

Incomplete miscarriage, expectant versus medical management and the use of Doppler sonography for patient selection

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Abstract:

Background: Miscarriage is the most common complication of early pregnancy, and remains an important clinical problem. Knowledge of the pathophysiology of this is limited and therefore therapeutic regimens are based on few data.

Objective: To study patients with first trimester incomplete miscarriage and to evaluate whether expectant or medical management is a feasible strategy and to assess the value of Colour Doppler ultrasonography for patient selection.

Patients and Method: A prospective comparative study of a total of 100 pregnant women with an estimated gestation age of up to 13 weeks from the last menstrual period (LMP) attending Al Yarmouk teaching hospital from November 2011 to November 2012, after confirmation of the diagnosis by transvaginal sonography, the patients were divided into two groups: expectant and medical management groups. The ultrasound examination included Colour Doppler Imaging to evaluate the vascularity of retained products.

Results: Out of a total of 100 women recruited, 50 patients (50%) elected to expectant management and 50 patients (50%) for medical management. The treatment groups were similar in age, gestational age, and proportion of patients who had post-treatment complications (12–13%). By 4 weeks after inclusion, 42 patients (84%) in the expectant management group had undergone a spontaneous complete miscarriage and 8 patients (16%) had undergone surgical evacuation. While in the medical management group, 46 patients (92%) had undergone complete miscarriage and 4 (8%) had undergone surgical evacuation. 54.3% of cases with detectable presumed intervillous pulsatile blood flow had a complete, spontaneous miscarriage within 1 week; this occurred in 77.8% of cases with no detectable flow. This suggests that conservative management is a successful approach for patients with first trimester incomplete miscarriage; Colour Doppler ultrasonography can be used to select the most suitable patients for this strategy, and thus reduces the need for hospital admission, surgery and prolonged follow up.

Key words: Incomplete miscarriage / Colour Doppler ultrasonography/Conservative management

Introduction:

Incomplete miscarriage is defined as vaginal bleeding that is ongoing where pregnancy tissue has already been passed but ultrasound suggests the presence of further products within the uterine cavity^[1]. Spontaneous miscarriage develops in 20–25% of women during early gestation^[2], with an overall incidence of spontaneous miscarriage of some 12–19% among clinically recognized pregnancies^[3].

The management of miscarriage has changed and conventional surgical evacuation of the uterus has been recommended when there are retained products of conception^[4, 5]. However, surgical management is associated with significant morbidity for example, infection, uterine perforation or bowel damage^[6]. The medical management of miscarriage, which can achieve complete uterine evacuation in up to 95% of early miscarriages, has been developed as a realistic alternative to surgical evacuation^[7, 8]. The methods involve the combined use of the antiprogesterone, mifepristone, and the prostaglandin E1 analogue, misoprostol, and has been shown to result in lower costs per patient, compared with surgical treatment^[9].

There is strong evidence supporting expectant management as a realistic alternative to surgical evacuation^[10]. We used transvaginal sonography (TVS) to evaluate the feasibility of medical or expectant management for first trimester incomplete miscarriages. Furthermore, we assessed the value of

colour Doppler Imaging (CDI) to identify those patients with incomplete miscarriage who would be most suitable for expectant or medical treatment.

Patients and method:

We undertook a prospective comparative study of a total of 100 pregnant women with an estimated gestation age of up to 13 weeks from the last menstrual period (LMP) attending Al Yarmouk teaching hospital from Nov. 2011 to Nov. 2012. All women included in the study were symptomatic and had reported abdominal pain, vaginal bleeding with or without passage of clots and stable vital signs at time of examination with no evidence of infection (fever, vaginal discharge and leukocytosis); all these women had previously confirmed intrauterine pregnancies. Inclusion was restricted to those shown by ultrasonography to have evidence of retained products of conception (the diagnosis of incomplete miscarriage was defined by the presence of a measurable focus of hyper echoic material within the endometrial cavity using two-dimensional (2D) TVS with endometrial cavity A–P diameter of 15 mm or more as shown in Figure 1) at the time of examination. The ultrasound examination included CDI to evaluate the vascularity of retained products. All patients received prophylactic antibiotics. Patients who were rhesus-negative received anti-D immunoglobulin. Patients were randomly divided into two groups in order to manage their miscarriage: either expectant management so that

the patient received a placebo drug, or medical management receiving 600 micrograms of misoprostol orally in two doses 12 hours apart. Follow up of the patients with ultrasound at weekly intervals after inclusion into the study. If the scan suggested the persistent presence of retained products 28 days after inclusion with or without vaginal bleeding, the patient was advised to have surgical evacuation. All patients gave a written informed consent.

Statistical analysis: The data were expressed in means, ranges and/or standard deviation. T test has been used to test the significance of difference between two groups. Significant difference was considered at p value less than 0.05.

Results:

Of the 100 women recruited, 50 patients (50%) elected to expectant management, and 50 patients (50%) for medical management. The two treatment groups were similar in age, parity, gestational age of the pregnancy, retained products size and hemoglobin concentration (Table 1).

By 4 weeks after inclusion, 42 (84%) patients in the expectant management group had undergone a spontaneous complete miscarriage and 8 (16%) had undergone surgical evacuation. While in the medical management group, 46 (92%) patients had undergone complete miscarriage and 4 (8%) had undergone surgical evacuation. For each gestational age category, the proportion of patients with

complete miscarriage after 1, 2, 3 and 4 weeks after inclusion was shown in Table 2. The chances of the miscarriage resolving were independent of gestational age. The number of women who had undergone a complete miscarriage increased each week up to 28 days.

Using CDI, all the patients were evaluated for the presence of vascular retained products (figure no 2 showing positive CDI and figure no 3 showing negative CDI).

44% of the expectant management group had vascular retained products and 48% of the medical management group had vascular retained products, there was no statistically significant difference among the two groups as shown in table 3.

The current study revealed that patients with avascular retained products had significantly higher rate of complete miscarriage after 7 days compared with those with vascular products, 87.6% versus 45.5% in the expectant management group and 76.9% versus 62.5% in the medical management group. The rate of miscarriage among those with vascular retained products was higher in the medical management group compared with those in the expectant group, 62.5% compared with 45.5%, and this was significant statistically since $P=0.01$. As shown in table 4.

Table 5 showing the frequency of complications among the two groups, there was no statistically significant difference among the two groups as $P=0.9$.

Table 1: The characteristics of patients in both groups. Data expressed as mean with standard deviation or range.

Parameter	Expectant group(n=50)	Medical group (n=50)
Age (years)	28.4 (± 6.5)	30.8 (± 5.6)
Parity	2.7 (1-5)	3.4 (2-5)
Previous miscarriage	0.4 (0-2)	0.5 (0-4)
Gestational age (weeks)	9.3 (7-12)	9.4 (7-12)
Retained products diameter (mm)	28.6 (12-49)	26.2 (16-50)
Hemoglobin (g/l)	10.8 (± 0.7)	11.2 (± 0.6)
P=0.98 (Not significant)		

Table 2: The proportion of patients having complete miscarriage after 1, 2, 3 and 4 weeks related to gestational age

Gestational age(weeks)	Expectant management (n=50), complete abortion after:					Medical management (n=50), complete abortion after:				
	1 week	2 weeks	3 weeks	4 weeks	All	1 week	2 weeks	3 weeks	4 weeks	All
7	3	2	0	0	5\6	4	1	0	0	5\5
8	5	1	1	0	7\7	7	0	1	0	8\9
9	6	1	1	0	8\9	6	0	1	1	8\8
10	4	0	0	1	5\6	5	2	0	0	7\8
11	7	0	1	0	8\10	6	1	0	1	8\9
12	7	0	1	1	9\12	7	2	1	0	10\11
All	32	4	4	2	42\50	35	6	3	2	46\50
P= 0.93 (Not significant)										



Figure 1: The transvaginal sonography showing retained products



Figure 2: The transvaginal sonography showing retained products with positive CDI

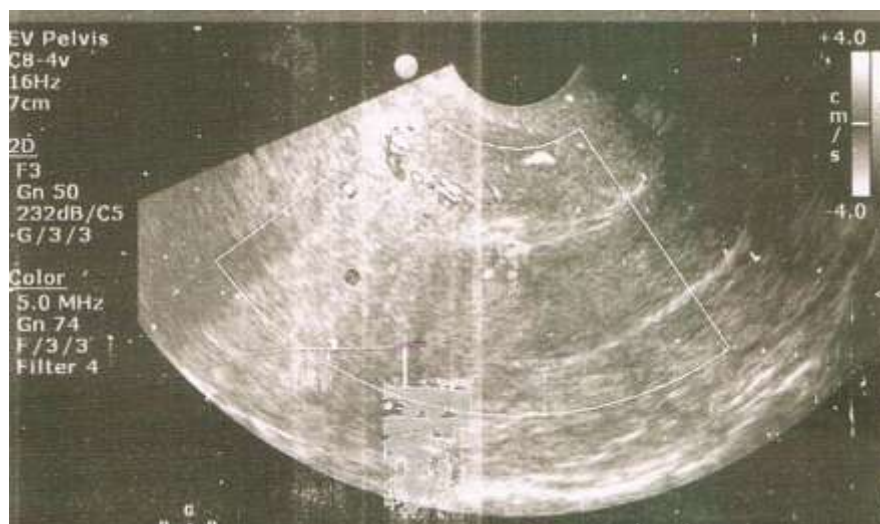


Figure 3: The transvaginal sonography showing retained products with negative CDI

Table 3: The detection of vascular retained products using Doppler study among the two groups:

	Vascular retained products by colour Doppler		
	Positive No(%)	Negative No(%)	All
Expectant management	22 (44 %)	28 (56 %)	50
Medical management	24 (48 %)	26 (52%)	50
All	46 (46 %)	54 (54 %)	100
P=0.11 (Not significant)			

Table 4: The presence of vascular retained products and the occurrence of complete miscarriage within 7 days in the two groups:

Complete miscarriage within 7 days	Vascular retained products by colour Doppler		
	Positive No(%)	Negative No(%)	All
Expectant management(n=50)	10\22 (45.5 %)	22\28 (87.6 %)	32
Medical management (n=50)	15\24 (62.5 %)	20\26 (76.9 %)	35
All	25\46 (54.3%)	42\54 (77.8%)	67
P=0.01 (Significant)			

Table 5: The complications experienced by patients in the two groups.

Complication	Expectant management (n=50)	Medical management (n=50)
Infection	1	1
Haemorrhage (Haemoglobin<10g/l)	3	1
Intolerable pain	0	2
Gastrointestinal symptoms	0	4
Curettage	8	4
Trophoblastic disease	1	0
Total	13%	12%
P=0.9 (Not significant)		

Discussion:

The current study revealed that both expectant and medical management are feasible strategies for incomplete miscarriage with high success rate in both groups after 4 weeks of inclusion, and these results were in agreement with those investigators (Luise *et al.*, Bagratee *et al.* and Trinder *et al.*) who demonstrated that incomplete miscarriages seem to be particularly appropriate for expectant management. Luise *et al.* in their study concluded that the majority of women with incomplete miscarriage achieved spontaneous resolution within 14 days, while~10% failed expectant management and needed curettage, in our study 12% curettage rate were seen^[11]. Bagratee *et al.* in their study found that medical management using 600 microg misoprostol vaginally is more effective than expectant management of early pregnancy failure. Misoprostol did not increase the side-effect profile and patient acceptability was superior to expectant management. However, there was no significant difference in success rate (100 versus 85.7%) in women treated with an incomplete miscarriage, in our study the success rates of medical was higher than expectant management but this was not significant^[12]. Results from the largest randomized controlled trial, the Miscarriage Treatment Trial (MIST), concluded that the rates of gynaecological infection were reassuringly low (2-3%) among those with conservative management^[13].

More recently, the 'two-week' rule for the expectant management of miscarriage was evaluated by Casikar *et al.*, In that study, women with an incomplete miscarriage were the most appropriate miscarriage group for expectant management with the highest rate of spontaneous resolution at 14 days^[14]. Blohm *et al.* in their study found that the treatment with 400 microg misoprostol administered vaginally increased the success rate of resolution of uncomplicated early miscarriages compared with placebo, However, women who received misoprostol experienced more pain and required more analgesics than those who did not, while in our study the success of medical treatment was higher but not significant and this possibly because we evaluate incomplete miscarriages only while in that study they evaluate both missed and incomplete miscarriages^[15]. Shelley *et al.* evaluated the Effectiveness at 8 weeks of medical, expectant and surgical treatment for incomplete miscarriage and it was lower for medical (80.0%) and expectant (78.6%) than for surgical management (100.0%), they conclude that expectant care appears to be sufficiently safe and effective to be offered as an option for women^[16]. Petrou *et al.* studied the economic costs of medical, expectant and surgical treatment of incomplete miscarriage and they conclude that expectant and medical management of first-trimester miscarriage possess significant economic advantages over traditional surgical

management ^[17]. *Nguyen et al.* found that oral misoprostol in doses (600 or 1,200 microg) offers a safe, effective and acceptable treatment for incomplete abortion, and it was equally effective but more side effects with higher doses, so in our study we chose 600 microgram to minimize the side effects ^[18].

In our study, we hypothesize that in an incomplete miscarriage, if there is persistent communication between the residual trophoblast and maternal circulation using CDI, these women are more likely to fail expectant management, as 45.5% of those with vascular retained products had complete abortion compared with 87.6% of those with avascular retained products in the expectant group versus 62.5% and 76.9% in the medical management group, and these results were in agreement with *Casikar et al.* who demonstrated that the absence of vascularity equates to an 89% success rate at 2 weeks. Conversely, the presence of vascularity equates to lower rates of success (60.9%). We believe that the use of CDI enables the clinician to appropriately counsel women with regard to their chances of success or failure with expectant and medical management.

In our clinical set up we used CDI to study the vascularity of retained products and its relationship to successful expectant management while other studies have used Power Doppler to confirm the presence of retained products of conception (RPC) after miscarriage ^[19-20] and although they have then managed their women with RPC expectantly, they didn't correlate Doppler findings with the likelihood of successful expectant management.

In our study we use positive or negative CDI rather than Power Colour Doppler scoring, this is because of inter and intra-observer variation of this subjective vascular scoring technique that may contribute to bias in the results.

Conclusion:

We have demonstrated that both expectant management and medical management are feasible strategies for those with incomplete miscarriage who are vitally stable with no evidence of infection to minimize the rate of surgical intervention with its complications. However the success rate of medical management is higher, it still not significant statistically. The absence of blood flow in residual trophoblastic tissue on colour Doppler is associated with a significant improvement in successful expectant management of incomplete miscarriage as it is a simple technique and can be adopted clinically. We believe that this study enables the clinician to counsel women appropriately regarding their chances of success or failure if they choose expectant management or medical management, women with vascular retained products had higher failure rate and longer follow up than those with avascular products.

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