Early Pregnancy Failure: Factors Affecting Successful Medical Treatment

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ABSTRACT: **Background:** The results of medical treatment for early pregnancy failure are conflicting.

Objectives: To determine whether gestational sac volume measurement as well as other variables can predict the success rate of medical treatment for early pregnancy failure.

Methods: The study group comprised 81 women diagnosed with missed abortion or anembryonic pregnancy who consented to medical treatment. Demographic data were collected and beta-human chorionic gonadotropin level was documented. Crown-rump length and the sac volume were measured using transvaginal ultrasound. TVU was performed 12–24 hours after intravaginal administration of 800 µg misoprostol. If the thickness of the uterine cavity was less than 30 mm, the women were discharged. If the sac was still intact or the thickness of the uterine cavity exceeded 30 mm, they were offered an additional dosage of intravaginal misoprostol or surgical uterine evacuation.

Results: Medical treatment successfully terminated 32 pregnancies (39.5%), 30 after one dose of misoprostol and 2 after two doses (group A); 49 underwent surgical evacuation (group B), 47 following one dose of misoprostol and 2 following two doses. There were no significant differences between the groups in age and gestational week. Gestational sac volume did not differ between groups A and B (10.03 and 11.98 ml respectively, $P = 0.283$). Parity (0.87 and 1.43, $P = 0.015$), previous pregnancies (2.38 and 2.88, $P = 0.037$), and βhCG concentration (6961 and 28,748 mIU, $P = 0.013$) differed significantly between the groups.

Conclusions: Gestational sac volume is not a predictor of successful medical treatment for early pregnancy failure. Previous pregnancies and deliveries and higher βhCG concentration negatively affect the success rate of medical treatment.

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KEY WORDS: early pregnancy failure, missed abortion, anembryonic pregnancy, gestational sac volume, misoprostol, medical treatment

TVU = transvaginal ultrasound
βhCG = beta-human chorionic gonadotropin

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Medical treatment for failed first-trimester pregnancy ("missed abortion") has become an acceptable alternative to surgical uterine evacuation. Several studies have compared medical treatment to other treatment modalities – such as expectant management [1,2] and surgical evacuation of the uterus [3-5] – and to treatment by placebo [6-8]. Conflicting success rates of medical treatment for missed abortion have been reported, ranging from 13% to 94%. The variance in these rates may be due to a lack of parameters to predict the success of medical treatment, to differences in the regimens used, and to the different definitions of successful outcome. The main purpose of our study was to compare the usefulness of certain parameters in predicting the outcome of medical treatment for early pregnancy failure. These parameters were gestational sac volume, crown-rump length, and clinical and demographic characteristics (age, number of previous pregnancies, abortions and deliveries).

PATIENTS AND METHODS

The Institutional Review Board (Helsinki Committee) of our hospital approved the study. Written informed consent was obtained from every patient. Patients admitted to our department diagnosed with missed abortion or anembryonic pregnancy, and with existing intrauterine pregnancy sac, were included. Missed abortion was diagnosed when the fetal pole was at least 4 mm in size [9] and there was no fetal heart activity, on two consecutive vaginal ultrasound examinations conducted at least 4 hours apart. Anembryonic pregnancy was diagnosed when a gestational sac of at least 20 mm in diameter was present without yolk sac [10]. Only patients with crown-rump length appropriate to less than 12 weeks were included, regardless of the gestational week. Demographic data and obstetric history were documented, such as age, gestational age according to last menstrual period, number of previous pregnancies and abortions, and number of deliveries. Human chorionic gonadotropin level was recorded when available. The same sonographer (M.O.) performed transvaginal ultrasound, using 5-9 MHz transducer (Voluson 730 Expert, GE Medical systems, Milwaukee,

Figure 1. Three-dimensional ultrasound measurement of the gestational sac volume in an 8 week missed abortion

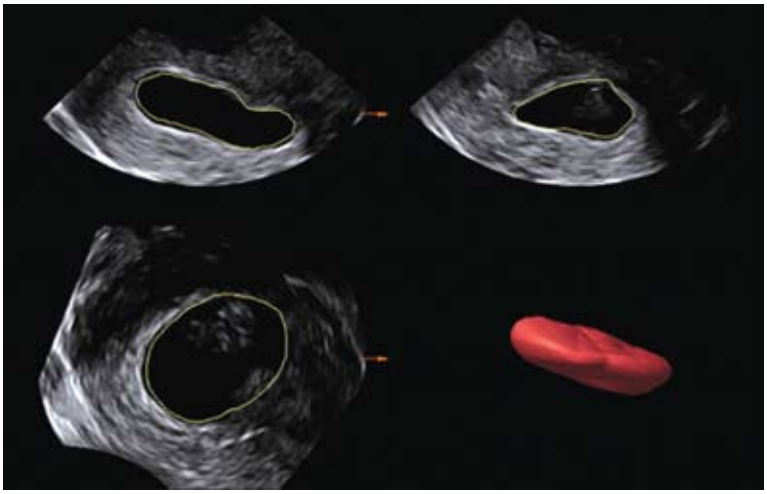

Table 1. Comparison between the group with successful medical treatment (A) and the group who underwent surgical evacuation (B)

	Group A (32)	Group B (49)	*P* value (one-sided)	*P* value (two-sided)
Age (yrs)				
Median (range)	25.5 (18–44)	30 (20–47)	0.109*	0.219*
Mean (SD)	27.9 (7.15)	29.8 (6.35)		
Gestational age (wks)				
Median (range)	9 (5–13)	9 (5–16)	0.212*	0.425*
Mean (SD)	9.4 (1.86)	9.1 (2.0)		
Past deliveries				
Median (range)	0 (0–4)	1 (0–7)	0.015**	0.029**
Mean (SD)	0.87 (1.15)	1.42 (1.35)		
Past abortions				
Median (range)	0 (0–4)	0 (0–4)	0.487**	0.971**
Mean (SD)	0.53 (0.95)	0.47 (0.82)		
No. of pregnancies				
Median (range)	2 (1–7)	3 (1–8)	0.037**	0.075**
Mean (SD)	2.38 (1.8)	2.88 (1.6)		
Crown–rump length (cm)				
Median (range)	1.2 (0.25–3.86)	0.52 (0.22–6.9)	0.036**	0.072**
Mean (SD)	1.27 (0.91)	1.17 (1.6)		
(n)	(26)	(42)		
GSV (ml)				
Median (range)	4.4 (0.04–37.6)	6.1 (0.14–78.3)	0.283**	0.566**
Mean (SD)	10.03 (11.7)	11.98 (17.3)		
hCG level (mIU)				
Median (range)	5638 (472–19, 744)	15,801(2145–155,180)	0.013**	0.026**
Mean (SD)	6961 (6308)	28,748 (39, 451)		
(n)	(7)	(15)		

* *t*-test, ** Wilcoxon test

WI, USA) for all participants. We measured the crown-rump length in participants with missed abortions. Virtual Organ Computer Aided Analysis (VOCAL) software, using maximal sweep angle, ensured that the entire gestational sac volume was included (Voluson 730 Expert Operation Manual, GE Medical Systems). We calculated volume measurements after patient discharge using 30^0 rotations, thus comprising a sequence of six sections. The GSV was measured manually by drawing the contour of each section [Figure 1].

Misoprostol 800 µg was administered intravaginally. Patients were reevaluated by TVU 12–24 hours later. Successful treatment was defined as an empty uterus or an endometrial lining with thickness less than 30 mm at reevaluation. A second intravaginal dose of misoprostol or surgical evacuation of the uterus was offered to women with an intact sac or with uterine content thickness of more than 30 mm.

STATISTICAL ANALYSIS

Qualitative data were described by frequencies and percentages; quantitative data were expressed as mean, standard deviation. Independent *t*-test, Fisher's exact test, chi-square test or Wilcoxon rank sum test were used as appropriate. The data were analyzed using the statistical software SPSS 11.5 (Chicago, IL, USA), and a *P* value less than 0.05 was considered significant.

RESULTS

The study group consisted of 81 women; 13 of them had an anembryonic pregnancy and the rest were diagnosed with missed abortion. The median age was 29 (range 18–47 years), median gestational age was 9 weeks (range 5–16). The median number of previous pregnancies was 2 (range 1–8), median number of previous deliveries 1 (range 0–7), median crown-rump length 0.59 cm (range 0.22–6.9), and median number of previous abortions 0 (range 0–4). Thirty-two women (39.5%) successfully aborted after misoprostol treatment (group A), and 49 (60.9%) underwent surgical evacuation (group B). In four patients a second intravaginal dose of misoprostol was administered. In two of them the pregnancy subsequently terminated; the other two underwent surgical evacuation. In five women (10.2%) who underwent surgical uterine evacuation there was no evidence of placental or fetal tissue at pathologic examination.

There was no statistically significant difference in gestational sac volume, age, or number of previous abortions between groups A (medical treatment) and B (surgical treatment) [Table 1]. A few patients (7 in group A and 15 in group B) had documented blood hCG level, indicating that higher levels of hCG were significantly associated with the need for surgical evacuation. In addition, as shown in Table 1, one or more previous deliveries were associated with a high failure rate of medical treatment. Differences in crown-rump length and number of previous pregnancies between the two groups were significant with a one-sided, but not two-sided test [Table 1].

GSV = gestational sac volume

DISCUSSION

We recently documented normal values (normograms) of gestational sac volume for normal pregnancies [11]. Another study documented values in pregnancies associated with chromosomal malformations [12]. The clinical significance of the gestational sac volume in predicting pregnancy outcome in normal and abnormal pregnancies has not been determined. Comparing GSV in missed abortion or anembryonic pregnancies to GSV in normal pregnancies, we found that GSV in missed and anembryonic pregnancies was significantly smaller after 7 weeks gestation (unpublished data) while GSV before 7 weeks of gestation was similar. In the present study we did not prove our hypothesis that gestational sac volume may predict successful medical treatment for early failed pregnancy. A study [13] similar to the present study also reported that gestational sac volume did not predict successful treatment in missed abortion followed expectantly. In that study [13] patients did not receive any treatment, whereas our patients were treated by misoprostol and yet gestational sac volume did not predict which patients will not need surgical intervention.

However, we did find that obstetric history can affect the success of medical treatment for failed pregnancy. Specifically, previous term pregnancy and higher number of pregnancies associated negatively with success of medical treatment for early pregnancy failure. A negative association was previously reported in cases of medical termination of pregnancy using mifepristone and gemeprost [14] and also mifepristone and misoprostol [15]. Bartley and colleagues [14] found that parous women were more likely to have incomplete or ongoing pregnancy following medical induction of abortion than nulliparous women (5.4% vs. 2.0%), although multiparous women presented earlier in the pregnancy for termination. Ashok et al. [15] found that women who had a previous live birth were more likely to have a failed abortion after medical treatment with mifepristone and misoprostol (odds ratio 2.03). Our study dealt only with misoprostol and not with mifepristone; and with treatment of early pregnancy failures and not with termination of viable pregnancies. Creinin and associates [16] similarly reported that the chances of successful medical treatment for early pregnancy failure are better in nulliparous women, especially in those presenting with vaginal bleeding or abdominal pain in the 24 hours preceding misoprostol administration. Their study [16] included patients with missed abortion and anembryonic gestation, but also incomplete and inevitable abortion. In contrast, our study included patients with intact intrauterine sac only, with either anembryonic or fetal pole present, excluding cases of incomplete abortion. The similar effect of nulliparity on the success rate of medical treatment for early pregnancy failure in both our study and that of Creinin et al. [16] needs to be elucidated. Possibly, implantation of trophoblastic tissue may be more successful in women following a previous term pregnancy.

Of note, our patients were hospitalized, even though outpatient treatment for early pregnancy failure is acceptable. One may argue that hospitalization may have influenced parous women who would be more anxious to leave the hospital to take care of their children than women without children waiting at home. Hence, multiparous women may prefer to undergo surgical evacuation and leave immediately thereafter, rather than wait for the results of the medical treatment.

We did not test βhCG in all patients prior to enrollment. However, in the few patients (7 in group A and 15 in group B) for whom βhCG was measured during the 24 hours before enrollment, higher levels of βhCG were significantly associated with the need for surgical evacuation. Conceivably, higher levels of hCG indicate a more recent pregnancy failure.

The crown-rump length was significantly smaller in the medically treated group (group A) when a one-sided statistical test was used. This finding might also reflect a smaller sized pregnancy or longer time interval since the occurrence of fetal demise and admission, resulting in a better chance of successful medical treatment.

In conclusion, our findings demonstrate that gestational sac volume does not correlate with the rate of successful medical treatment for early failed pregnancy, while the following variables – previous term pregnancy, higher number of previous pregnancies and a higher blood βhCG level – negatively affect the success rate of medical treatment for early pregnancy failure. These findings should be considered and explained to patients when selecting the type of treatment for early pregnancy failure.

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