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Fertility and obstetric outcomes after curettage versus expectant management in randomised and non-randomised women with an incomplete evacuation of the uterus after misoprostol treatment for miscarriage

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ABSTRACT

Objective: To assess fertility and obstetric outcomes in women treated with curettage or undergoing expectant management for an incomplete miscarriage after misoprostol treatment.
Study
Design: Between June 2012 and July 2014, we conducted a multicentre randomised clinical trial (RCT) with a parallel cohort study for non-randomised women, treated according to their preference. In the RCT 30 women were allocated curettage and 29 expectant management. In the cohort 197 women participated; 65 underwent curettage and 132 women underwent expectant management. Primary outcome was curation, defined as either an empty uterus on sonography at six weeks or an uneventful clinical follow-up. We used questionnaires to assess fertility and obstetric outcome of the first new pregnancy subsequent to study enrolment.
Results: Curation was seen in 91/95 women treated with curettage (95.8%) versus 134/161 women managed expectantly (83.2%) (p = 0.003). The response rate was 211/255 (82%). In 198 women pursuing a new pregnancy, conception rates were 92% (67/73) in the curettage group versus 96% (120/125) in the expectant management group (OR 0.96, 95% CI 0.89;1.03, p = 0.34), with ongoing pregnancy rates of 87% (58/67) versus 78% (94/120), respectively (OR 1.12, 95% CI 0.99;1.28, p = 0.226). Preterm birth rates were 1/46 in the curettage group versus 8/81 in the expectant management group (OR 0.22, 95% CI 0.03;1.71 P = 0.15). Caesarean section rates were 23% and 24% for women in the curettage group and expectant management group respectively.
Conclusion: In women with an incomplete evacuation of the uterus after misoprostol treatment, curettage and expectant management does not lead to different fertility and pregnancy outcomes, as compared to expectant management.

Introduction

Miscarriage occurs in around 15% of all clinical pregnancies [1]. Women experiencing a miscarriage can either be managed expectantly, medically with misoprostol or surgically by performing a curettage. Since the beginning of the 20th century, curettage is performed for miscarriage and induced abortion [2,3]. Despite it

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being highly effective, curettage can lead to complications such as bleeding, perforation of the uterus, bladder or bowel, the formation of intrauterine adhesions known as Asherman's syndrome and is associated with preterm birth in future pregnancies [4–6].

More recently, treatment with misoprostol has gained popularity [7]. In the Netherlands in 2005, 50% of Dutch gynaecologists used misoprostol, while in 2014 almost all Dutch gynaecologists offered misoprostol to women as treatment for a first trimester miscarriage [8,9]. Misoprostol is a non-invasive alternative to curettage, it is cost-effective and has little adverse effects [1,3]. Although the duration of vaginal bleeding after misoprostol treatment is longer than after curettage, haemoglobin levels are similar for both treatments [10,11]. In approximately 15–50% of the women treated with misoprostol for first trimester miscarriage, sonographic examination will show signs of incomplete evacuation of the uterus. [2,3,12] This finding generally leads to additional curettage. The MisoREST trial compared the effectiveness of surgical versus expectant management in these women. In this trial, curettage was effective in 96% of the women, and expectant management was safe, and effective in over 80% [13].

Previous studies have assessed fertility after misoprostol treatment and have found no impairment of misoprostol treatment on future fertility [14,15]. It is unknown whether in women with an incomplete evacuation of the uterus, curettage leads to differences in fertility rates and obstetric outcomes in the subsequent pregnancy, compared to expectant management. The present study explores these questions.

Methods

Study design

In the MisoREST trial 256 patients participated, originating from over 27 hospitals in The Netherlands; 59 women were randomly assigned curettage (N = 30), or expectant management (n = 29) while 197 women declining randomization received the treatment of their own choice (65 curettage, 132 expectant management). Women were included in the study between June 2012 and June 2014. For details regarding the design of the study we refer to the original publication of the MisoREST trial [13].

All participating women were send two questionnaires regarding their fertility (one year after participation in the MisoREST trial) and obstetric outcome of any pregnancy subsequent to participation in the MisoREST trial (2.5–4.5 years after participation in the MisoREST trial). In order to increase the response rate up to three reminder emails were sent. If women, in spite of these efforts, did not respond, we contacted their hospitals to ascertain if a pregnancy had occurred and if so, we asked for the outcome.

Outcome

The fertility related questions regarded; conception since study participation, planning thereof, time to conception and details of any pregnancy: miscarriage, ectopic, termination, pregnancy outcomes (miscarriage, intra-uterine death, EUG, delivery), gestational age at time of delivery, type of delivery (i.e. caesarean or vaginal) and baby's general health after birth.

Statistical analysis

We compared the survey outcomes for the two treatments, and analysed the data using independent T−tests or Mann-Whitney *U* tests for continuous variables and Pearson's chi-square tests or Fisher's exact test for categorical variables. A Kaplan Meier curve was constructed to report time to conception and log rank to determine significance. P-values less than 0.05 were considered to indicate statistical significance. All tests were executed two-sided using SPSS version 22.

Results

Baseline characteristics were comparable among both groups, with the exception AP diameter of the uterine cavity and empty uterus six weeks after study inclusion. Since the interaction term of group allocation and treatment preference between the

Table 1
Baseline characteristics.

Baseline Characteristics	Treatment		*p*-Value
	Curettage N = 95	Expectant N = 161	
Age in years, mean (SD)	31.5 (±5.4)	32.6 (±4.7)	0.10
Nulliparous, n (%)	50 (52.6)	75 (46.6)	0.35
Obstetric History, n (%)			
Previous miscarriage	33 (34.7)	67 (41.6)	0.28
Previous curettage	13 (13.7)	22 (13.7)	0.93
Number of previous curettages:			
0	82 (86.3)	130 (86.3)	1.0
1	8 (8.4)	17 (10.6)	0.58
≥2	5 (5.3)	5 (3.1)	0.39
Previous misoprostol treatment	10 (10.5)	20 (12.4)	0.70
GA at misoprostol use in weeks, mean (SD)	10.5 (±1.8)	10.6 (±1.5)	0.40
AP diameter uterine cavity in mm, median (IQR)	17 (14,25)	15 (12,17.5)	*0.001*
Ethnicity, n (%)			
Caucasian	79 (83.2)	128 (79.5)	0.47
Middle-Eastern/North African	4 (4.2)	15 (9.3)	Ns
Afro-Caribbean	6 (6.3)	5 (3.1)	Ns
African (Sub-Sahara)	2 (2.1)	3 (1.9)	Ns
Other	1 (1.0)	7 (4.3)	Ns
Unknown	3 (3.2)	3 (1.9)	Ns
MisoREST outcomes, n (%)			
Empty uterine cavity six weeks after randomization	91 (95.8)	134 (83.2)	*0.003*

Means ± SDs are presented for Age, BMI and GA.
GA = gestational age, AP = anteroposterior, Ns = not significant.