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Original Article

Very early medical abortion before confirmed intrauterine pregnancy

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ABSTRACT

INTRODUCTION. Medical abortion using mifepristone and misoprostol is effective and safe, but evidence is limited in very early gestation before ultrasound confirmation of an intrauterine pregnancy (IUP).

METHODS. This single-centre prospective cohort study included 100 women between 2023 and 2025 who requested medical abortion up to 6+0 weeks of gestation and had a non-confirmed IUP on ultrasound (empty cavity or sac-like structure without embryonic pole). Participants initiated immediate medical abortion according to the WHO-recommended protocol. The primary outcome was complete abortion without the need for surgical intervention.

RESULTS. Complete abortion was achieved in 95% of the participants without the need for surgical intervention. The ectopic pregnancy rate was 2%, all of which were diagnosed before rupture. 2% required additional medical treatment, and 2% surgical intervention. No serious adverse events occurred.

CONCLUSIONS. Medical abortion before visible IUP is as effective as standard treatment. Very early medical abortion can be implemented safely and effectively with structured follow-up, allowing for earlier treatment without compromising safety.

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TRIAL REGISTRATION. The study was approved by the University Hospital of Southern Denmark, Sygehus Sønderjylland, record no.:24/44840.

Medical abortion using a combination of mifepristone and misoprostol is a well-documented, effective, safe and accepted method for induced abortion in the first trimester [1, 2]. Compared with surgical abortion, medical abortion offers the advantage that medication, treatment and follow-up can often be self-administered [2].

Although medical abortion is recommended by national and international organisations and

supported by increasing evidence at very early gestational ages, many clinical guidelines still refrain from providing specific recommendations when an intrauterine pregnancy (IUP) has not yet been confirmed [2-5].

With improved access to medical abortion and the removal of barriers like waiting periods and referral requirements, more women are expected to seek abortion services before an IUP is visible on an ultrasound [6, 7]. In clinics where ultrasound is routinely performed prior to abortion, many women are classified as having a pregnancy of unknown location (PUL) – defined as a positive pregnancy test without ultrasound evidence of an IUP) or a probable IUP (a sac-like intrauterine structure (gestational sac) without yolk sac or embryonic structures) [8].

In these cases, some providers opt to delay treatment or recommend a diagnostic uterine evacuation (curettage) due to concern that the pregnancy could be ectopic [9, 10].

However, observational studies have shown that when serum human chorionic gonadotropin (S-hCG) levels are measured before and after abortion treatment, the diagnosis of pregnancy location is not delayed compared with postponing treatment until an IUP is confirmed [3, 11, 12].

A small number of observational studies of medical abortion performed before ultrasound-confirmed IUP have reported treatment success rates ranging from 85% to 100% [3, 11, 13-17]. However, the inclusion criteria for these studies vary with respect to gestational age, ultrasound criteria for inconclusive IUP and treatment failure definitions [18].

This study was inspired by our experience as co-investigators in a large, multicentre, multinational, randomised non-inferiority trial of very early medical abortion (VEMA) coordinated by the Karolinska Institutet in Sweden [12].

The VEMA found that early initiation of medication abortion, before confirmation of an IUP, was noninferior to standard delayed treatment, achieving similarly high rates of complete abortion (~ 95%) with low and comparable rates of ectopic pregnancy and serious adverse events (SAEs).

This prompted us to examine whether the results from that trial could be replicated in a smaller regional hospital setting in Denmark. Accordingly, this prospective cohort study aimed to assess the efficacy and safety of VEMA in women presenting before IUP confirmation.

METHODS

The prospective cohort study was conducted at the Department of Obstetrics and Gynaecology, University Hospital of Southern Denmark, Aabenraa, between April 2023 and December 2025. The study was approved by the Research Centre of the Region of Southern Denmark (approval number: 24/44840).

We included 100 women seeking medical abortion with an estimated gestational age of no more than 42 days (6+0 weeks), in whom an IUP had not been confirmed by transvaginal ultrasound. Ultrasound findings included either a thickened endometrium and/or a gestational sac without a

yolk sac or embryonic structures [8].

The exclusion criteria were: clinical symptoms or signs of pathological pregnancy (e.g., heavy bleeding, unilateral pelvic pain), risk factors for ectopic pregnancy (such as previous ectopic pregnancy or intrauterine device in situ) and contraindications to medical abortion.

All participants received the WHO-recommended standard protocol for medical abortion: mifepristone 200 mg administered orally, followed after 24-48 hours by misoprostol 800 µg, administered vaginally, sublingually or buccally [2]. Pain relief was offered using a combination of NSAIDs and paracetamol, with the option of repeated doses as needed.

Blood samples for measurement of S-hCG levels were obtained at baseline (on the day of mifepristone administration) and on day seven after initiation of treatment. For participants with a baseline S-hCG concentration ≥ 5,000 IU/l, a senior gynaecologist evaluated the patient for potential risk of ectopic pregnancy.

The abortion was considered complete if S-hCG levels decreased by ≥ 80% between baseline and day seven. Complete abortion was defined as the absence of an ongoing pregnancy with no need for surgical intervention within 30 days. Treatment failure included both ongoing pregnancy and the need for medical or surgical management of incomplete abortion.

If the decrease was <80%, patients were followed per the local PUL guideline for further evaluation and management.

Data on bleeding events were collected through clinical observations within the electronic patient journal (EPJ) system. Bleeding was specifically monitored during laparoscopic procedures for ectopic pregnancies and surgical procedures for retained tissue of conception.

SAEs were defined as any event that resulted in death, required hospitalisation or prolonged an existing hospitalisation, caused persistent disability or incapacity, or was considered life-threatening based on the investigator's judgement.

Statistical analyses

Statistical analyses were performed using R version 4.5.1. The primary outcome measure was complete abortion, defined as the absence of an ongoing pregnancy and no need for surgical intervention due to incomplete abortion within 30 days after treatment [19]. The standardised incidence ratio (SIR) was calculated based on the estimated incidence compared with the observed incidence in the Danish Quality Database for Early Pregnancy and Abortion. 95% CIs for the observed cases were calculated from the Poisson distribution using the exact method based on the χ^2 distribution.

Clinical data were extracted from the EPJ record system and included: demographic characteristics (age, parity and previous pregnancies), baseline ultrasound findings, S-hCG levels, treatment course and any complications (**Table 1**).

TABLE 1 Baseline characteristics of women included in the study (N = 100).

Age, median (Q1; Q3), yrs	25 (20; 31)
No. of pregnancies, including current pregnancy, n (%)	
1	36 (36)
2	30 (30)
≥ 3	34 (34)
Nulliparous, n (%)	50 (50)
Previous miscarriage, n (%)	36 (36)
Previous ectopic pregnancy, n (%)	3 (3.0)
Previous missed abortion, n (%)	1 (1.0)
Last menstrual period, n (%)	
Certain	83 (83)
Unknown	17 (17)
Length of gestation, median (Q1; Q3), days	36 (35; 38)
Ultrasound finding, n (%)	
Pregnancy of unknown location	15 (15)
Probable intrauterine pregnancy	85 (85)
S-hCG	
Day 1:	
S-hCG concentration, median (Q1; Q3), IU/l	3,300 (1,300; 8,200)
Unknown, n	3
Day 7:	
S-hCG concentration, median (Q1; Q3), IU/l	140 (56; 290)
Unknown, n	3

Q = quartile; S-hCG = serum human chorionic gonadotropin.

Trial registration: The study was approved by the University Hospital of Southern Denmark, Sygehus Sønderjylland, record no.:24/44840.

RESULTS

A total of 100 women with unintended pregnancies were included in the study. Among these, 15% (n = 15) were included based solely on the presence of a thickened endometrium, whereas the remaining 85% (n = 85) were included based on visualisation of a gestational sac but without a yolk sac or embryonic structures. Complete abortion was achieved in 95% (n = 95) of participants.

Ongoing pregnancies were recorded in 3% (n = 3) of cases, a rate similar to that reported in previous studies of women treated using traditional abortion methods [12, 20]. In 1% (n = 1) of cases, the complete abortion was achieved following an additional dose of mifepristone and misoprostol. As part of the evaluation or treatment of suspected ectopic pregnancy, three women (3%) underwent laparoscopic procedures. The overall incidence of ectopic pregnancy was 2% (n = 2), all of which were diagnosed prior to rupture. Surgical management (uterine evacuation) for incomplete abortion was performed in 2% (n = 2) of the participants (SIR = 1.38; 95% CI: 0.17-4.98). The mean blood loss per patient was 50 ml.

In 9% (n = 9) of cases, follow-up was incomplete due to missed blood test appointments. However, treatment outcomes could be verified and documented from the EPJ.

Retained products of conception after medical abortion were identified in 4% (n = 4) of participants. Additional medical treatment (a single dose of misoprostol) for retained products of conception was administered to 1% (n = 1). Only 2% (n = 2) underwent dilation and curettage, and 1% (n = 1) underwent diagnostic hysteroscopy under local anaesthesia for retained tissue of pregnancy.

The amount of bleeding was generally described as minimal to moderate, and no patients experienced severe haemorrhage. No SAEs related to the treatment were recorded.

DISCUSSION

In this prospective cohort study, we examined the efficacy and safety of medical abortion at a very early gestational age, before an IUP could be confirmed by ultrasound. Our results indicate that the VEMA protocol can be applied safely and effectively in clinical practice when systematic follow-up with S-hCG level measurements and clinical assessment are performed.

Using the reduction in S-hCG levels over seven days as the primary criterion for treatment success, it was possible to identify both treatment failures and ectopic pregnancies at an early stage. This approach is consistent with previous observational studies, which have shown that VEMA does not delay the diagnosis of pregnancy location, provided patients are monitored closely [3, 11, 12].

Our experience confirms that timely and structured follow-up is crucial. In cases where patients adhered to the follow-up programme with blood tests and/or ultrasound, ectopic pregnancies could be diagnosed and treated early, reducing the risk of rupture and severe bleeding.

The efficacy of medical abortion in very early pregnancy in our study falls within the range

reported in previous studies (85-100%) [3, 11, 13-17]. This supports the notion that treatment need not be postponed until ultrasound visualisation of the IUP, provided a well-organised follow-up strategy is in place.

Our results also show that a small proportion of women required additional medical or surgical treatment for incomplete abortion. This corresponds to rates reported in a previous study [12] and is also comparable to standard medical abortion at later gestational ages.

Other key limitations of this study were the small sample size, which resulted in a wide 95% CI for the SIR, and the absence of a control cohort.

CONCLUSIONS

Overall, our findings support that VEMA can be performed safely and effectively without waiting for ultrasound confirmation of an IUP if patients receive close follow-up and clear guidance.

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References can be found with the article at ugeskriftet.dk/dmj

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REFERENCES

1. Upadhyay UD, Coplon L, Atrio JM. Society of Family Planning Committee Statement: abortion nomenclature. Contraception. 2023;126:110094. https://doi.org/10.1016/j.contraception.2023.110094
2. World Health Organization. Abortion care guideline. World Health Organization, 2022. www.who.int/publications/i/item/9789240039483 (21 Nov 2025)
3. Bizjak I, Fiala C, Berggren L, et al. Efficacy and safety of very early medical termination of pregnancy: a cohort study. BJOG. 2017;124(13):1993-1999. https://doi.org/10.1111/1471-0528.14904
4. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins - Gynecology, Society of Family Planning. Medication abortion up to 70 days of gestation: ACOG Practice Bulletin, Number 225. Obstet Gynecol. 2020;136(4):e31-e47. https://doi.org/10.1097/AOG.0000000000004082

5. Royal College of Obstetricians and Gynaecologists. Best practice in abortion care (best practice paper). Royal College of Obstetricians and Gynaecologists, 2022. www.rcog.org.uk/guidance/browse-all-guidance/best-practice-papers/best-practice-in-abortion-care-best-practice-paper/ (21 Nov 2025)
6. Fiala C, Bombas T, Parachini M, et al. Management of very early medical abortion - an international survey among providers. Eur J Obstet Gynecol Reprod Biol. 2020;246:169-176. https://doi.org/10.1016/j.ejogrb.2020.01.022
7. Kortsmit K, Nguyen AT, Mandel MG, et al. Abortion surveillance - United States, 2021. MMWR Surveill Summ. 2023;72(9):1-29. https://doi.org/10.15585/mmwr.ss7209a1
8. Barnhart K, van Mello NM, Bourne T, et al. Pregnancy of unknown location: a consensus statement of nomenclature, definitions, and outcome. Fertil Steril. 2011;95(3):857-866. https://doi.org/10.1016/j.fertnstert.2010.09.006
9. Axelsson PB, Løkkegaard ECL, Helm P. A ruptured ectopic pregnancy during early termination of pregnancy before ultrasound confirmation. Ugeskr Læger. 2020;182:V11190651
10. Flynn AN, Schreiber CA, Roe A, et al. Prioritizing desiredness in pregnancy of unknown location: an algorithm for patient-centered care. Obstet Gynecol. 2020;136(5):1001-1005. https://doi.org/10.1097/AOG.0000000000004124
11. Borchert K, Thibodeau C, Varin P, et al. Medication abortion and uterine aspiration for undesired pregnancy of unknown location: a retrospective cohort study. Contraception. 2023;122:109980. https://doi.org/10.1016/j.contraception.2023.109980
12. Brandell K, Jar-Allah T, Reynolds-Wright J, et al. Randomized trial of very early medication abortion. N Engl J Med. 2024;391(18):1685-1695. https://doi.org/10.1056/NEJMoa2401646
13. Goldberg AB, Fulcher IR, Fortin J, et al. Mifepristone and misoprostol for undesired pregnancy of unknown location. Obstet Gynecol. 2022;139(5):771-780. https://doi.org/10.1097/AOG.0000000000004756
14. Goldstone P, Michelson J, Williamson E. Effectiveness of early medical abortion using low-dose mifepristone and buccal misoprostol in women with no defined intrauterine gestational sac. Contraception. 2013;87(6):855-858. https://doi.org/10.1016/j.contraception.2012.10.013
15. Heller R, Cameron S. Termination of pregnancy at very early gestation without visible yolk sac on ultrasound. J Fam Plann Reprod Health Care. 2015;41(2):90-95. https://doi.org/10.1136/jfprhc-2014-100924
16. Schaff EA, Fielding SL, Eisinger S, et al. Mifepristone and misoprostol for early abortion when no gestational sac is present. Contraception. 2001;63(5):251-254. https://doi.org/10.1016/S0010-7824(01)00200-1
17. Tai NQR, Reynolds-Wright JJ, Cameron S. Very early medical abortion: treatment with mifepristone and misoprostol before ultrasonographic visualisation of an intrauterine pregnancy. BMJ Sex Reprod Health. 2023;49(2):97-104. https://doi.org/10.1136/bmjsrh-2022-201677
18. Fiala C, Safar P, Bygdeman M, et al. Verifying the effectiveness of medical abortion: ultrasound versus hCG testing. Eur J Obstet Gynecol Reprod Biol. 2003;109(2):190-195. https://doi.org/10.1016/S0301-2115(03)00012-5
19. Whitehouse KC, Stifani BM, Duffy JMN, et al. Standardizing abortion research outcomes (STAR): results from an international consensus development study. Contraception. 2021;104(5):484-491. https://doi.org/10.1016/j.contraception.2021.07.004
20. Kallfa E, Lauszus F, Ravn P. Control of the level of human chorionic gonadotropin in urine compared to the level of serum after medically provoked abortion is a safe alternative. Ugeskr Læger. 2021;183:V03210262

