=modules/unregistered
16. Day 14–21 – after 14–21 days from the administration of the medicinal product containing the active substance mifepriston (Mifegyne®), the follow up ultrasound examination is performed to exclude ongoing pregnancy – MToP failure (or it is possible to monitor the decrease in the level of human chorionic gonadotropin in serum)

17. EVALUATION OF THE RESULT
    - "Ongoing pregnancy" – a medical abortion has failed, if the pregnancy continues
    - "Incomplete abortion" – presence of a non-vital embryo/fetus in the uterine cavity; another abnormal ultrasound finding in the area of uterine cavity or cervical canal, and simultaneously presence of clinical symtoms; persistent value of human chorionic gonadotropin (hCG) in serum of more than 1000 IU/l (positive low sensitivity urine hCG test)
    - "Complete abortion" – a medical abortion is successful when the expulsion has occured without the need of any other observation (Expectant management) or additional treatment (misoprostol alone or Surgery)

18. MANAGEMENT
    - "Ongoing pregnancy" – repetition of the pharmacological method – MToP (up until the 9th week of gestation, CRL ≤ 25 mm), or surgical method – SToP (up until the 12th week of gestation, CRL ≤ 55 mm); continuing the pregnancy – Prenatal care
    - "Incomplete abortion" – Expectant management or additional misoprostol or Surgery

CAVE!

MToP failure "Ongoing pregnancy" is rare (1–3% of cases). The main goal of the follow up ultrasound examination is to exclude ongoing pregnancy, because in case the pregnancy continues, it is possible to proceed, depending on the actual gestational age and the patient's wish, in the following way:

- repetition of the pharmacological method – MToP (up until the 9th week of gestation, CRL ≤ 25 mm),
- surgical method - SToP (up until the 12th week of gestation, CRL ≤ 55 mm),
- in case the patient decides to continue the pregnancy, it is necessary to inform the patient in detail about the potential risk of abnormal fetus development (approx. 1% of cases, damage to central nervous system and/or extremities have been reported), it is necessary to obtain the **INFORMED CONSENT** from the patient, it is recommended to make detailed fetal anomaly scan by ultrasound.

Scheme 3 Medical Termination of Pregnancy (MToP) up until the 7th week of gestation - methodology and informed consent

CONCLUSION

A medical facility performing MToP in the 1st trimester should develop its own methodology in accordance with the legislation in force, Summaries of Product Characteristics, and recommendations of professional associations. The methodology should also include a method of evaluation of the result and management. The subsequent surgical intervention should only be performed in indicated cases. The main goal of MToP follow up is to exclude ongoing pregnancy (MToP failure), and the patient should be informed in detail about the risks involved and possibilities of their solution, it is necessary to obtain an informed consent.

REFERENCES

1. **CZECH REPUBLIC.** Act No. 66/1986 Coll., Czech National Council Act on the induced termination of pregnancy, Collection of Laws of the Czech Republic.
2. **CZECH REPUBLIC.** Decree No. 75/1986 Coll., implementing Act No. 66/1986 Coll., on Abortion, Collection of Laws of the Czech Republic.
3. **CZECH REPUBLIC.** Decree No. 273/2015 Coll., setting up the reimbursement conditions for the year 2016, Collection of Laws of the Czech Republic.
4. **CZECH REPUBLIC.** Decree No. 350/2015 Coll., amending decree No. 134/1998 Coll., which issues a list of health care services with point values, as amended by later regulations, Collection of Laws of the Czech Republic.
5. **CZECH REPUBLIC.** Act No. 378/2007 Coll., on pharmaceuticals and on amendments to some related acts (Act on Pharmaceuticals), Collection of Laws of the Czech Republic.
6. Educational material on safe use and minimizing risks in use of medicinal products Mifegyne® and Mispregnol® (in the version approved by the State Institute for Drug Control from 11 November 2013 and 16 December 2013)
7. **Fiala C., Cameron S., Bombas T., et al.** Early medical abortion, a practical guide for healthcare professional. Editions de Santé, 2012, ISBN 978-2-86411-268-6.
8. **Gemzell-Danielson K., Fiala C.,, Agostini A., et al.** Medical abortion beyond the 1st trimester including fetal death in utero, a practical guide for healthcare Professional. Editions de Santé, 2015, ISBN 978-9553002-0-6.
9. Good practice guidelines: Medical termination of Pregnancy, Haute Autorité de Santé, 2010.
10. **Lubusky M., Prochazka M., Simetka O., Holuskova I.** Doporučení k provádění prevence RhD aloimunizace u RhD negativních žen – Doporučený postup ČGPS ČLS JEP. Čes. Gynek., 2013, 78 (2), p. 132–133. (Guideline for prevention of RhD alloimmunization in RhD negative women – recommendation of Czech National OB/GYN Society)
11. **Metodický pokyn ČGPS ČLS JEP.** Farmakologické ukončení těhotenství do 63. dne amenorey (gestačního stáří). Čes. Gynek., 2014 (2), p. 240–241. (Medical Termination of Pregnancy up until the 7th week of gestation – recommendation of Czech Nationl OB/GYN Society)
12. **Morris JL., Winikoff B., Dabash R., et al.** FIGO's updated recommendations for misoprostol used alone in gynecology and obstetrics. Int. J. Gynaecol. Obstet., 2017, 138, No. 3, pp. 363–366.
13. **Orioli I. M., Castilla E. E.** Epidemiological assessment of misoprostol teratogenicity. BJOG, 2000, 107, No. 4, p. 519–523.
14. **Papageorghiou AT, Kennedy SH, Salomon LJ, et al.** International standards for early fetal size and pregnancy dating based on ultrasound measurement of crown-rump length in the first trimester of pregnancy. International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st). Ultrasound Obstet. Gynecol., 2014, 44, No. 6, p. 641–648.
15. **Strasilova P., Durdova V., Kratochvilova T., Lubusky M.** Farmakologické ukončení těhotenství v I. trimestru. Postgrad. Med. 2016, 18, No. 4, pp. 381–390. (Medical abortion in the 1st trimester)
16. **SÚKL (State Institute for Drug Control).** Summary of product characteristics, Mifegyne 200mg tablets.
17. **SÚKL (State Institute for Drug Control).** Summary of product characteristics, Mispregnol 400mg tablets.
18. **SÚKL (State Institute for Drug Control).** Summary of product characteristics, Medabon. Combipack of Mifepristone 200 mg tablet and Misoprostol 4 x 0.2 mg vaginal tablets.
19. **SÚKL (State Institute for Drug Control).** Information on the marketing authorization of medicinal products for medical termination of pregnancy Mifegyne, Mispregnol (25 June 2013), Medabon (27 June 2013) and a decision on the classification as: Restricted medical prescription.
20. The Care of Women Requesting Induces Abortion (Evidence-based Clinical Guideline Number 7). Royal College of Obstetrics and Gynecologists UK, November 2011.
21. **WHO.** Safe abortion: technical and policy guidance for health systems. World Health organisation, Second edition, 2012, ISBN 978-92-4-154843-4.

Petra Slunska, MD
Department of Obstetrics and Gynecology
University Hospital Olomouc
I. P. Pavlova 6, 775 20 Olomouc, Czech Republic
E-mail: strasilova.petra@seznam.cz

Corresponding author

Professor Marek Lubusky, MD, PhD, MHA
Department of Obstetrics and Gynecology
University Hospital Olomouc
I. P. Pavlova 6, 775 20 Olomouc, Czech Republic
E-mail: marek@lubusky.com