

Verifying the effectiveness of medical abortion; ultrasound versus hCG testing

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Abstract

Objectives: The combination of mifepristone and misoprostol is an established method for termination of pregnancy. However, there is no general agreement about how best to evaluate the treatment outcome.

Study design: In 217 women with an unwanted pregnancy below 49 days of amenorrhoea, ultrasound examination and serum hCG test were performed before treatment and at follow-up.

Results: Treatment was successful in 98.2%. At follow-up their hCG dropped to a mean of 3% (S.D. 3) of initial levels and the endometrium measured a mean of 10 mm (S.D. 4). Interpretation of endometrium was difficult in some cases because of inhomogeneous structure. Using hCG was reliable in 98.5% of successful abortions. For ultrasound the corresponding figure was 89.8% for the cases with a confirmed intrauterine pregnancy before treatment but only 66% if all pregnancies were included.

Conclusion: Measuring serum hCG before treatment and at follow-up is more effective than ultrasound to confirm a successful medically induced abortion in early pregnancy.

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1. Introduction

Treatment with a combination of mifepristone (Mifegyne[®], Exelgyn, France) and the prostaglandin analogue, misoprostol (Cytotec[®], Searle AG, USA), both administered orally, has been shown to be a safe, effective method for termination of early pregnancy [1–7]. Medical abortion with mifepristone and misoprostol is licensed for use in about 30 countries including most of Europe, USA, Russia and China.

The method is highly effective up to 49 days of amenorrhoea. The estimation of duration of pregnancy before treatment is therefore of importance and is in most cases based on medical history, gynaecological examination and an ultrasound examination. For the evaluation of the outcome of treatment, complete abortion, incomplete abortion, missed abortion or continuing pregnancy various methods are used. Beside clinical events and a gynaecological examination

either measurement of serum hCG or an ultrasound examination is performed at a follow-up visit 1–3 weeks following start of treatment [8,9].

The aim of the present study was to compare the usefulness of hCG measurement and ultrasound examination before and after medical abortion in determining the outcome of treatment.

2. Material and methods

Two-hundred and seventeen women with an unwanted pregnancy up to 49 days of amenorrhoea, requesting medical abortion, were treated between 26 April and 10 November 1999. The treatment was performed on an outpatient basis at a general public hospital in Austria. A vaginal ultrasound (Toshiba Powervision 6000, vaginal probe 7.5 MHz) was performed to confirm pregnancy gestation in all women. A crown-rump length (CRL) of 10 mm was used as upper limit for treatment, consistent with 49 days amenorrhoea [10,11]. Furthermore serum hCG levels were determined in all women. All patients gave an informed consent for the abortion.

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The patients received 600 mg mifepristone orally at the hospital. They returned 48 h later to take 400 µg misoprostol orally once or twice. A second dose of 400 µg misoprostol orally after 3 h was given, according to routine, if bleeding had not started at that time or if bleeding was less than on the first day of menstruation [1].

The first follow-up to assess the treatment outcome was performed on day 6–18. The ultrasound examination and hCG testing was repeated at this time. If there was a continuing pregnancy, vacuum aspiration was performed. Surgical intervention was also performed if there was heavy bleeding or if requested by the patient. If it was unclear whether the woman had aborted completely a further follow-up visit was scheduled. The treatment was regarded as successful only if no surgical treatment was necessary up to the first menstruation.

Women who wanted combined oral contraceptives (OC) were advised to start on day 3 (day 1 being the day of mifepristone treatment). If there was suspected retention or heavy bleeding at follow-up, women on OC were asked to stop taking the pill after the fourteenth tablet.

The hCG levels at follow-up are given as the percentage of the value before the treatment and presented as mean and (S.D.). Measurements of endometrial thickness are given in mm and presented as mean and (S.D.).

3. Results

All patients completed the treatment and returned for follow-up.

The distribution of the gestational age of the pregnancies before treatment based on the ultrasound findings is shown in Table 1.

The hCG levels ranged from as low as 28 in the earliest up to 190,750 mU/ml in the most advanced pregnancy. The correlation between ultrasound findings and the hCG levels before treatment is shown in Table 2. Examples of ultrasound images of the endometrium are shown in Figs. 1–6.

A second dose of misoprostol was given to 28 women (12.9%) who had not started to bleed or had a minimal bleeding within 3 h following the first dose. One hundred and eight (49.7%) women obtained OC on day 3 following start of treatment.

Table 1
Ultrasound findings before treatment, $n = 217$

No gestational sac	6 (2.7%)	(see patient 1, Fig. 1)
Gestational sac but no yolk sac or foetal pole	44 (20.3%)	(see patient 2, Fig. 2)
Gestational sac with yolk sac but no foetus or CRL <2 mm	105 (48.4%)	(see patient 3, Fig. 3)
CRL >2 mm	62 (28.6%)	(see patient 4, Fig. 4)

CRL: crown-rump length.

Table 2
Correlation between ultrasound findings and serum hCG level before treatment

No gestational sac	28–1,752 mU/ml, (median 558 mU/ml)
Gestational sac, no yolk sac	802–54,443 mU/ml, (median 4.072 mU/ml)
Yolk sac	2,700–107,400 mU/ml, (median 17.295 mU/ml)
CRL >2 mm	22,900–190,750 mU/ml, (median 63.600 mU/ml)

CRL: crown-rump length.

Treatment was successful without the need for surgical intervention in 98.2% of cases. A total of four vacuum aspirations had to be performed; two for continuing pregnancy and two for haemorrhage.

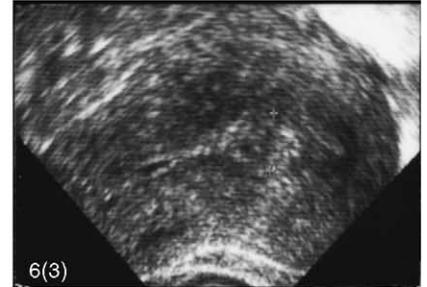
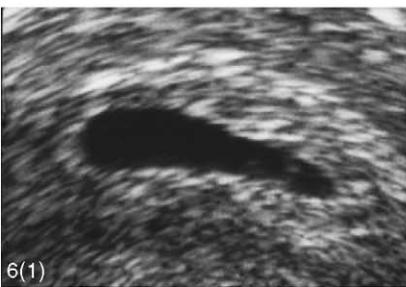
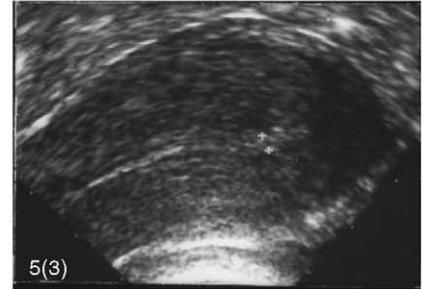
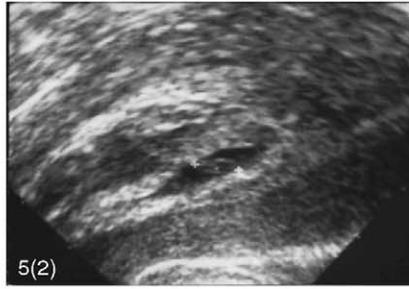
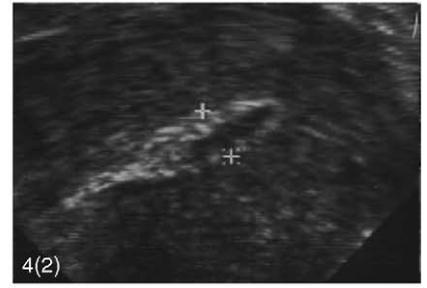
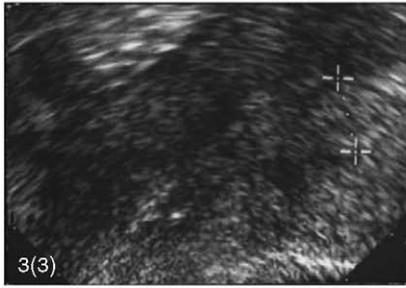
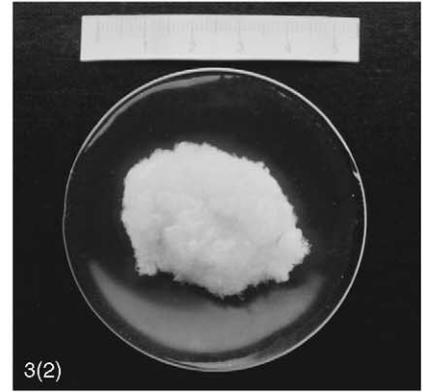
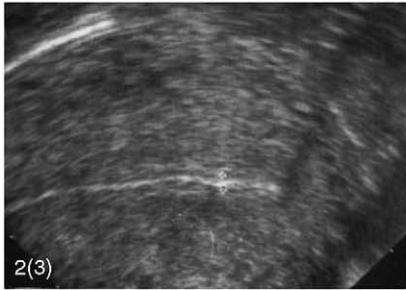
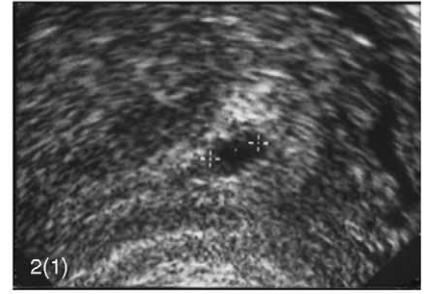
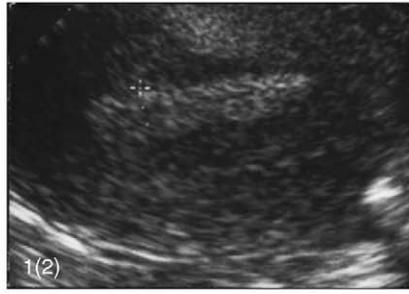
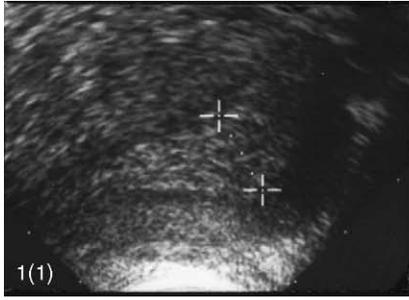
The hCG levels dropped to a mean of 3% (S.D. 3) of the value before treatment, ranging from 1 to 44% of the initial value in the cases of successful abortion (Fig. 7). The hCG value was above 17%, range 27–44%, in only three cases. Expulsion was confirmed by ultrasound in all of them, without the need for further follow-up. The two women with a continuing pregnancy had elevated hCG levels, 159% on day 10 and 7900% on day 8, respectively. Two patients were found to have a missed abortion. In each a gestational sac was seen on ultrasound which failed to grow from treatment to the time of the first follow-up at days 8 and 9 respectively. The drop in hCG was 91% in one and 3%, in the other woman. At a second follow-up visit, 8 and 15 days later respectively, both subjects had expelled the gestational sac without further treatment.

When 20% of the initial hCG value was used as cut-off, a positive predictive value for successful expulsion of 0.995 was obtained (Table 3).

If the reduction of the hCG level is less than 80%, the negative predictive value is 0.5 and further evaluation using ultrasound examination and repeated hCG measurements are needed to confirm the outcome of treatment.

The date of follow-up had been scheduled between day 6–18 according to the preferences of the patients. Due to the wide variation between treatment and follow-up, any cut off value of the hCG level has to be interpreted with caution. Nevertheless we found the cut-off at 20% valid, as all cases with complete abortion and early follow-up were far below this value.

Verification of successful abortion by ultrasound was possible only for the cases where the initial ultrasound examination had shown the presence of an intrauterine pregnancy (yolk sac or CRL). This was the case in 167 women (77%). Endometrium at follow-up measured 10 mm (mean, S.D. 4) in cases of successful abortion, ranging from 1 to 24 mm (Fig. 8). The content of the uterine cavity was inhomogeneous in some cases, making interpretation difficult (see Figs. 3 and 5). Complete abortion could not be verified at first follow-up (performed on days 7–12) by ultrasound alone in 17 of these cases (10.2%) due to the inhomogeneous picture. A further follow-up was scheduled in these cases (Fig. 5).



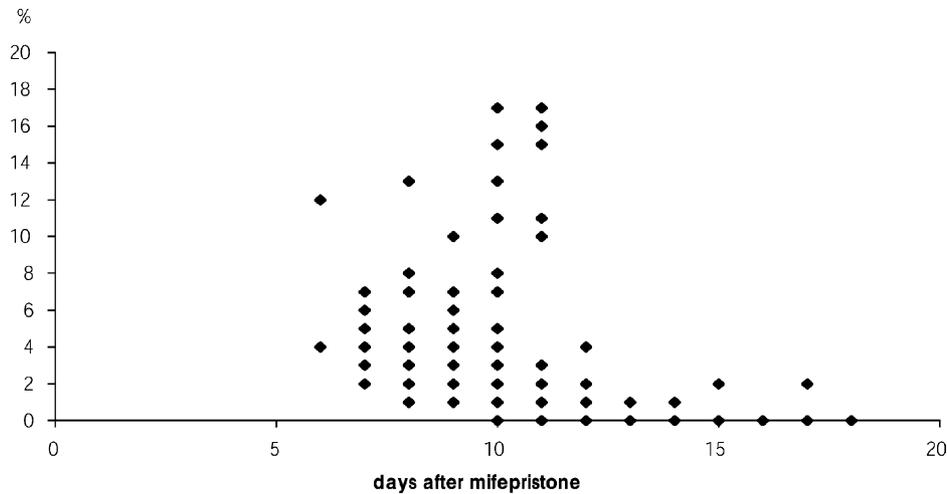


Fig. 7. S-hCG at follow-up in percentage of initial value, $n = 213$. Mean level 3% (0.1–44) of the hCG values before treatment.

Table 3

Positive and negative predictive value for expulsion at follow-up using a cut-off value of 20% of the initial value in hCG decrease

	True expulsion	True non-expulsion	Total	
hCG <20% per expulsion	210	1	211	Positive predictive value = 0.995
hCG >20% per non-expulsion	3	3	6	Negative predictive value = 0.5
Total	213	4	217	

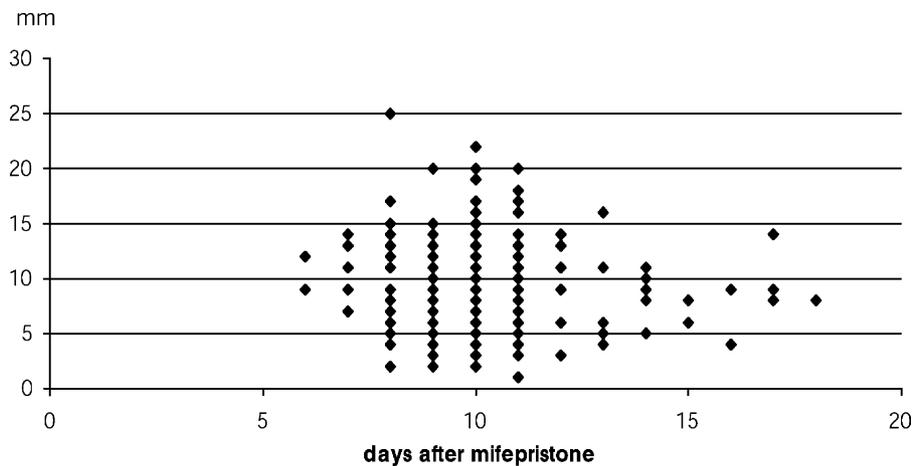


Fig. 8. Endometrial thickness at follow-up, $n = 213$. Mean 10 mm (1–24).

Figs. 1–6. Examples of patients with various duration of pregnancies up to 49 days counted from last menstrual period (LMP). Ultrasound images of the endometrium and S-hCG levels before and after treatment with 600 mg mifepristone (day 1) followed by 0.4 mg of misoprostol orally, 48 h later (day 3).

- (1) Day 1 S-hCG 269 mU/ml. Day 9 S-hCG 20 mU/ml.
- (2) Day 1 gestational sac 5 mm. S-hCG 862 mU/ml. Day 3 expelled gestational sac. Day 7 thin endometrium. S-hCG 7 mU/ml.
- (3) Day 3 expelled gestational sac. Day 7 endometrium 12 mm. S-hCG 837 mU/ml.
- (4) Day 1 CRL 1/4 10 mm. S-hCG 83439 mU/ml. Day 8 endometrium 8 mm. S-hCG 312 mU/ml.
- (5) Day 1 CRL 1/4 6 mm. S-hCG 104 900 mU/ml. Started OC on Day 3. Day 10 endometrium 20 mm. S-hCG 16 841 mU/ml. Day 21 withdrawal bleeding. Day 28 S-hCG 100 mU/ml.
- (6) Day 1 gestational sac and yolk sac. S-hCG 11947 mU/ml. Started OC on Day 3. Day 9 ultrasound image consistent with a missed abortion. S-hCG 10819 mU/ml. Day 18 withdrawal bleeding (stopped OC on day 16). Day 19 endometrium 8 mm. S-hCG 718 mU/ml.

4. Discussion

Treatment with 600 mg mifepristone and 0.4 mg misoprostol orally followed 3 h later by a second dose of 0.4 mg misoprostol if the woman had not started to bleed was found to be a highly effective method to terminate pregnancy in women with a duration of amenorrhoea up to 49 days. Out of the 217 women treated, 213 aborted without surgical intervention giving an overall success rate of 98.2%. Vacuum aspiration was performed in four women due to continuing pregnancy (two women) or heavy bleeding (two women). The outcome corresponds well with previous results using the same treatment [1].

The success of treatment is dependant on gestational age. If the duration of amenorrhoea is more than 49 days the efficacy of mifepristone and oral misoprostol is less effective [12]. The duration of pregnancy can usually be determined by menstrual history and a gynaecological examination. However, in some subjects these parameters are not sufficient and an ultrasound examination can be of considerable value.

There is no general agreement on how to verify the outcome of medical abortion. Some centres use ultrasound before administration of mifepristone and at follow-up, others rely on serum hCG levels or use a less sensitive urine pregnancy test (500 mU/ml) at follow-up. Whether ultrasound examination or serum hCG measurement is more suitable depends on several factors (Table 4). Ultrasound is not reliable in very early pregnancy before the yolk sac is visible. It could be useful to exclude a persisting extra uterine pregnancy after treatment but not in all cases. On the other hand it gives an immediate result in most cases and is inexpensive where available. Also, it can sometimes be of great relief for women in early pregnancy to see for herself that no foetal heart rate can be demonstrated.

The use of ultrasound to determine the outcome of medical abortion and possible need for surgical intervention

clearly requires knowledge of the ultrasound finding following medical abortion. In the present study follow-up was performed according to the wish of the patient between days 6 and 18. Ultrasound at follow-up was sometimes difficult to interpret. The endometrium was often thick and sometimes inhomogeneous resembling an incomplete abortion (Figs. 3 and 5). It might be difficult to abstain from surgical intervention in such cases. However, no negative consequences were observed whilst waiting for the next menstrual bleeding to occur. Thus, the need for curettage in cases with missed abortion or a thick endometrium at follow-up could be reduced by refraining from immediate surgical intervention. An increasing hCG level at follow-up on the other hand, indicates a need for surgical intervention.

To measure serum hCG levels is especially helpful in early pregnancy. Measuring hCG is also reliable in detecting a persistent pregnancy or incomplete expulsion, even when extra uterine. Successful expulsions were consistent with a marked decline in hCG value at follow-up. Using 20% of the initial value as cut-off at follow-up gave a high sensitivity. It allowed correct diagnosis in 98.5% of the patients with successful expulsion. Only one patient with missed abortion at follow-up discovered by ultrasound had a marked decrease of hCG. She expelled the gestational sac with time without complications. There is probably a high frequency of spontaneous expulsion until or during the next menstruation in such cases. Measuring hCG can easily be done in most places and might be more convenient for the woman than an ultrasound examination. Furthermore there is no need to have it performed in the same institution that provided the medical abortion.

Even following medical abortion an ovulation could occur before the first menstruation. It is therefore of importance to provide the woman with an effective contraceptive method immediately after treatment. It has previously been demonstrated that OC can be given immediately after treatment without influencing outcome or bleeding [13].

In conclusion, hCG levels are a safe and effective way to verify complete abortion following medical treatment. Performing hCG is recommended especially in very early pregnancy. It's advantage over ultrasound is less pronounced at a later gestational age, as soon as an intrauterine pregnancy can be diagnosed by ultrasound. Plasma hCG level at follow-up compared to the initial value gave a reliable result in 98.5% of successful abortions, when using 20% of the initial value as cut-off. In contrast the reliability of ultrasound examination in diagnosing successful expulsion was 89.8% in the cases with a prior diagnosis of an intrauterine pregnancy. Ultrasound at follow-up showed a thick endometrium in many cases, sometimes with an inhomogeneous structure even when the abortion was complete. The ultrasound findings might be difficult to interpret and may lead to unnecessary surgical interventions. Conservative management i.e. waiting for the menstruation or an withdrawal bleeding proved to be safe. Surgical intervention was performed only in cases of continuous evolving pregnancy or

Table 4
Comparing ultrasound and hCG measurement to verify the effectiveness of the treatment

Advantages	Disadvantages
Ultrasound Usually done before starting the treatment Easy to perform Immediate result Great relief for the woman when there is no foetal structure visible	No reliable result in very early pregnancy Sometimes difficult to interpret at follow-up Vaginal ultrasound necessary
hCG Always a definite result Easy to perform	Not possible to exclude a gestational age >49 days LMP Some time needed to obtain the result

heavy bleeding. Thus if ultrasound is used alone to verify outcome of treatment, caution should be made to avoid unnecessary interventions.

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References

- [1] Aubeny E, Peyron R, Turpin CL, Renault M, Targosz V, Silvestre L, et al. Termination of early pregnancy (up to 63 days of amenorrhea) with mifepristone and increasing doses of misoprostol (corrected). *Int J Fertil Menopausal Stud* 1995;40(Suppl 2):85–91.
- [2] Aubeny E. Trends since 1989, in France, of induced abortions by mifepristone (RU486) combined with a prostaglandin analogue. *Contracept Fertil Sex* 1997;25:777–81.
- [3] Peyron R, Aubeny E, Targosz V, Silvestre L, Renault M, Elkik F, et al. Early termination of pregnancy with mifepristone (RU 486) and the orally active prostaglandin misoprostol. *N Engl J Med* 1993;328:1509–13.
- [4] Winikoff B, Ellertson C, Elul B, Sivin I. Acceptability and feasibility of early pregnancy termination by mifepristone–misoprostol. Results of a large multicenter trial in the United States. Mifepristone clinical trials group. *Arch Fam Med* 1998;7:360–6.
- [5] WHO. Medical Methods For Termination Of Pregnancy. 1997.
- [6] Spitz IM, Bardin CW, Benton L, Robbins A. Early pregnancy termination with mifepristone and misoprostol in the United States. *N Engl J Med* 1998;338:1241–7.
- [7] Bygdeman M, Gemzell-Danielsson K, Marions L. Medical termination of early pregnancy: the Swedish experience. *J Am Med Womens Assoc* 2000;55:195–6204.
- [8] Jourdan MC v d B M. Intert des beta HCG dans. 1991.
- [9] Creinin MD, Spitz IM. Use of various ultrasonographic criteria to evaluate the efficacy of mifepristone and misoprostol for medical abortion. *Am J Obstet Gynecol* 1999;181:1419–24.
- [10] Robinson HP, Fleming JE. A critical evaluation of sonar crown-length measurements. *Br J Obstet Gynaecol* 1975;82:702–10.
- [11] Chervenak FA, Brightman RC, Thornton J, Berkowitz GS, David S. Crown-rump length and serum human chorionic gonadotropin as predictors of gestational age. *Obstet Gynecol* 1986;67:210–3.
- [12] el-Refaey H, Rajasekar D, Abdalla M, Calder L, Templeton A. Induction of abortion with mifepristone (RU 486) and oral or vaginal misoprostol. *N Engl J Med* 1995;332:983–7.
- [13] Tang OS, Gao PP, Cheng L, Lee SW, Ho PC. A randomized double-blind placebo-controlled study to assess the effect of oral contraceptive pills on the outcome of medical abortion with mifepristone and misoprostol. *Hum Reprod* 1999;14:722–5.