Medical termination of first trimester pregnancy

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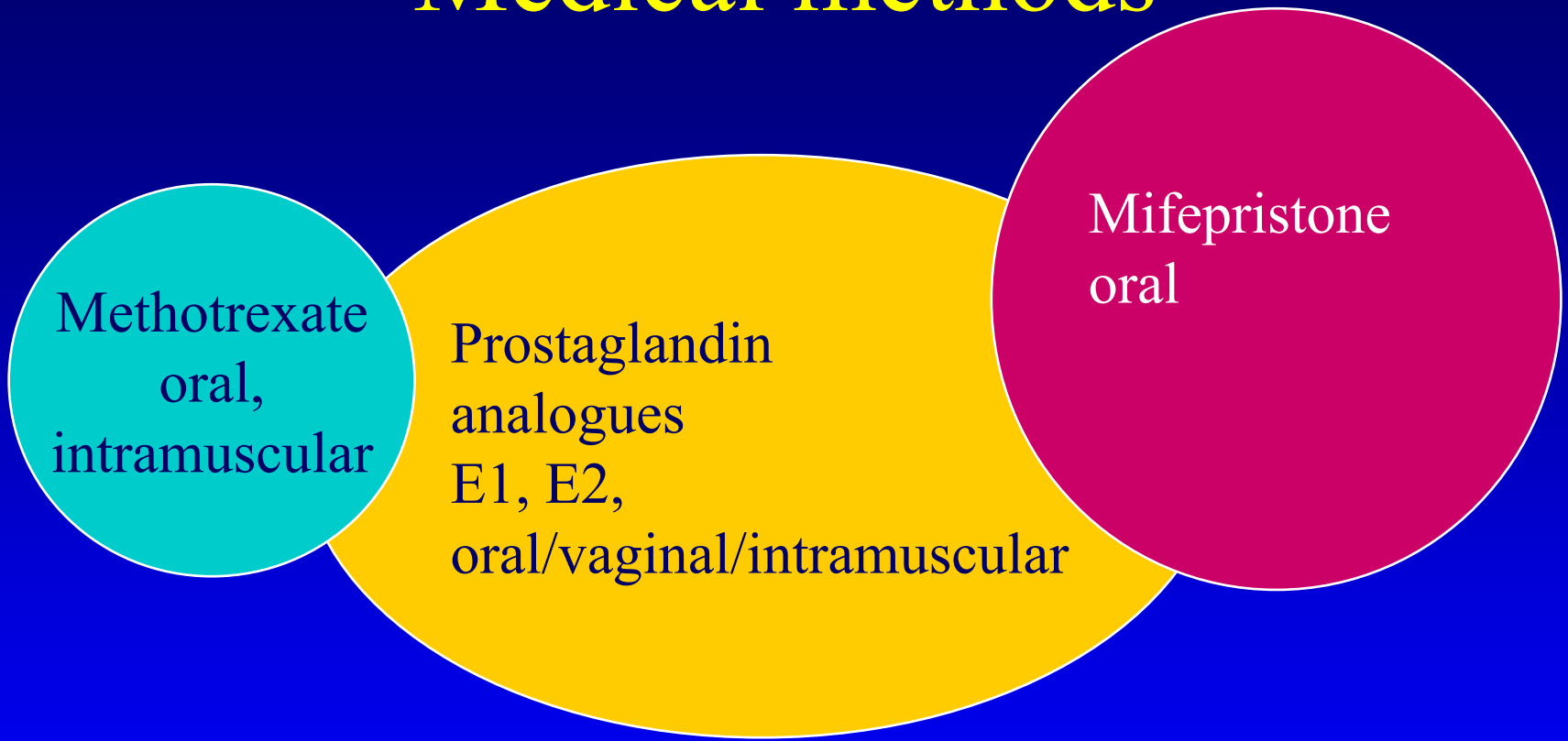
Medical Methods

- Mifepristone (RU 486, Mifegyne®)
- Prostaglandins
  - Misoprostol (oral, vaginal), Gemeprost (vaginal)(E1 analogue)
  - Dinoprostone, Sulprostone* (vaginal, intramuscular)(E2 analogue)
- Methotrexate
- Laminaria, Tamoxifen

Medical methods



Rationale

- Mifepristone
  - antiprogestogen, antiglucocorticoid
- Prostaglandins
  - uterine contractions, cervical ripening
- Methotrexate
  - folic acid antagonist, toxic to trophoblast
- Combinations

Prostaglandin alone

- complete abortion rate varies: 66% - 83%
  - Koopersmith 1996, Bugalho 1996
- repeat doses of 800 mcg: success rate up to 93%
  - Carbonell 1997

Mifepristone/prostaglandin

- Mifepristone 600 mg/oral
- Misoprostol 800 mcg or Gemeprost 1mg after 36-48 hours

Table 1. Selected Randomized Controlled Trials of Mifepristone and Prostaglandin

Author	Year	Gestational limit (d)	Regimens	*N*	Complete abortions	95% CI	Blood transfusion	Vomiting	Diarrhea	Narcotics
World Health Organization[9]	1991	49	Mifepristone 25 mg orally every 12 h × five doses, gemeprost 1 mg vaginally at 60 h	192	93	89, 97	*	NR	NR	4
			Mifepristone 600 mg orally, gemeprost 1 mg vaginally at 60 h	193	92	87, 95	*	NR	NR	7
McKinley et al[10]	1993	63	Mifepristone 600 mg orally, misoprostol 600 μg orally at 48 h	110	94	87, 97	0	NR	NR	7
			Mifepristone 200 mg orally, misoprostol 600 μg orally at 48 h	110	94	87, 97	0	NR	NR	8
World Health Organization[11]	1993	Menstrual delay ≤28	Mifepristone 600 mg orally, gemeprost 1 mg vaginally at 48 h†	389	94	92, 96	NR	23	NR	13
			Mifepristone 400 mg orally, gemeprost 1 mg vaginally at 48 h†	391	94	91, 96	NR	23	NR	11
			Mifepristone 200 mg orally, gemeprost 1 mg vaginally at 48 h†	388	94	91, 96	NR	24	NR	15
El-Refaey and Templeton[12]	1994	56	Mifepristone 200 mg orally, misoprostol 800 μg orally at 36–48 h	75	95	87, 99	NR	40	33	12
			Mifepristone 200 mg orally, misoprostol 400 μg orally every 2 h × two doses at 36–48 h	75	92	83, 97	NR	31	21	12
Sang et al[13]	1994	49	Mifepristone 50 mg orally, then 25 mg orally every 12 h up to 150 mg, misoprostol 600 μg orally at day 3	301	94	91, 97	0	20	22	NR
			Mifepristone 50 mg orally, then 25 mg orally every 12 h up to 150 mg, PGO5 1 mg vaginally at day 3	150	97	93, 99	0	23	39	NR
			Mifepristone 200 mg orally, misoprostol 600 μg orally at day 3	149	95	90, 98	0	21	20	NR
El-Refaey et al[14]	1995	63	Mifepristone 600 mg orally, misoprostol 800 μg orally at 36–48 h	130	87	80, 92	0	44	36	16
			Mifepristone 600 mg orally, misoprostol 800 μg vaginally at 36–48 h	133	95	89, 98	0.8	31	18	10
Baird et al[15]	1995	63	Mifepristone 200 mg orally, gemeprost 0.5 mg vaginally at 48 h	391	97	94, 98	0	12	7	7
			Mifepristone 200 mg orally, misoprostol 600 μg orally at 48 h	386	95	92, 97	0.3	22	8	5

CI = confidence interval; NR = not reported; PG = prostaglandin.
Complete abortions, blood transfusion, vomiting, diarrhea, and narcotics reported as rate per 100.
* One blood transfusion (regimen not specified).
† Sixteen women received antibiotics for suspected infections (regimen not specified).

Mifepristone/misoprostol

- n=1182
- <56 days gestation
- Mifepristone 200, 400, 600mg
- Gemeprost 1mg/vaginal

WHO 1993

Mifepristone/misoprostol

Mifepristone	200mg (n=388)	400 mg (n=391)	600 mg (n=389)
Complete abortion	364 (93.8%)	368 (94.1%)	367 (94.3%)
Incomplete abortion	14 (3.6%)	15 (3.8%)	14 (3.6%)
Continuing pregnancy	2 (0.5%)	2 (0.5%)	1 (0.3%)

WHO 1993

Mifepristone/misoprostol

Mifepristone	200 mg n=386	400 mg n=387	600 mg n=384
Duration of vaginal bleeding (median days)	12 (4-71)	12 (4-72)	12 (4-66)
time to return of menstruation (median)	for all three groups: 35 - 36 days		

WHO 1993

Mifepristone/misoprostol

- n=266
- Mifepristone 600mg
- Misoprostol 800mcg oral versus vaginal
- < 63 days

El-Refaey 1995 NEJM;332:983

Mifepristone/misoprostol

	Misoprostol oral (n=130)	Misoprostol vaginal (n=133)
Complete expulsion	113 (87%)	126 (95%)
Expulsion within 4 hours	102 (78%)	124 (93%)
Vomiting	51 (44%)	38 (31%)
Diarrhea	42 (36%)	22 (18%)

El-Refaey 1995

Mifepristone /misoprostol - repeat dose

- Mifepristone 600mg/ misoprostol 400mcg
- repeat dose misoprostol 200 mcg/after 3h
- N=1029, cohort
- < 63 days gestation

Aubeny 1995 Int J Fertil;Suppl 21:85

Mifepristone/misoprostol -repeat dose

	42-49 days n=364	50-56 days n=380	57- 63 days n=235
Complete abortion	345 (94.8%)	355 (93.4%)	204 (86.8%)
Incomplete abortion	13 (3.6%)	16 (4.2%)	1 (5.5%)
Hemostatic procedure	1 (0.3%)	3 (0.8%)	6 (2.6%)

Aubeny 1995

Mifepristone/misoprostol - repeat dose

< 49 days	Misoprostol 400 mcg + repeat 200 mcg	Misoprostol 400 mcg
Termination before or during monitoring period	69.7 %	64.9%
Complete abortion	95.5%	95.4%

Aubeny 1995

Methotrexate/misoprostol

- MTX 50 mg/m2/im
- Misoprostol 800 mcg after 5-7 days, repeat dose if required
- n=178
- < 63 days

Hausknecht 1995 NEJM;333:537

Methotrexate/misoprostol

N=178

Complete abortion, total	171 (96%)
Complete abortion after 1st dose	146 (82%)

Hausknecht 1995

Methotrexate/misoprostol

- MTX 50mg/m2/intramuscular
- Misoprostol 800mcg/vaginal
  - » after 3 days or 7 days
- n=88
- < 56 days gestation

Creinin 1995 AJOG;173:1578

Methotrexate/misoprostol

	Misoprostol after 3 days	Misoprostol after 7 days
Complete abortion	83%	98%
Ongoing pregnancies	9%	0%

Surgical versus Medical

- Mifepristone 600mg PLUS Gemeprost 1mg/vaginal/48h

  versus

- Vacuum aspiration
- n=363; < 63 days

Henshaw 1994, Hum Reprod 9(11);2167

Surgical versus medical - efficacy

	Vacuum aspiration	Medical
35 – 49 days		
n	59	51
complete abortion rate	98.3%	98%
50 – 63 days		
n	132	121
complete abortion rate	97.7%	92.6%

Henshaw 1994

Surgical versus medical - complications

Major complications	Vacuum aspiration (n=191)	Medical abortion (n=172)
Haemorrhage (>500ml)	0	1 (0.6%)
Pelvic infection (requiring ivi antibiotics)	2 (1%)	0

Henshaw 1994

Surgical versus medical - effects

	Prefer medical abortion	Prefer vacuum aspiration	Randomised to medical abortion	Randomised to vacuum aspiration
n	73	95	99	96
Duration of post-abortal bleeding (days)	12.7* (SD 2.7)	10.2* (SD 5.1)	13.1* (SD 2.9)	10.2* (SD 4.4)
Fall in haemoglobin (g/L)	3.3 (SD 7.9)	2.4 (SD 6.1)	3.3 (SD 6.8)	1.4 (6.4)
Time off work	1.1* (SD 2.3)	2.6* (SD 2.9)	1.3* (SD 2.0)	2.4* (3.0)

Henshaw 1994

Surgical versus medical - acceptability

Method of abortion that women would opt to undergo in future

Group	Opt for medical abortion	Opt for surgical abortion	Undecided
Chose medical abortion (n=72)	68 (95%)	3 (4%)	1 (1%)
Chose vacuum aspiration (n=84)	3 (4%)	76 (90%)	5 (6%)
Randomised to medical abortion (n=94)	70 (74 %)	21 (22%)	3 (3%)
Randomised to vacuum aspiration abortion (n=95)	2 (2%)	83 (87%)	10 (11%)

Conclusions

- Prostaglandins alone are not as effective as in combination with mifepristone
- severe side effects are rare and the procedure is highly acceptable with combination regimen
- > 49 days the efficacy decreases, side effects increase

WHO 1997

- Mifepristone, followed by a suitable prostaglandin analogue is a safe and effective method of inducing abortion up to < 63 days of amenorrhoea
- Optimal dose of mifepristone is uncertain, but 200 mg seems to be as effective as 600 mg; no advantage in giving divided doses
- Mifepristone and Prostaglandins used at 9-14 weeks of gestation has a higher incidence of of incomplete abortion, side effects and complications than vacuum aspiration

WHO Technical Report Series;871, WHO 1997

Recommendations WHO 1997

- Appropriate back-up facilities for surgical evacuation must be available
- More research needed to evaluate and improve current treatment regimens
- Evaluation of the appropriateness of current medical guidelines regarding the use of Mifepristone/misoprostol is needed

WHO Technical Report Series;871, WHO 1997