Original paper

Extra-amniotic saline instillation versus combination of oral mifepristone and vaginal misoprostol for second trimester termination of pregnancy in women with previous one caesarean section: A randomized controlled trial

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Abstract

Background: To study and compare the efficacy and safety of extra-amniotic saline instillation (EASI) and combination of oral mifepristone and vaginal misoprostol for second trimester termination of pregnancy in women with previous one caesarean section.

Methods: This randomized controlled trial was conducted in Puducherry, South India. Pregnant women aged 18-45 years with history of previous one caesarean section at 16-27^{+6} weeks of gestation admitted for pregnancy termination were randomized to receive EASI or combination of oral mifepristone and vaginal misoprostol. Efficacy and safety were compared between the groups in an intention-to-treat analysis.

Results: There were 50 patients randomized to the EASI (n=25) and oral mifepristone + vaginal misoprostol (n=25) groups. The median induction to abortion interval was 48 vs 60 hours (p value=0.029), need for another method of termination was 16% vs 44% and side effects were 36% vs 8% with combination of oral mifepristone and vaginal misoprostol in comparison to EASI.

Conclusion: Combination of oral mifepristone and vaginal misoprostol appears to be more effective than EASI in reducing the induction-abortion interval, need for another method of termination and duration of hospital stay. The maternal safety profile appears to be comparable but requires further studies.

Key words: extra-amniotic saline instillation, combination of oral mifepristone and vaginal misoprostol, second trimester termination of pregnancy, previous caesarean section.

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Introduction

Termination of pregnancy in women with a prior caesarean delivery is becoming common[1-3]. Although most of the abortions are done in the early trimester (within 12 weeks) there is a need for termination of pregnancy between 13-28 weeks of gestation due to missed abortion, congenital anomalies etc. Difficulty in accessing abortion service and a delayed diagnosis of unwanted pregnancy also calls for second trimester abortion[1-3]. The options for pregnancy termination between 13-28 weeks of gestation are mechanical, pharmacological and surgical[4-8]. Mechanical options include insertion of foleys catheter followed by extra amniotic instillation of saline /prostaglandins/ hyper-osmotic solutions. Pharmacological methods of second trimester pregnancy termination include combination of mifepristone and misoprostol, carboprost and oxytocin. Surgical methods of termination are dilatation and evacuation and hysterotomy in some instances when other methods have failed.

The safety of the use of misoprostol is questionable in women undergoing pregnancy termination between 13-28 weeks of gestation with a uterine scar. The incidence of scar rupture has been found to be 0.2-4.8%[9-12] although some studies have found no cases of scar rupture with use of misoprostol[13-14]. As misoprostol is associated with risk of uterine rupture in women with a scarred uterus an alternative mechanical nonpharmacological method namely extra amniotic saline instillation (EASI) might be safer and more effective for second trimester termination of pregnancy in women with a scarred uterus. The data is limited on use of EASI for termination of pregnancy[15-17]. There has been only one study on EASI in combination with prostaglandins for second trimester pregnancy termination in women with a caesarean scar which found it to be effective and safe[18].

The purpose of this study was to compare the efficacy and safety of extra amniotic saline instillation with combination of oral mifepristone and vaginal misoprostol for pregnancy termination between 13-28 weeks of gestation in women with previous one caesarean scar.

Materials and methods

This open label randomized controlled trial was carried out in the Department of Obstetrics and Gynecology, JIPMER, Puducherry, India. The study protocol was approved by Post Graduate Research Monitoring Committee [No:PGRMC-18.04.2017/9], Ethics Committee of JIPMER [JIP/IEC/2017/1089] and Clinical Trials Registry- India [No: CTRI/2017/09/009947]. Women aged 18-45 years with history of previous one caesarean section at 16-27^{+6} weeks of gestation with missed abortion, congenital anomalies, intrauterine death and medical indications were included. Exclusion criteria were known allergy to misoprostol, recent history of asthma, previous rupture uterus, placenta covering the os and pre-viable premature rupture of membranes. The purpose of the study was explained clearly to potential participants and written informed consent was obtained from all participants.

Computer-generated randomization schedules were produced and placed in sequentially numbered, sealed, opaque envelopes. Block randomization with a block size of four was used with a 1:1 ratio for the EASI and combination of oral mifepristone and vaginal misoprostol groups. **Group A** – received tablet mifepristone 200mg oral and 36-48 hours later tablet misoprostol 400µg was administered vaginally every 3 hourly up to five doses. [MIFEGEST KIT, Zydus Cadila, INDIA] **Group B** – Cervix was visualized by use of a vaginal speculum under aseptic precautions. Foley's catheter (22 French) was introduced transcervically by using sponge holder. After passing the catheter through internal os, the balloon was inflated with 60ml of normal saline, and the external end of the catheter was taped to the thigh. Infusion set was fixed to the Foley's catheter at the opening of its drainage side. Then 150 ml 0.9% saline was instilled extra amniotically through Foley's catheter over 10 minutes.

Prophylactic broad-spectrum antibiotics namely capsule doxycycline100mg and tablet metronidazole 400 mg orally twice daily was administered for 5 days in both groups. If the patient did not expel products within 72 hours with the use of either method, the induction was considered as a failure and other methods were administered. Induction to abortion interval, need for another method of termination, total dose of misoprostol, duration of hospital stay, side effects like nausea, vomiting, fever, diarrhea, shivering and complications like uterine rupture, cervical tear, need for blood transfusion, infection or hysterotomy were noted.

Sample size calculation was done by using n-Master (CMC, Vellore, India) and was calculated to be 138 (69 in each group) considering the expected difference in failure rate to be 10% in between the groups[17-19], non-inferiority margin of 25%, 80% power and confidence limit 95%. However due to time and resource constraints as the sample size could not be achieved, the number of participants in each group was restricted to 25. All statistical analyses were performed using the intention-to-treat analysis method. Significance level for all analyses was set as $p<0.05$. SPSS software version 20.0 (IBM, Armonk, NY) was used for statistical analysis. Data were expressed as mean ± SD or median (range) for continuous variables and as frequency and percentage for categorical variables. The χ^2 test was used for comparison between groups for categorical variables and the independent t test or Mann-Whitney test was used for continuous variables.

Results

A total of 55 pregnant women with one previous caesarean section admitted for second trimester pregnancy termination were assessed for eligibility to participate in the study. Five women did not meet the eligibility criteria, leaving 50 eligible patients who were then randomized into the EASI (25) and the combination of oral mifepristone and vaginal misoprostol group (25). No women were excluded from the study after randomization (Figure 1).

Baseline characteristics in both groups were comparable. There was no significant difference between the two groups concerning maternal age, parity, gestational age of previous caesarean section and body mass index (BMI). There was a statistically significant difference with regard to indication for previous caesarean section (p value=0.018) and period of gestation/ indication for termination in the present pregnancy (p value=0.002) (Table1).

Majority of the study participants in combination of oral mifepristone and vaginal misoprostol group (72%) and EASI group (52%) expelled the abortus within 48 hours. Two patients in EASI group expelled the fetus after 192 hours and 240 hours respectively and they were the outliers (Figure 2).

There was a statistically significant difference between the groups with respect to induction to abortion time interval (p value=0.029). The success rate of abortion was 84% in combination of oral mifepristone and vaginal misoprostol group when compared to 56% in the EASI group. (p=0.031) majority (44%) of the participants in combination of oral mifepristone and misoprostol group aborted with mifepristone alone, 20% required 1 dose of misoprostol, 24% required 2 doses and 4% each required 3/ 4/ 5 doses. Mean dose of misoprostol used in combination of oral mifepristone and vaginal misoprostol group was 1.29 + 0.458 (Table1).

All patients in combination of oral mifepristone and vaginal misoprostol group were managed by instrumental evacuation whereas in EASI group either medical methods namely mifepristone, misoprostol, oxytocin, dinoprostone, mechanical methods like extra amniotic prostodin and surgical methods like instrumental evacuation or hysterotomy were needed. There was a statistically significant difference between two groups with regard to need for other methods of termination (p value=0.031) (Table1).

There was no statistically significant difference between two groups in terms of side effects/complications (p value >0.05). Proportion of shivering was higher in combination of oral mifepristone and vaginal misoprostol group (8% compared to 4% in EASI group) and this was not statistically significant. Fever was present in EASI group (4%), while it was nil in combination of oral mifepristone and vaginal misoprostol group. In contrast diarrhea, nausea and vomiting was found in combination of oral mifepristone and vaginal misoprostol group (4%, 12% and 12% respectively), while there were no cases in the EASI group. In EASI group 8% had complications of which one participant (4%) needed blood transfusion and one (4%) underwent hysterotomy (because of failure of both methods), while in combination of oral mifepristone and vaginal misoprostol group none of the participants had complications. The mean duration of hospital stay was 2.4 days higher in the EASI group when compared to the combination of oral mifepristone and vaginal misoprostol group (p value=0.003) (Table1).

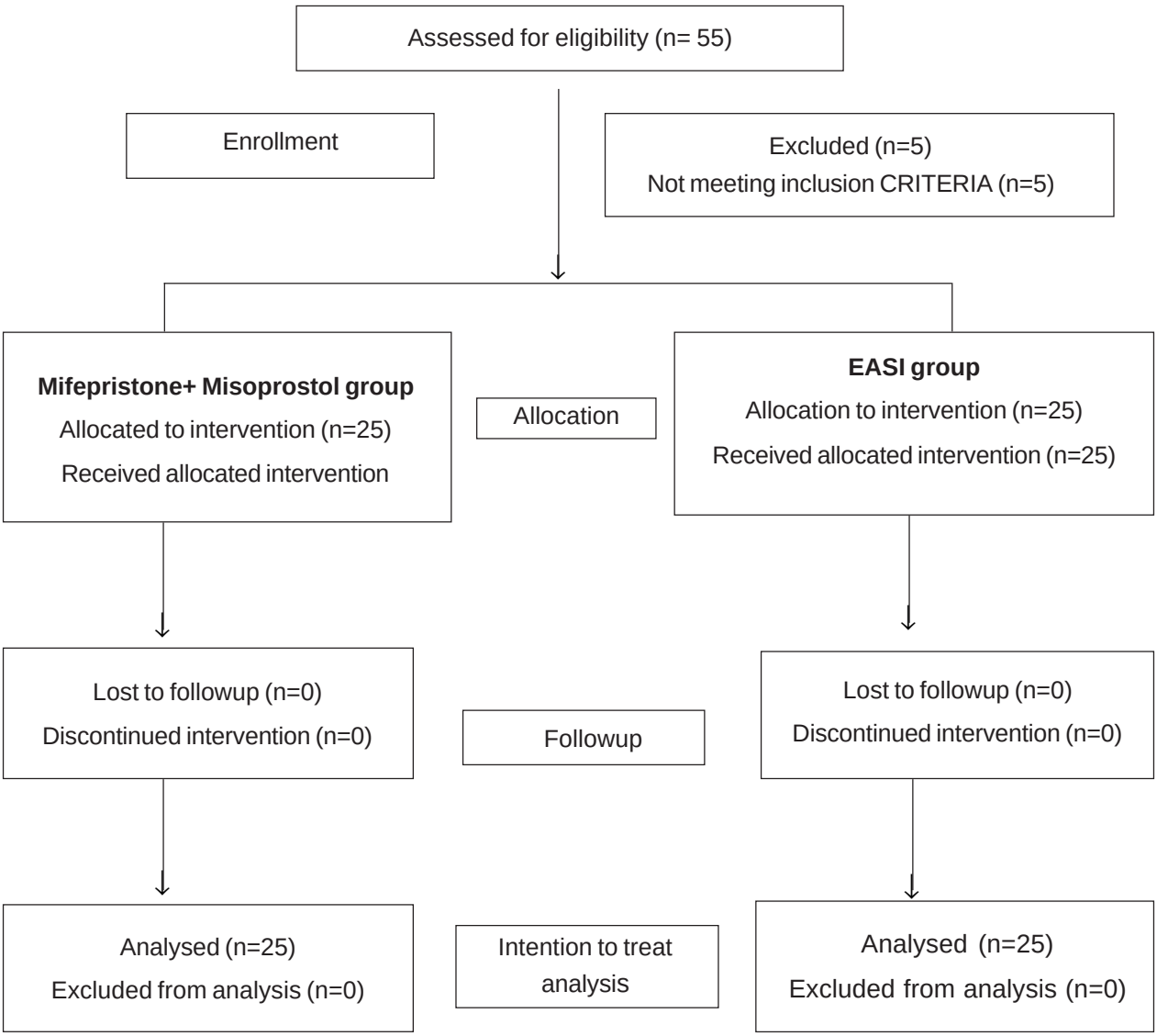

Figure 1. **Flow diagram of study participants.**

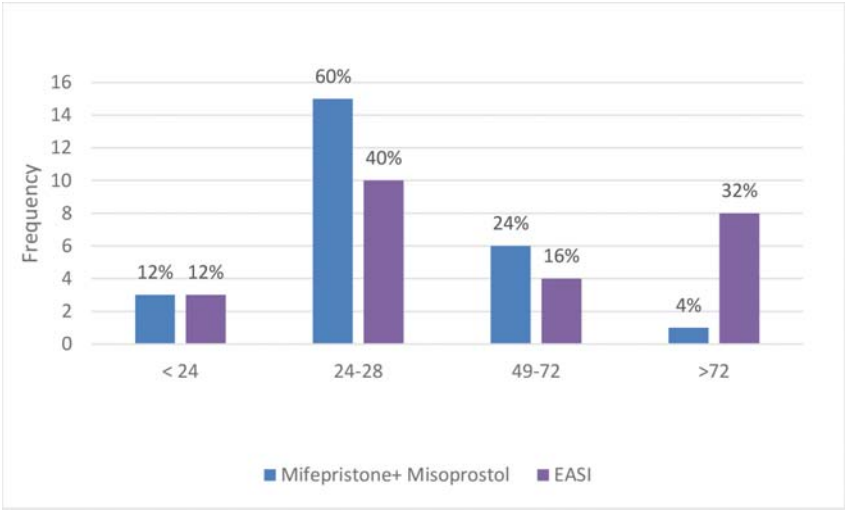

Figure 2. **Induction to abortion interval (hours).**

Table 1. Comparison of EASI versus combination of oral mifepristone and vaginal misoprostol

Characteristic	**Oral mifepristone and vaginal misoprostol (n=25)**	**EASI** (n=25)	**p value**
1. Age-Mean (SD)	28.6 (4.42)	27.4 (3.6)	0.315
2. BMI (kg/m^2)-Mean (SD)	23.1 (2.9)	22.8 (2.2)	0.149
3. Parity-Mean (SD)	1.48 (0.83)	1.4 (0.57)	0.561
4. Period of gestation-n (%)			
16-20 weeks	21 (84%)	9 (36%)	0.002
20^{+1}-24 weeks	1 (4%)	3 (12%)	
24^{+1}-28 weeks	3 (12%)	13 (52%)	
5. Indication for termination of pregnancy-n (%)			
Congenital anomalies	11 (44%)	10 (40%)	0.002
Intrauterine death	4 (16%)	9 (36%)	
Missed abortion	9 (36%)	1 (4%)	
6. Indication for previous caesarean section-n (%)			
Foetal distress	8 (32%)	17 (68%)	0.018
Non progress of labour	4 (16%)	0 (0%)	
PROM (preterm rupture of membranes)	5 (20%)	2 (8%)	
7. Induction abortion interval – Median (range) hours	48 (16.5-75)	60 (24-240)	0.029
8. Need for another method of termination-n (%)	4 (16%)	11 (44%)	0.031
9. Side effects-n (%)	9 (36%)	2 (8%)	<0.05
10. Blood transfusion-n (%)	0 (0%)	1 (4%)	1
11. Duration of hospital stay – Mean (SD) days	5.6 (2.3)	8 (2.9)	0.03

Discussion

There are no studies which have compared EASI with combination of oral mifepristone and vaginal misoprostol in women with a caesarean scar. A few studies have used either a combination of mifepristone and misoprostol[12-14] or EASI[18] for pregnancy termination between 13-28 weeks of gestation in women with a caesarean scar. In our study, most (84%) of the participants in combination of oral mifepristone and vaginal misoprostol group were between 16-20 weeks of gestation, which was lesser than other studies where the gestational age ranged from 14-34 weeks[10,11]. Most (52%) of the participants in EASI group were between 24-28 weeks of gestation and this was higher when compared to a study where EASI was used in combination with PG's + oxytocin, in which the gestational age was 12-20 weeks[18].

The median induction to abortion interval in the combination of oral mifepristone and vaginal misoprostol group which was longer (range 16.5-75 hours) than two other studies[9-11] where it ranged from 4 hours 20 minutes to 12 hours. This could have been because the starting time of induction was from the time of administration of first dose of misoprostol in the other studies, whereas in our study the starting time of induction was from administration of mifepristone. The median induction to abortion interval in EASI group was 60 hours (range 24-240 hours), this was longer when compared to a retrospective study where the mean interval was 15.7 hours[18] and this might have been due to use of the combination of EASI with PG's+ Oxytocin. Induction to abortion interval was significantly higher in EASI group when compared to the combination of oral mifepristone and vaginal misoprostol group in our study (p value=0.029) and this was probably because of advanced gestational age and need for additional methods of termination.

The success rate of complete abortion in the combination of oral mifepristone and vaginal misoprostol group was 84% in our study, which was lesser when compared to three other studies[9-11] where the success rate ranged from 90-98%. A higher initial dose of misoprostol (600-800µg) was used in these studies in addition to a higher dose of mifepristone (600mg)[11], although the interval of administration was similar to our study[9-11]. In our study, the success rate in the EASI group was 56%. As per review of literature there are no studies which have evaluated EASI alone for second trimester termination of pregnancy in women with a caesarean scar. There is only one retrospective study which has evaluated its use in combination with PG's namely dinoprostone + misoprostol 200µg+ oxytocin in which a high success rate of 93% was observed[18]. The success rate was significantly higher in combination of oral mifepristone and vaginal misoprostol group when compared to EASI group (p value=0.031) in our study and this could be attributed to lower gestational age of patients in combination group. 44% of the participants in combination of oral mifepristone and vaginal misoprostol group in our study expelled the fetus with mifepristone alone, which was much higher when compared to 0.5% in another study[10]. Mean dose of misoprostol (1.29 + 0.458) in our study was less when compared to other studies where the mean and median doses were 2.1+1.6 and 2 respectively[9-11].

The need for other methods of termination in our study was higher in combination of oral mifepristone and vaginal misoprostol group when compared to the other studies (2-9.6%)[9-11] probably due to lower dose of misoprostol/mifepristone although the interval of administration was the same[9-11]. The need for other methods of termination was higher in EASI group in this study when compared to a retrospective study[18] where 7% needed hysterotomy / D and E and this might be due to advanced gestational age. 2% in EASI group underwent hysterotomy due to failure of all other methods of termination, and it was comparable to another study[18] where hysterotomy rate was 2.2%.

The proportion of shivering, nausea, diarrhea was 8%, 4% and 12% respectively in combination of oral mifepristone and vaginal misoprostol group. This was not mentioned in other studies[9-11]. Vomiting (12%) was higher in our study when compared to 4% in another study[9] and this was probably because of lower dose of misoprostol (200µg) used in that study. In EASI group, the proportion of shivering was 4% in our study, it was higher when compared to one retrospective study where it was nil[18] and 4% had fever in our study, which was comparable to another study where the proportion of fever was 2%.

None of the patients developed infection or required blood transfusion in combination of oral mifepristone and vaginal misoprostol group whereas other studies which have used mifepristone + misoprostol have reported a rupture rate of 0.2-4.8%[9-11], proportion of cervical tear - 9.3%,[10] hysterectomy rate of 0.2% and 1.49%[10-11], sepsis in 2.9%[11] and the need for blood transfusion of 0.5-3%[10,11]. The above mentioned

complications were not observed in our study as opposed to other studies where these might have been due to a higher dose of misoprostol /mifepristone[10-11]. In EASI group in our study, 8% required blood transfusion in contrast to no patients in another study where EASI was used in combination with PG's + oxytocin[18] probably due to advanced gestational age (24-28 weeks) and the need for additional methods of termination.

The mean duration of hospital stay (5.6 days) in combination of oral mifepristone and vaginal misoprostol group in our study was higher when compared to 4-4.5 days in other studies[9-11]. In EASI group the mean duration of hospital stay was 8 days in this study and this has not been mentioned in another study which has used EASI with PG's+ oxytocin[18]. Hospital stay was significantly longer in the EASI group when compared to combination of oral mifepristone and vaginal misoprostol group (p value=0.003) and this was probably due to prolonged induction – abortion time interval and an increased need for other methods of termination in EASI group.

Limitation of the study was that the participants were not blinded to the method of termination although the use of block randomization at study enrolment should have reduced the bias. Also, we did not elicit views and satisfaction of the participants regarding the methods of termination of pregnancy.

Conclusion

The combination of oral mifepristone with vaginal misoprostol appears to be more effective than extra amniotic saline instillation for second trimester pregnancy termination in women with a caesarean scar by reducing induction-abortion interval, need for another method of termination and duration of hospital stay. The maternal safety profile appears to be comparable, but requires further studies.

Synopsis

Combination of oral mifepristone and vaginal misoprostol appears to be more effective than EASI for second trimester pregnancy termination in previous one caesarean section.

Author contributions

KM contributed to designing the study, patient recruitment, data collection, and writing the manuscript. HS contributed to designing the study, data analysis, and writing and revising the manuscript.

Acknowledgement

None.

Conflics of interest

The authors have no conflicts of interest.

Clinical trial registration information

This trial has been registered with Clinical Trials Registry of India [No: CTRI/2017/09/009947].

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Sl. No.	age	hospital no	booked or unbooked	educational status	socioeconomical status	obstetric index	pog	single or multiple pregnancy	indication for termination	medical illness	surgical illness	height in cm	weight in kg	BMI	HB in gm	blood grouping	BT/CT	hiv/hbsag	induction with	induction-abortion interval	Total doses of misoprostol used in mifepristone-misoprostol arm	nausea	vomiting	diarrhoea	shivering	fever	uterine rupture	cervical tear	need for blood transfusion	infection	hysterotomy	duration of hospital stay	need for another method of termination	Additional methods	Indication for previous caesarean section	previous caesarean section elective or emergency	induction-abortion interval in hours	duration of hospital stay in day
1	22	h-442175	A	2	B	1	3	A	A	A	B	160	54	21	10	A1+	A	A	B	2	B	1	A	A	A	A	A	A	A	A	A	2	2		1	1	42	4
2	29	f-1696 A	A	1	A	1	1	A	B	B	B	165	64	24	10.3	A+	A	A	B	1	B	1	A	A	A	A	A	A	A	A	A	A	3	2		1	1	48	10
3	27	h-604687	A	3	C	1	2	A	B	B	B	160	52	20	10.1	B+	A	A	B	1	C			A	A	A	A	A	A	A	A	A	3	2		1	1	72	8
4	32	H-648734	A	3	C	1	3	A	A	B	B	162	60	23	12	B+	A	A	B	1	B			A	A	A	A	A	A	A	A	A	2	2		1	1	40	6
5	25	g-382947	A	2	C	1	1	A	A	B	B	162	58	22	10	B+	A	A	B	1	C			A	A	A	A	A	A	A	A	A	2	2		1	1	60	6
6	24	h-582204	A	3	C	1	3	A	C	A	B	151	57	25	10.4	A1+	A	A	B	1	B			A	A	A	A	A	A	A	A	A	3	2		1	1	47	8
7	28	h-241986	A	2	B	1	1	A	B	B	B	153	43	23	9.8	A+	A	A	B	1	D			A	A	B	A	A	A	A	A	A	3	1	pge1	1	1	120	8
8	25	H-306277	A	2	B	2	1	A	B	B	B	160	00	20	11.6	o+	A	A	B	1	B			A	A	A	A	A	A	A	A	A	2	2		8	2	48	4
9	22	H-048871	A	3	D	1	3	A	A	B	B	160	52	20	10	A1+	A	A	A	1	A			A	A	A	A	A	A	A	A	A	4	2		7	2	24	12
10	28	H-565610	A	3	D	3	3	A	C	B	B	155	62	26	10	A1+	A	A	B	1	D			A	A	A	A	A	A	A	A	A	3	1	pge2,oxytocin	6	1	108	8
11	26	H-563568	A	3	C	3	3	A	C	A	B	160	60	23	11	A1+	A	A	B	1	C			A	A	A	A	A	A	A	A	A	3	1	pge1	6	1	72	8
12	28	f-799382	A	2	C	1	3	A	B	B	B	160	62	24	10	A1+	A	A	B	2	B	2		A	A	A	A	A	A	A	A	A	2	2		6	1	48	4
13	26	H-639012	A	2	C	2	3	A	A	B	B	162	69	26	11	B+	A	A	B	2	A	0		A	A	A	B	A	A	A	A	A	3	2		6	1	24	8
14	34	h-511764	A	1	B	1	1	A	B	B	B	156	60	25	10	o+	A	A	B	2	B	2		A	A	A	A	A	A	A	A	A	3	2		5	1	45	9
15	30	H-519530	A	1	B	1	1	A	E	B	B	162	61	21	10	O+	A	A	B	2	B	0		A	A	A	A	A	A	A	A	A	3	2		6	1	48	8
16	30	H-203926	A	2	B	1	1	A	B	B	B	155	22	22	9.8	o+	A	A	B	2	B	0		A	A	A	A	A	A	A	A	A	1	2		6	1	48	2
17	27	h-521907	A	3	C	2	1	A	B	A	B	160	00	25	11	o+	A	A	B	2	B	0		A	A	A	A	A	A	A	A	A	4	2		6	1	48	11
18	26	h-542267	A	3	C	1	1	A	E	B	B	154	22	22	13.2	B+	A	A	B	1	B			A	A	A	A	A	A	A	A	A	2	2		1	1	48	6
19	31	h-508426	A	3	B	2	3	A	A	B	B	155	05	25	11	O+	A	A	B	1	B			A	A	A	A	A	A	A	A	A	2	2		1	1	72	6
20	29	py2/154/2018	A	3	B	1	1	A	B	B	B	160	93	23	9	B+	A	A	B	1	C			A	A	A	A	A	A	A	A	A	3	1	Pge2	1	1	72	10
21	28	f-708152	A	3	C	4	3	A	B	*B	B	150	02	22	11	B+	A	A	B	1	A			A	A	A	A	A	A	A	A	A	4	2		1	1	24	12

22	28	G-542859	A	2	C	1	1	A	E	B	B	164	62	23	10	O+	A	B	2	B	0	A	A	A	A	A	A	A	A	A	A	3	2		1	1	48	8
23	26	H-593369	A	1	A	3	1	A	E	B	B	156	60	24	10	A1 +	A	B	2	C	2	A	A	A	A	A	A	A	A	A	A	2	2		1	1	72	4
24	25	H-517372	A	2	B	1	1	A	B	B	B	162	52	20	10	O+	A	B	1	D		A	A	A	A	A	A	A	A	A	A	2	1	pge1	1	1	120	5
25	27	H-488141	A	2	B	1	2	A	B	B	B	160	62	24	10	O+	A	B	1	D		A	A	A	A	A	A	A	A	A	A	3	1	pge1,pge2	1	1	192	9
26	28	H-426848	A	2	B	1	1	A	B	A	B	154	62	26	10	O+	A	B	1	D		A	A	A	A	A	A	A	A	A	A	3	1	eap	1	1	120	8
27	33		A	2	B	1	1	A	B	B	B	160	56	21	10	o+	A	B	2	B	0	A	A	A	A	A	A	A	A	A	A	2	2		1	1	36	5
28	39	H-499355	A	4	C	1	3	A	A	A	B	162	50	19	10	o-	A	B	1	D		A	A	A	A	A	A	A	A	A	B	4	1	hysterotomy	1	1	240	18
29	26	py2/128/2018	A	2	B	2	1	A	B	A	B	154	60	25	10	A1 +	A	B	2	C	3	A	A	A	A	A	A	A	A	A	A	2	1	IE	2	1	72	5
30	32	H-436472	A	1	A	1	1	A	E	B	B	156	60	25	9.9	A1 +	A	B	2	B	0	A	A	A	A	A	A	A	A	A	A	2	2		2	1	48	5
31	26	H-589706	A	2	B	1	1	A	B	B	B	160	59	23	10	A1 +	A	B	2	B	1	A	A	A	A	A	A	A	A	A	A	2	2		2	1	48	6
32	32	G-134922	A	3	C	1	1	A	B	A	B	150	76	34	10.2	A1 +	A	B	1	B		A	A	A	A	A	A	A	A	A	A	2	2		2	1	48	5
33	25	H-509741	A	1	B	1	1	A	E	B	B	160	62	24	11	O+	A	B	2	A	0	A	A	A	A	A	A	A	A	A	A	1	2		3	1	24	3
34	28	h-875067	A	4	D	2	1	A	E	B	B	146	46	22	9.8	B+	A	B	2	C	2	A	A	A	A	A	A	A	A	A	A	2	2		3	1	50.5	4
35	27	H-128344	A	1	B	2	1	A	F	B	B	152	54	23	9	AB +	A	B	2	B	2	A	A	A	A	B	A	A	A	A	A	2	2		2	1	44	4
36	23	H-203489	A	2	B	2	1	A	E	B	B	152	56	24	10.5	B+	A	B	2	B	5	A	A	A	A	A	A	A	A	A	A	3	2		2	1	48	9
37	20	G-232310	A	3	C	1	1	A	E	B	B	152	50	22	9.9	AB +	A	B	2	B	4	A	A	A	A	A	A	A	A	A	A	3	1	IE	3	1	48	10
38	28	H-231490	A	1	B	2	1	A	B	B	B	156	56	23	8.8	B+	A	B	2	C	2	A	A	A	A	A	A	A	A	A	A	2	2		3	1	54	4
39	31	H-506128	A	1	B	1	1	A	B	B	B	160	40	16	10	B+	A	B	2	C	1	A	A	A	A	A	A	A	A	A	A	2	2		4	1	47.5	4
40	29	H-182069	A	4	E	1	1	A	E	B	B	165	64	23	11.1	A1 +	A	B	2	A	0	A	A	A	A	A	A	A	A	A	A	2	1	IE	4	1	16.5	5
41	27	H-526762	A	2	B	1	3	A	A	B	B	150	56	24	10	AB +	A	B	1	D		A	A	A	A	A	A	A	A	A	A	3	1	mifepristone 22mg	4	1	120	8
42	24	E-862938	A	3	C	2	3	A	C	A	B	150	54	24	10.7	AB +	A	B	1	B		A	A	A	A	A	A	A	A	A	A	2	2		1	1	48	7
43	25	H-633354	A	2	B	1	3	A	C	A	B	162	56	21	9	A1 B+	A	B	1	B		A	A	A	A	A	A	A	B	A	A	2	2		1	1	48	6
44	34	H-205979	A	3	C	2	3	A	A	A	B	156	56	23	9	A1 +	A	B	1	D		A	A	A	A	A	A	A	A	A	A	3	1	Pge1, oxytocin	4	1	168	9
45	26	H-607892	A	2	B	1	3	A	A	A	B	155	56	23	11.7	A1 +	A	B	1	B		A	A	A	A	A	A	A	A	A	A	3	2		4	1	25.5	8
46	29	F-863304	A	2	B	2	2	A	A	B	B	156	52	21	11.8	A1 +	A	B	1	A		A	A	A	A	A	A	A	A	A	A	2	1	pge1,IE	1	1	24	5

47	22	h-581036	A	3	B	1	2	A	A	A	B	154	60	25	10.1	A+	A	B	2	B	0	A	B	B	B	A	A	A	A	A	A	2	2		1	1	25	6
48	24	h-232249	A	2	C	1	1	A	B	B	B	156	55	23	9.7	A-	A	B	2	B	0	A	A	A	A	A	A	A	A	A	A	2	2		1	1	27	4
49	30	g-073814	A	2	B	1	1	A	B	B	B	156	57	23	10.2	B+	A	B	2	C	1	A	A	A	A	A	A	A	A	A	A	2	2		1	1	72	5
50	32	h-665601	A	3	B	2	1	A	B	B	B	160	55	22	11	A+	A	B	2	D	1	A	A	A	A	A	A	A	A	A	A	2	1	IE	1	1	75	5