Assistance Publique
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Mifepristone and misoprostol for cervical ripening in surgical abortion between 12 and 14 weeks of gestation: a randomized controlled trial

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Introduction

Misoprostol and **mifepristone** are the two substances recommended for cervical preparation during the first trimester.

HAS. Support for the abortion up to 14 weeks. Clinical practice guidelines in March 2001, reviewed in 2010.
RCOG. The care of women requesting induced abortion (evidence-based clinical guideline number 7); 2011.
WHO.Safe abortion: technical and policy guidance for health systems. 2nd ed. 2012

Nonetheless, the benefit of **combining both drugs** during the first trimester has not been assessed.

Material and Method

This study was a single-center randomized, controlled, single (physician)-blinded trial conducted at the Conception University Hospital Centre

Three groups: the combination group, receiving a combination of mifepristone and misoprostol, the misoprostol group, and the mifepristone group.

Inclusion criteria
women aged 18 years or older, requesting an elective abortion under general anesthesia for an intrauterine singleton pregnancy between 12 and 14 weeks of gestation and who provided written informed consent.

Exclusion criteria
women with a uterine malformation, coagulation disorders, known allergy or hypersensitivity to one of the active substances or excipients of either mifepristone or misoprostol or a contraindication to its use or refusal to provide informed consent.

Material and Method

The primary objective of this study was to compare the effectiveness, assessed by intraoperative blood loss, of misoprostol, mifepristone, and the combination of the two treatments, in cervical preparation for elective surgical abortions between 12 and 14 weeks of gestation.

The secondary objectives were to compare the 3 treatment strategies in terms of duration of intervention, ease of dilatation, satisfaction regarding the procedure, women's anxiety and complications.

Material and Method

Combination group, 200 mg of oral mifepristone to take 36 h before the procedure, and 400 mcg of oral misoprostol to take 3 h before the procedure.

Misoprostol group, 400 mcg of oral misoprostol to take 3 h before the procedure.

Mifepristone group, 200 mg of oral mifepristone to take 36 h before the procedure.

Material and Method

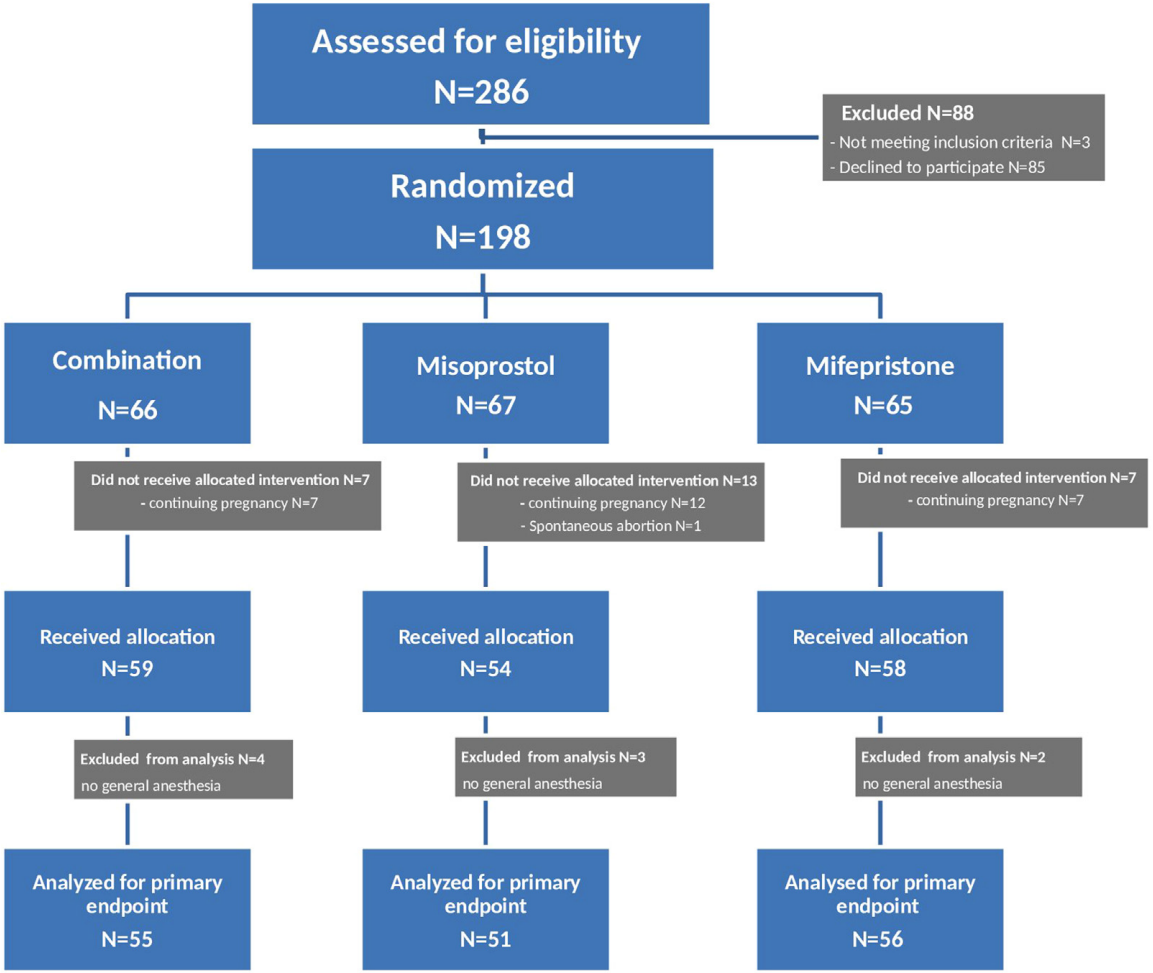
The primary endpoint was the quantity of intraoperative bleeding. It is the quantity of blood collected during the intrauterine aspiration, beginning after the mechanical cervical dilatation and ending with the withdrawal of the cannula at the end of the procedure

The duration of the intervention was defined as the time from the beginning of the supplemental mechanical cervical dilatation to the end of the intrauterine aspiration.

The spontaneous cervical dilatation was assessed by the diameter of the Hegar dilator that entered the cervix without force, before the supplemental mechanical cervical dilatation began.

Ease of mechanical dilatation and **physician satisfaction** for procedure were evaluated on VAS by physician.

Results


Assessed for eligibility
N=286
Excluded N=88
- Not meeting inclusion criteria N=3
- Declined to participate N=85
Randomized
N=198
Combination
N=66
Misoprostol
N=67
Mifepristone
N=65
Did not receive allocated intervention N=7
- continuing pregnancy N=7
Did not receive allocated intervention N=13
- continuing pregnancy N=12
- Spontaneous abortion N=1
Did not receive allocated intervention N=7
- continuing pregnancy N=7
Received allocation
N=59
Received allocation
N=54
Received allocation
N=58
Excluded from analysis N=4
no general anesthesia
Excluded from analysis N=3
no general anesthesia
Excluded from analysis N=2
no general anesthesia
Analyzed for primary endpoint
N=55
Analyzed for primary endpoint
N=51
Analysed for primary endpoint
N=56

Results

Women characteristics.

		Combination group ($N=59$)	Misoprostol group ($N=54$)	Mifepristone group ($N=58$)
Age (years)	$M \pm SD$	25.9 ± 5.7	26.2 ± 6.0	26.6 ± 6.3
BMI (kg/m^2)	$M \pm SD$	23.6 ± 5.3	22.1 ± 4.3	23.1 ± 4.6
Previous pregnancies, *n*	Med [IQR]	2.0 [1.0–4.0]	2.5 [2.0–4.0]	3.0 [2.0–5.0]
Parity, *n*	Med [IQR]	0 [0–2.0]	0.5 [0–1.0]	0.5 [0–1.3]
Gestational age (weeks)	$M \pm SD$	13.1 ± 0.7	13.2 ± 0.7	13.2 ± 0.7
		Combination group	Misoprostol group	Mifepristone group
		n (%)	*n* (%)	*n* (%)
Smoker active		38 (64)	38 (70)	37 (64)
Vaginal delivery ≥1		24 (41)	23 (43)	22 (38)
Cesarean ≥1		7 (12)	5 (9)	10 (17)
Elective abortion ≥1		26 (44)	24 (44)	33 (57)
Early pregnancy loss ≥1		8 (14)	7 (13)	14 (24)
Therapeutic abortion ≥1		2 (3)	1 (2)	0
Ectopic pregnancy ≥1		0	0	1 (2)

BMI: body mass index; Med [IQR]: median [interquartile range]; $M \pm SD$: mean ± standard deviation; combination group: group receiving mifepristone and misoprostol.

Results

Characteristics of the surgical procedure.

	Combination group	Misoprostol group	Mifepristone group	*p*-values			
	M ± SD	*M* ± SD	*M* ± SD	Global	Combination vs. misoprostol	Combination vs. mifepristone	Misoprostol vs. mifepristone
Intraoperative bleeding (mL)	222 ± 64	329 ± 129	276 ± 118	**0.001**	**0.001**	**0.032**	**0.035**
Duration of intervention (min)	5 ± 2	7 ± 5	7 ± 3	**0.001**	**0.001**	**0.012**	0.98
Spontaneous dilatation (mm)	9.4 ± 2.2	8.1 ± 1.5	8.3 ± 1.6	**0.001**	**0.001**	**0.003**	1.0
Dilatation maximum (mm)	12 ± 0.9	12 ± 1.0	12+-1.1	**0.1**			
Ease of mechanical dilatation[a]	8.8 ± 1.6	6.8 ± 2.5	7.7 ± 2.3	**0.001**	**0.001**	**0.029**	0.09
Physician satisfaction[b]	8.8 ± 1.3	6.8 ± 2.1	7.7 ± 1.9	**0.001**	**0.001**	**0.004**	**0.03**
Woman satisfaction[b]	7.6 ± 1.7	7.9 ± 1.6	7.5 ± 2.3	**0.6**			
Anxiety pre-intervention (STAI 20–80)	50 ± 11	46 ± 12	48 ± 12	**0.2**			
Anxiety post-intervention (STAI 20–80)	37 ± 12	35 ± 12	40 ± 15	**0.2**			
Perioperative satisfaction (EVAN-G 0–100)	70 ± 15	70+/14	75 ± 12	**0.1**			

M ± SD: mean ± standard deviation; STAI: State-Trait Anxiety Inventory, 20–80, higher score corresponding to higher level of anxiety; EVAN-G: Anesthesia Experience questionnaire for general anesthesia, 0–100, higher score corresponding to better experience; combination group: group receiving mifepristone and misoprostol.

[a] Visual analog scale, 0–10, higher score corresponding to easier dilatation.

[b] Visual analog scale, 0–10, higher score corresponding to higher satisfaction level.

Results

Side effects before intervention.

	Combination group (*N*=55) *n* (%)	Misoprostol group (*N*=51) *n* (%)	Mifepristone group (*N*=56) *n* (%)	*p*-value
Headaches	1 (2)	1 (2)	1 (2)	1.0
Nausea	0	4 (8)	2 (4)	0.1
Vomiting	1 (2)	1 (2)	3 (5)	0.5
Diarrhea	0	0	0	1.0
Abdominal pain	5 (9)	4 (8)	6 (11)	0.9
Cutaneous reaction	0	0	0	1.0
Malaise (faintness, etc.)	0	0	0	1.0
Hot flushes	1 (2)	1 (2)	0	0.6
Vertigo	0	1 (2)	0	0.3
Shivering	0	1 (2)	1 (2)	0.6
Fever	0	0	0	1.0
Bleeding	9 (16)	6 (12)	8 (14)	0.8
At least one	9 (16)	8 (16)	12 (21)	0.7

Combination group: group receiving mifepristone and misoprostol.

Discussion

In our study, **less intraoperative bleeding** was observed in the **combination group** compared to the misoprostol or the mifepristone group. Moreover, the quantity of **intraoperative bleeding was also significantly lower** in the **mifepristone** group than in the misoprostol group.

Spontaneous dilatation was **significantly greater** and the duration of the procedure significantly shorter in the **combination group**.

Discussion

The choice of primary outcome should be discussed. The complication rate would be most pertinent for distinguishing the most effective intervention. But the rarity of these events means that a much higher sample size would be needed.

We can assume that the primary outcome, defined by the quantity of intraoperative bleeding, allows us to **indirectly assess the risk of complications,** especially the risk of hemorrhage.

Results of **this monocentric** study should be confirmed by a **larger multicentric study**.

Thank You!

Lisboa

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