

Expectant management of spontaneous first-trimester miscarriage: prospective validation of the '2-week rule'

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KEYWORDS: empty sac; expectant management; incomplete miscarriage; miscarriage; missed miscarriage

ABSTRACT

Objectives To assess uptake and success of expectant management of first-trimester miscarriage for a finite 14-day period, in order to evaluate our '2-week rule' of management.

Methods This was a prospective observational study evaluating our proposed 2-week rule of expectant management, which is based on the finding that women managed expectantly are most likely to miscarry in the first 14 days and that to wait longer than 2 weeks without intervention does not confer a greater chance of successful resolution. Eligible women diagnosed with first-trimester miscarriage were offered a choice of expectant management or surgical evacuation under general anesthesia. Inclusion criteria for expectant management were: diagnosis of incomplete miscarriage (heterogeneous tissue, with or without a gestational sac, seen on ultrasound in the uterine cavity and distorting the endometrial midline echo), missed miscarriage (crown–rump length (CRL) ≥ 6 mm with absent fetal heart activity) or empty sac (anembryonic pregnancy) based on transvaginal ultrasonography. Women with complete miscarriage, missed miscarriage at the nuchal translucency scan, molar pregnancy or miscarriage ≥ 3 weeks in duration (missed miscarriage in which the CRL was ≥ 3 weeks smaller than the gestational age based on last menstrual period), or with signs of infection or hemodynamic instability were excluded. Expectant management consisted of weekly ultrasonography for 2 weeks. If after 2 weeks resolution was not complete, surgery was advised.

Results 1062 consecutive pregnant women underwent transvaginal ultrasound examination. Of these, 38.6% (410/1062) were diagnosed with miscarriage, of whom 241 (59%) were symptomatic at the time of presentation

and 282 were eligible for the study. These were offered expectant management and 80% (227/282) took up this option. 11% (24/227) were lost to follow-up; therefore, complete data were available on 203 women. Overall spontaneous resolution of miscarriage at 2 weeks was observed in 61% (124/203) of women. Rates of spontaneous resolution at 2 weeks according to the type of miscarriage were 71% for incomplete miscarriage, 53% for empty sac and 35% for missed miscarriage. The incidence of unplanned emergency dilatation and curettage due to gynecological infection or hemorrhage was 2.5% (5/203).

Conclusions Expectant management based on the 2-week rule is a viable and safe option for women with first-trimester miscarriage. Women with an incomplete miscarriage are apparently the most suitable for expectant management. Copyright © 2010 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Approximately 11–15% of pregnancies end in spontaneous first-trimester miscarriage^{1,2}. Diagnosis of miscarriage has traditionally been followed by surgical evacuation of retained products of conception (RPOC), on the assumption that this decreases the risk of subsequent gynecological infection. However, surgical management is not without its complications; for example, infection, uterine perforation or bowel damage may arise from dilatation and evacuation (D&E)³. The largest randomized controlled trial to date, the miscarriage treatment trial (MIST), concluded that the rates of gynecological infection, whatever the type of management chosen, were reassuringly low (2–3%). The study found, however, that medical and expectant management resulted in more

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unplanned admissions and emergency surgery (e.g. for increased pain or bleeding) than did traditional surgical management⁴.

Success rates for expectant management have been reported to be between 75% and 80%^{4,5}. Incomplete miscarriages seem to be particularly appropriate for expectant management. Preliminary data from small randomized controlled trials found higher rates of success for expectant management in cases of incomplete miscarriage (79%) compared with the missed miscarriage group (37%)^{6–8}. Medical management of miscarriage, especially in those women with a missed miscarriage or empty sac, has been shown to be beneficial³. However, the use of misoprostol is not licensed for use universally and expectant management has not been embraced as a form of therapy in many countries. Thus, many clinically stable women still undergo surgical management in the form of D&E.

Luise *et al.*⁵ diagnosed women undergoing miscarriage and found that those women managed expectantly were most likely to miscarry in the first 14 days and that to wait longer than 2 weeks without intervention did not confer a greater chance of successful resolution of the pregnancy by expectant management. Based on the results of this study, it would seem intuitive to offer expectant management to clinically stable women diagnosed with miscarriage for a finite period, i.e. 14 days, after which surgery would be deemed appropriate. There are no published data, however, to support such a practical approach to these women. In this study, therefore, we aimed to evaluate the uptake as well as the success of expectant management of miscarriage for a finite 14-day period; we refer to this as the '2-week rule'.

METHODS

This was a prospective observational study of pregnant women with miscarriage at < 13 weeks' gestation, based on last menstrual period (LMP), attending the Acute Gynaecology Unit (AGU) at Nepean Hospital, Sydney, from November 2006 to July 2008, inclusive. Ethics approval was obtained from the Human Research Ethics Committee prior to commencement of the study. All women, irrespective of the presence or absence of symptoms, who presented to the AGU during this period underwent transvaginal ultrasound (TVS) of the pelvis using a 7.5-MHz transvaginal probe (LOGIQ-e -I, GE Medical Systems, Zipf, Austria). The diagnosis of miscarriage was ultrasound-based and defined according to the guidelines published by the UK's Royal College of Obstetricians and Gynaecologists⁹; each woman's miscarriage was classified as complete, incomplete, missed or empty sac (anembryonic pregnancy) (Table 1). Each woman was counseled about the diagnosis and those who fulfilled the entry criteria for expectant management were given the choice of either expectant or surgical management.

We included women diagnosed by transvaginal ultrasound with incomplete, missed and anembryonic miscarriages who were clinically stable with no signs of infection

Table 1 Sonographic classification of miscarriage

Miscarriage type	Products of conception
Complete miscarriage	Nil retained products of conception in the endometrial cavity and endocervical canal*
Incomplete miscarriage	Heterogeneous tissue (with or without gestational sac) seen on ultrasound in the uterine cavity and distorting the endometrial midline echo
Empty sac (anembryonic pregnancy)	Gestational sac (diameter > 20 mm, no embryonic pole or yolk sac) seen on ultrasound in the uterine cavity; if diameter ≤ 20 mm, no change on rescan 7 days later
Missed miscarriage	Fetal pole (crown–rump length > 6 mm, no heart beat); if crown–rump length ≤ 6 mm, no change on rescan 7 days later

Adapted from RCOG Green-top Guideline No. 25 (2006)⁹. *No specific endometrial thickness used to define complete miscarriage; previous work⁵ used ET < 15 mm.

(signs included raised white blood cell count, temperature > 38°C, tachycardia, malodorous vaginal discharge and lower abdominal tenderness). Exclusion criteria included severe vaginal hemorrhage with hemodynamic instability, infection, complete miscarriage diagnosed at the first scan (in the context of a previously documented intrauterine pregnancy), molar pregnancy, missed miscarriage diagnosed at the nuchal translucency (NT) scan, and missed miscarriage when the crown–rump length (CRL) was ≥ 3 weeks smaller than the gestational age based on the LMP. Women who were diagnosed with a missed miscarriage at the NT scan were scheduled for surgery because they had already failed expectant management (by default) and these women tend to bleed very heavily if managed expectantly¹⁰. Women who were diagnosed with a missed miscarriage when the CRL was ≥ 3 weeks smaller than the gestational age based on LMP had also already failed expectant management (by default) and were scheduled for surgery. Women who declined expectant management or who were excluded were placed on the emergency list for day surgery, and were treated in the standard way, i.e. by D&E performed by experienced operators.

Expectant management meant that a 'wait-and-watch' approach was adopted. Those women who chose expectant management underwent TVS on a weekly basis for 2 weeks. Success, i.e. complete resolution of the miscarriage, was defined as the resolution of symptoms (vaginal bleeding) and the absence of RPOC on follow-up TVS at 14 days. Women who had persistent RPOC on TVS at 14 days were deemed to have failed expectant management and advised to have surgery. Those women keen to continue expectant management, despite advice for surgical intervention at day 14, were again rescanned at the end of the 3rd week, i.e. on day 21; these women were not excluded. Women undergoing expectant management could change their mind at any time

and opt for surgery. If, at any time during expectant management follow-up, the woman developed fever, chills or malodorous vaginal discharge, then expectant management was ceased and surgery was arranged for that day. Surgery involved D&E under general anesthesia.

The main outcome measures included uptake of expectant management, overall success of expectant management at 2 weeks and success of expectant management for the different types of miscarriage. A secondary outcome measure was the rate of infection or need for emergency D&E.

RESULTS

A total of 1062 consecutive pregnant women at < 13 weeks' gestation based on LMP presented to the AGU during the study period. Of these women, only 410 were diagnosed with miscarriage. The remaining 652 women had diagnoses such as viable intrauterine pregnancy, intrauterine pregnancy of uncertain viability and ectopic pregnancy. Of the 410 women diagnosed with miscarriage, 241 (59%) were symptomatic at the time of presentation. The 169 who were asymptomatic presented for various reasons, such as previous ectopic, twin or molar pregnancy, previous pregnancy of unknown location (PUL), previous miscarriage, maternal anxiety, uncertain dates, suspected twin pregnancy (clomid-assisted ovulation) and confirmation of pregnancy. All women with

incomplete miscarriage were symptomatic; the women with empty sac or missed miscarriage were either symptomatic or asymptomatic. Of the 410 women diagnosed with miscarriage, 31% ($n = 128$) women were ineligible for the study and excluded from the final analysis.

All 282 women who were eligible for expectant management were offered it, and 80% (227/282) took up the offer. Of these, 11% ($n = 24$) were lost to follow-up, so complete data were available for 203 women. Successful spontaneous completion of the miscarriage at 2 weeks was observed in 124 (61%) (Figure 1). All 79 of the remaining women, who failed expectant management, underwent D&E within 2 weeks of the start of expectant management. The overall rate of spontaneous completion of the miscarriage at 14 days for incomplete miscarriage was 71%, for empty sac (anembryonic pregnancy) it was 53% and for missed miscarriage it was 35% (Table 2).

Specific information regarding planned vs. unplanned D&E was not collected in this study. However, to our knowledge, 2.5% ($n = 5$) of the 203 women who chose to undergo expectant management had unplanned emergency D&E due to gynecological infection or hemorrhage. Of these, three had developed signs of infection (elevated temperature, raised white blood cell count, malodorous vaginal discharge and abdominal pain) and two, who had been diagnosed with missed miscarriage, required emergency surgery and blood transfusion.

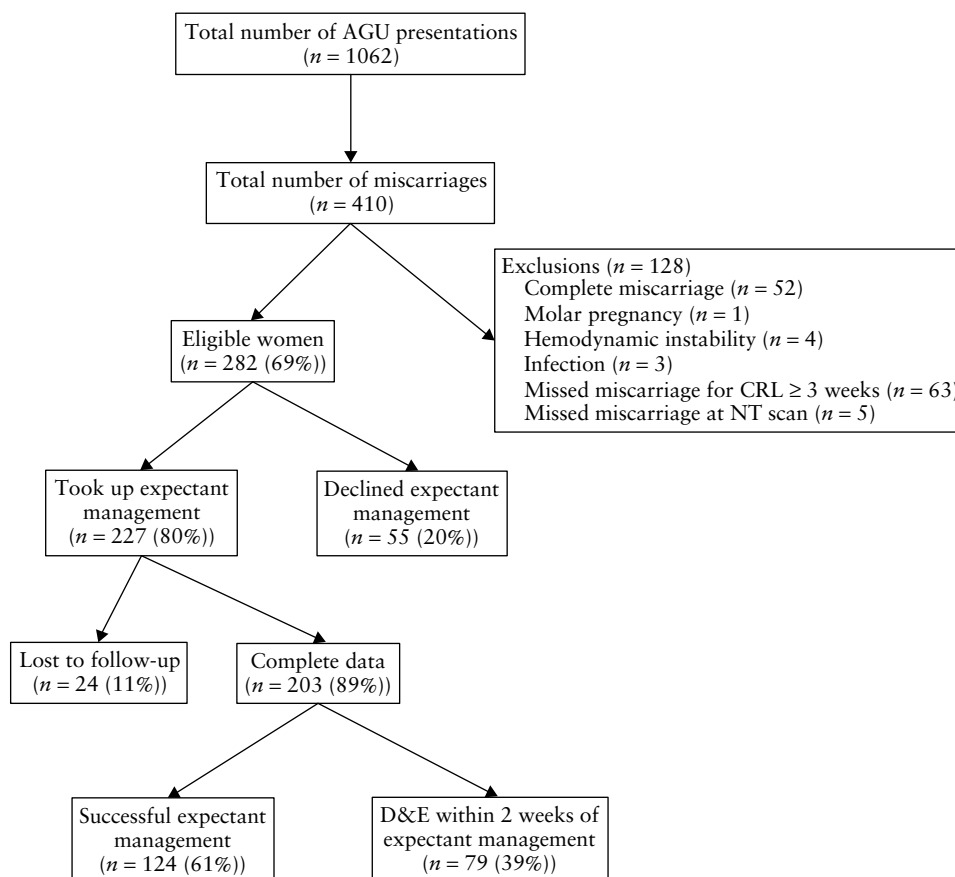


Figure 1 Summary of results. AGU, Acute Gynaecology Unit; CRL, crown-rump length; D&E, dilatation and evacuation; NT, nuchal translucency.

Table 2 Types of miscarriage and outcomes of expectant management

Diagnosis	Total	Offered expectant management	Took up expectant management	Expectant management results at 14 days	
				Successful	Failed
Incomplete miscarriage	185 (45)	150 (81)	130 (87)	92 (71)	38 (29)
Empty sac	82 (20)	59 (72)	36 (61)	19 (53)	17 (47)
Missed miscarriage	143 (35)	73 (51)	37 (51)	13 (35)	24 (65)
Total	410	282 (69)	203 (72)	124 (61)	79 (39)

Data are shown as *n* (%). The 24 women lost to follow-up are not included.

DISCUSSION

The objective of this study was to validate prospectively expectant management of miscarriage offered to women with first-trimester miscarriage for a finite time period, i.e. 2 weeks. Our 2-week management rule suggests that women with an incomplete miscarriage are the most suitable for expectant management. While it is safe to offer expectant management to women with a missed miscarriage or empty sac, the rates of resolution may not be sufficiently high for these women to choose such a management approach. The rule allows women to make an informed choice about the likelihood of success within a finite, acceptable period of time.

The success rates in this study on initial inspection appear somewhat discouraging (incomplete miscarriage, 71%; empty sac, 53%; missed miscarriages, 35%; overall, 61%; Table 2). However, it must be remembered that we defined failure as the unsuccessful resolution of miscarriage at 2 weeks. Our 2-week outcomes are comparable to the 14-day outcomes of Luise *et al.*⁵ (incomplete miscarriage 84%, missed miscarriage 59%, empty sac 52% and overall 70%). The slightly higher rates of success of Luise *et al.* may be due to their definition of complete miscarriage. We did not use a specific endometrial thickness (ET) cut-off, whereas Luise *et al.* defined a complete miscarriage as an ET < 15 mm. Specific cut-offs for complete miscarriage have not been validated prospectively¹⁰ and a cut-off for ET or endometrial volume that can be used to differentiate between an incomplete and a complete miscarriage has not been identified¹¹. Their use of an ET cut-off of 15 mm may have resulted in the over-classification of complete miscarriages, which in turn could account for their higher success rates.

Most women in this study who were diagnosed with first-trimester miscarriage and were offered the choice chose expectant management in preference to surgery. The high uptake and success of expectant management in this study may have been influenced by the knowledge that women could receive rapid surgical intervention if required. Our unit fulfils the recommendations of the Royal College of Obstetricians and Gynaecologists that expectant management should be offered only in units where immediate admission can be arranged⁹. The lower rates of successful expectant management at

2 weeks in the empty sac (53%) and missed miscarriage (35%) groups would suggest that these women should be offered alternatives. Higher success rates of around 95% have been reported in trials involving intervention with misoprostol^{12,13}.

As reported in other studies¹⁴, our study also demonstrated a low rate of pelvic infection and unplanned surgical management in women undergoing expectant management for first-trimester miscarriage, our infection rate following expectant management being approximately 2%, similar to levels in other studies^{4,8,15}. This reassuringly low rate of complications allows expectant management to be offered safely to the majority of patients. However, two women in the expectant management arm of the study with a diagnosis of missed miscarriage did have significant hemorrhage requiring emergency surgical D&E. They also needed blood transfusion to correct the significant drop in hemoglobin levels resulting in symptoms of tachycardia and hypotension. Both these women were deemed retrospectively to be inappropriate for expectant management as they were more than 10 weeks' gestation based on CRL at the time of diagnosis. We know that women with a missed miscarriage diagnosed around the time of the NT scan tend to bleed heavily when managed expectantly¹⁰.

Potential limitations to the study include the fact that women diagnosed with a missed miscarriage when the CRL was ≥ 3 weeks smaller than the gestational age based on LMP were excluded from expectant management. In retrospect, a limitation of this was that no distinction was made between women with regular and irregular cycles, even though dating by LMP in the latter group is unreliable. Also, eligible women were included in the study whether or not they were symptomatic and final outcomes of successful expectant management based on the presence or absence of symptoms was not analyzed. This may represent a shortcoming as there may be considerable differences between these two groups in the final outcome of successful expectant management. This will be the remit of future work performed by our unit.

As well as the medical consequences of miscarriage, there may be psychological complications. The available data suggest that there is no difference in psychological morbidity between those undergoing expectant

and those undergoing surgical management¹⁰. Although our study did not formally assess psychological sequelae, a small percentage (<1%) of women who were emotionally distraught following the diagnosis of miscarriage were still offered, but declined, expectant management. According to a subanalysis of the MIST trial, all women undergoing management of first-trimester miscarriage value being offered alternatives to expectant management¹⁶.

In conclusion, expectant management based on the 2-week rule is a viable and safe option for women with first-trimester miscarriage. The results from this practical approach to a common problem would suggest that women with an incomplete miscarriage are the most suitable for expectant management. The differences in the outcomes between symptomatic and asymptomatic women on the day of diagnosis of miscarriage are unknown. This will be the remit of future studies from this unit.

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