

Access this article online
Quick Response Code:

Website: www.jehp.net
DOI: 10.4103/jehp.jehp_582_22

# Comparison of the clinical efficacy of surgical versus medical method for first trimester pregnancy termination in Iran: A quasi-experimental research

Saeed Husseini Barghazan, Mohamad Hadian, Aziz Rezapour<sup>1</sup>, Setare Nassiri<sup>2</sup>

## Abstract:

**BACKGROUND:** The surgical and medical options for management of pregnancy termination procedures are acceptable in practice but differ in clinical efficacy, costs, and patient experiences, and deciding what the best method is not clear always. This study aimed to compare clinical efficacy, outcomes, and patient acceptance of dilatation and curettage (D and C) versus medical abortion using misoprostol for first trimester of gestation in Iranian context.

**MATERIALS AND METHODS:** A prospective, multicenter, quasi-experimental research conducted from July 2021 to January 2022. The primary outcomes were the rate of composite complications or complete abortion. Data were analyzed with SPSS 18 using descriptive statistics, independent t-test, analysis of variance and non-parametric tests. Secondary outcomes were quality of life using EQ5D questionnaire, estimated blood loss, pelvic infection, pain level, hospital stay, and acceptability of intervention and relative risk as the effect size.

**RESULTS:** Finally, 168 patients were included in this study. The composite complication rate among medical abortion patients is significantly more than that of surgical abortion patients (39.3% vs. 4.76%). The relative risk calculated 8.25 (3.05–22.26 CI). Medical abortion patients have experienced higher levels of ongoing bleeding, pain, and symptoms of pelvic infection. The higher level of acceptance has been reported by surgical group patients in comparison to the medical group patients (85.7% vs. 59.5%). Quality of life scores for surgical and medical group estimated 0.6605 and 0.5419, respectively.

**CONCLUSION:** Surgical method of abortion using D and C is a very safe and highly successful option in comparison to the medical method using misoprostol alone and is associated with better clinical outcomes, acceptance, and quality of life in first trimester of pregnancy among Iranian women.

## Keywords:

Dilatation and curettage, first pregnancy trimester, misoprostol, non-randomized controlled trials, quality of life

## Background

Pregnancy termination and induced abortion are very commonly practiced interventions worldwide. It is safe when carried out using a method recommended by World Health Organization, appropriate to the pregnancy gestational age and by sufficiently skilled practitioner.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow\_reprints@wolterskluwer.com

Pregnancy termination and abortion-related complications remain as potential cause of maternal deaths and morbidities and can lead to physical and mental health complications and social and financial burden for women, communities, and health systems.<sup>[1,2]</sup>

About 60% of unintended pregnancies end in an induced abortion, and it is estimated

**How to cite this article:** Barghazan SH, Hadian M, Rezapour A, Nassiri S. Comparison of the clinical efficacy of surgical versus medical method for first trimester pregnancy termination in Iran: A quasi-experimental research. J Edu Health Promot 2023;12:132.

Department of Health Economics, School of Health Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran, <sup>1</sup>Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran, <sup>2</sup>Endometriosis Research Center, Iran University of Medical Sciences, Tehran, Iran

## Address for correspondence:

Dr. Mohamad Hadian, Department of Health Economics, School of Health Management and Information Sciences, Iran University of Medical Sciences, Rashid Yasemi St, Tehran, Iran. E-mail: hadian.m@iums.ac.ir

Received: 22-04-2022  
Accepted: 19-07-2022  
Published: 28-04-2023

that 73 million induced abortions are performed each year, an increase by 30% since 1999. Approximately, 45% of all abortions are performed under unsafe conditions, of which 97% take place in developing countries. More than 50% of all unsafe abortions occur in Asia, mainly in south and central Asia. Notwithstanding misclassification of pregnancy-related maternal mortality, abortion and its complications are the cause of 2.3% of maternal mortality in Iran.<sup>[3]</sup> Lack of access to safe, timely, affordable, and respectful abortion care is a critical public health concern and human rights issue.<sup>[4,5]</sup>

The traditional treatment option of pregnancy termination and induced abortion has been uterine aspiration that also known as aspiration curettage, suction curettage, dilatation and curettage (D and C), dilatation and evacuation, or surgical abortion. In the last decade, efforts to develop alternative pregnancy termination methods largely focused on medical methods. Medical abortion using prostaglandins, mifepristone alone, mifepristone with prostaglandins, and methotrexate with prostaglandins have been gaining popularity as a noninvasive alternative in recent years and plays a crucial role in providing access to safe, effective, and acceptable abortion and post-abortion cares.<sup>[6,7]</sup>

Abortion is a simple health care intervention that can be effectively managed by a wide range of service providers using surgical or medical procedures. In the first trimester of pregnancy (until the end of week 12), a medical abortion can also be safely self-managed by the pregnant women outside of a health care facility (e.g., at home), in whole or in part. This requires that the women have access to accurate information, sufficient education and counseling, quality medicines, and support from the trained service providers.<sup>[8]</sup>

Currently, both surgical and medical options are acceptable in practice but differ in clinical efficacy, costs, and patient experiences, and deciding what the best method is not clear always.<sup>[9-11]</sup> This study was, therefore, set up to compare clinical efficacy, patient acceptance, and other outcomes of surgical D and C versus medical abortion using misoprostol in women with pregnancies in first trimester of gestation in Iranian context through a quasi-experimental research.

## Materials and Methods

### Study design and setting

A prospective, open-label, and multicenter quasi-experimental research (non-randomized clinical trial) was designed to compare the clinical efficacy of D and C versus misoprostol for first trimester pregnancy termination in Iranian women under the guidance and supervision of a gynecologist.

### Study participants and sampling

Eligible participants were woman aged 18 or over who admitted or referred to study settings for first trimester pregnancy termination, including legal abortions or treatment of incomplete pregnancy termination for whatever reason. Patients with underlying conditions, including diabetes, high blood pressure, thyroid, and neoplasms were excluded from study. The study was carried out in three general hospitals and their obstetrics and gynecology clinics affiliated to Iran University of Medical Sciences from July 2021 to January 2022. The sample size was calculated for each group based on the results of a previous similar study. The following equation (formula for sample size calculation for comparison between two groups when endpoint is qualitative such as alive/dead, diseased/non-diseased)<sup>[12]</sup> was used for sample size calculation:

$$n = \frac{2(Z\alpha/2 + Z\beta)^2 P(1-P)}{(p1 - p2)^2}$$

In this equation,  $Z\alpha/2 = 1.96$  (from Z table) at type 1 error of 5%,  $Z\beta = 0.842$  (from Z table) at 80% power.  $P$  scores (complete abortion rates in two methods) were extracted from most similar studies.<sup>[13-15]</sup> The total number of participants in each sample group was calculated to be at least 78.

### Data collection tool and technique

Patients received three doses of misoprostol 400 mg (Cytotec®) sublingual and vaginal 6 h apart in medical group or D and C; the dilatation of the cervix and surgical removal of part of the lining of the uterus and/or contents of the uterus by scraping and scooping along with 200 mg of misoprostol at the time of surgery and 6 h after that in surgical group. The primary outcomes were the rate of composite complications or complete abortion without any additional interventions. Those having one or more bad outcomes (failed abortion, observation for bleeding need for blood transfusion, symptoms of infection, and additional procedures required to complete the abortion) are considered as composite complication. Secondary outcomes were quality of life using EQ5D questionnaire, estimated blood loss, pelvic infection, pain level, hospital stay and acceptability of intervention, and relative risk as the effect size. Data were analyzed using SPSS 18, independent  $t$ -test, and analysis of variances and non-parametric equivalents. The univariate analyses were performed using proportions, means, standard deviations, and  $P$ -values. To understand the magnitude of the difference between the groups, we estimated the overall relative risk effect size and confidence interval. To improve the quality of reporting, transparent reporting of evaluations with nonrandomized designs guideline was applied.<sup>[16]</sup>

## Ethical consideration

The ethical approval and permission to perform the research as a part of PhD thesis in Health Economics was obtained from Research Ethics Committees of Iran University of Medical Sciences (Ethical code: IR.IUMS.REC.1399.068). The study was conducted after receiving an official approval letter from Iranian Registry of Clinical Trials (Registration Number: IRCT20210916052504N1). An informed consent form is read by the participants, signed, and handed back to the researcher.

## Results

During the 6 months of study period, a total of 209 women were assessed for eligibility and assigned for surgical or medical group. Then, the study was prolonged for additional two months to have equal number of patients in each group. Finally, 168 patients were included in this study (84 patients in each group). The medical group was divided into the hospital-based medical (42 patients) or clinic-based medical (42 patients) subgroup participants [Figure 1].

The largest age range of women was 25–34 in both surgical (41.6%) and medical (54.8%) group. About 38% of surgical and 35.7% of medical group participants had their second birth order let to pregnancy termination. The significant differences between two groups were observed for education levels, gestational age, and having previous abortion. More details of participant characteristics are provided in Table 1.

At the time of the 2-week follow-up, the observed composite complication rate among medical abortion patients is significantly different and more than that of surgical abortion patients (39.3% vs. 4.76%;  $P = 0.000$ ). Medical abortion patients have experienced higher levels of bleeding, pain, and symptoms of pelvic infection. The higher level of acceptance has been reported by surgical group patients in comparison to the medical group patients ( $P = 0.000$ ). Based on EQ5D tool, the quality of life scores for surgical and medical group estimated 0.6605 and 0.5419, respectively. More details of each group clinical outcomes are provided in Table 2.

The result finds that 39.28% of medical group patients and 4.76% of surgical group patients showed at least one of the composite complications and bad outcomes; then, we can calculate the relative risk of composite complications in medical method arm versus surgical arm as:  $\text{Relative Risk} = 39.28\%/4.76\% = 8.25$  (3.05 to 22.26 confidence interval 95%). Thus, medical group patients are 8.25 times more likely to show composite complications than surgical group patients. Relative risk calculation process detail is shown in Table 3.

## Subgroup analysis

As the final step in our quasi-experimental analysis, we estimated the clinical outcomes and treatment effects in the medical arm subgroups. The analysis showed that there were meaningful differences between hospital-based medical and clinic-based medical subgroups in majority of considered clinical outcomes.

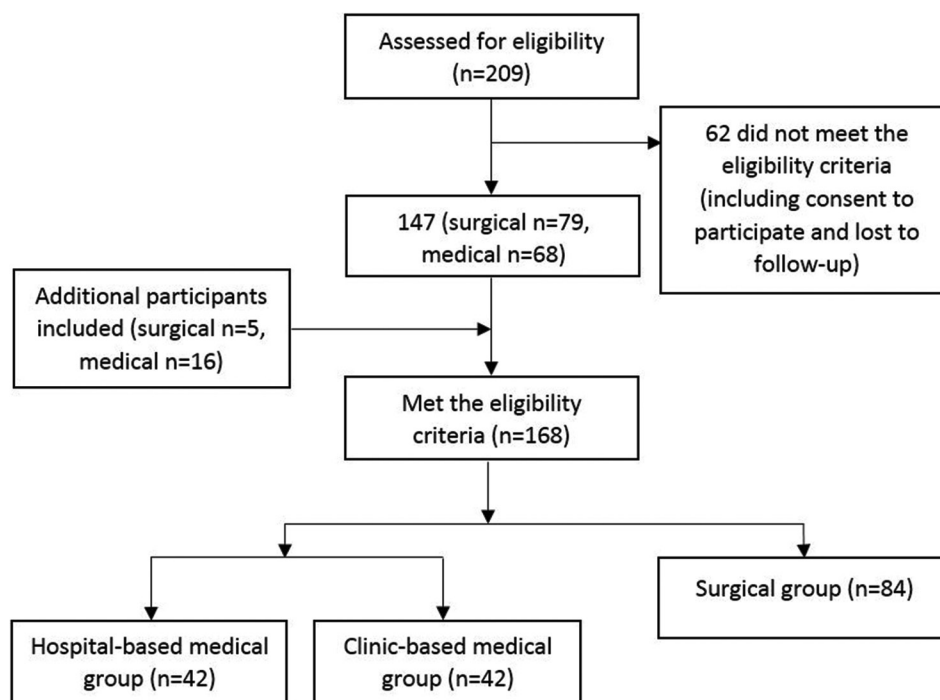


Figure 1: Patient enrollment flow chart

**Table 1: Participant baseline characteristics**

Characteristic	Level	Surgical (n=84)	Medical (n=84)	P
Age	Years	Mean 33 (6.5 S.D)	Mean 31 (6.5 SD)	0.137
Age range	<20	1 (1.2%)	3 (3.6%)	0.100
	20-24	8 (9.5%)	7 (8.3%)	
	25-34	35 (41.6%)	46 (54.8%)	
	35-40	27 (32.2%)	19 (22.6%)	
	>40	13 (15.5%)	9 (10.7%)	
Education	No formal education	12 (14.3%)	3 (3.6%)	0.000
	Grade 1-9 complete	16 (19%)	10 (11.9%)	
	Grade 12 complete	46 (54.8%)	35 (41.6%)	
	College graduate	10 (11.9%)	36 (42.9%)	
Income	Iranian Rials	32760504	40464685	0.017
Insurance coverage	Covered	60 (71.4%)	64 (76.2%)	0.626
	Uncovered	24 (28.6%)	20 (23.8%)	
Birth order	1	23 (27.4%)	27 (32.2%)	0.677
	2	32 (38%)	30 (35.7%)	
	3	26 (31%)	21 (25%)	
	4, >4	3 (3.6%)	6 (7.1%)	
Gestational age (weeks)	1-13 weeks	10.58	9.65	0.001
Previous abortion	Yes	11 (13.1%)	25 (29.7%)	0.009
	No	73 (86.9%)	59 (70.3%)	

**Table 2: Procedure details and complications of study participants**

Factor	Surgical (n=84)	Medical (n=84)	P
Complete abortion	80 (95.24%)	51 (60.72%)	<0.001
Composite complication	4 (4.76%)	33 (39.28%)	
Bleeding Scale			
No bleeding	53 (63.1%)	43 (51.2%)	0.070
Mild bleeding	19 (22.6%)	20 (23.8%)	
Moderate bleeding	9 (10.7%)	14 (16.7%)	
Severe bleeding	3 (3.6%)	7 (8.3%)	
Symptoms of pelvic infection	2 (2.4%)	11 (13.1%)	
Duration of hospital stay (hours)	Mean 54.57 (27.11 SD)	Mean 46.00 (24.02 SD)	0.043
Pain Scale			
No pain	62 (73.8%)	38 (45.2%)	<0.001
Mild pain	6 (7.2%)	19 (22.6%)	
Moderate pain	12 (14.3%)	18 (21.5%)	
Severe pain	4 (4.7%)	9 (10.7%)	
Acceptance (recommend to other)	72 (85.7%)	50 (59.5%)	<0.001
Quality of life	Mean 0.6605 (0.2882 SD)	Mean 0.5419 (0.3143 SD)	0.007

**Table 3: Comparison of relative risk in surgical and medical group**

Outcomes	Comparison of relative risk in surgical and medical group	
	Surgical (n=84)	Medical (n=84)
Composite complication (bad outcome)	4	33
Complete abortion (good outcome)	80	51
Relative Risk	Relative Risk = $\frac{33 / (33 + 51)}{4 / (4 + 80)} = 8.25$	

Clinic-based medical subgroup patients have experienced higher level of bleeding, pain, and symptoms of pelvic infection and have reported less acceptance level and

quality of life scores in comparison to the hospital-based medical subgroup. Based on EQ5D tool, the quality of life scores for hospital-based medical patients and clinic-based medical patients estimated 0.6891 and 0.3947, respectively. Furthermore, clinic-based medical patients are 2.30 times more likely to show composite complications than hospital-based medical patients. The relative risk (between subgroups) = 54.8%/23.8% = 2.30 (1.25 to 4.21 confidence interval 95%). Subgroup analysis results are shown in Table 4.

## Discussion

This study revealed substantial differences between surgical and medical methods for management of

**Table 4: Hospital-based and clinic-based medical subgroups analysis details**

Factor	Hospital-based medical (n=42)	Clinic-based medical (n=42)	P
Complete abortion	32 (76.2%)	19 (45.2%)	0.007
Composite complication	10 (23.8%)	23 (54.8%)	
Bleeding Scale			
No bleeding	26 (62.0%)	17 (40.5%)	0.015
Mild bleeding	11 (26.2%)	9 (21.4%)	
Moderate bleeding	3 (7.1%)	11 (26.2%)	
Severe bleeding	2 (4.7%)	5 (11.9%)	
Symptoms of pelvic infection	3 (7.1%)	8 (19%)	0.108
Duration of hospital stay (hours)	Mean 52 (24 SD)	Mean 39 (22 SD)	0.007
Pain Scale			
No pain	27 (64.3%)	10 (23.8%)	0.001
Mild pain	7 (16.7%)	13 (31.0%)	
Moderate pain	4 (9.5%)	14 (33.3%)	
Severe pain	4 (9.5%)	5 (11.9%)	
Acceptance (recommend to other)	31 (73.8%)	19 (45.2%)	0.008
Quality of life	Mean 0.6891 (0.2756 SD)	Mean 0.3947 (0.2858 SD)	<0.001

pregnancy termination procedures in Iran. Patients received D and C experienced significantly better clinical outcomes. This finding was backed up by differentiated statistical analyses and was shown for various clinical outcome parameters, such as estimated bleeding, experienced pain level, symptoms of pelvic infection, hospitalization, and quality of life.

Even though these results differ from some previously published studies,<sup>[14,15,17,18]</sup> they have a number of similarities with Westfall *et al.*,<sup>[19]</sup> Kim *et al.*,<sup>[20]</sup> and Niinimäki *et al.*<sup>[21]</sup> studies, who reported encouraging findings on safety and effectiveness of surgical methods of abortion in comparison to the medical methods. Furthermore, our results are in good agreement with Cochrane collaboration review study concluded that prostaglandins used alone seems to be less effective and more painful compared to the surgical methods of first trimester abortion.<sup>[22]</sup>

Furthermore, our subgroups analysis showed that the clinic-based medical patients have experienced worse clinical conditions and lowest acceptance rate in comparison to the surgical and hospital-based medical group patients. It would seem that clinic-based medical patients face major lack of enough self-management skills for medical abortion method. This may be because of poor patient counseling and education services for this kind of cares in Iran. Counseling and education are correlated with pregnancy outcomes, overall complete abortion rate, clinical outcomes, and patient's satisfaction because the patient is a more active participant in the process of pregnancy termination.<sup>[23-26]</sup>

As the current study investigated comprehensive clinical factors on women in all ages, all types of abortions including legal abortions, and at different settings, it can be expected that the entire women seeking an abortion

in first trimester would benefit from using the surgical method of pregnancy termination.

Results from this analysis should not be interpreted as underestimating the benefits of medical methods of abortion. Medical methods of abortion provide good alternatives to unsafe procedures, increases access and affordability of services in low resource settings, and women's range of options.<sup>[22]</sup> Undoubtedly, attempts to develop combination of misoprostol with other prostaglandins such as mifepristone as studies showed<sup>[7,27-30]</sup> would improve the clinical efficacy, acceptability, and patient's experiences in medical methods of abortion.

### Limitations and recommendations for future research

Given that our findings are based on quasi-experimental analysis and not fulfill the highest methodological research quality associated with a randomized controlled trial (RCT) design,<sup>[31]</sup> RCTs with longer follow-up periods, larger sample of clinical participants, and more analysis from different aspects such as cost-effectiveness analysis are needed to confirm these findings.

### Conclusion

According to the findings of this study, the surgical method of abortion using D and C is a very safe and highly successful option in comparison to the medical method using misoprostol alone and is associated with better clinical outcomes, acceptance, and quality of life in first trimester of pregnancy among Iranian women. Therefore, it is recommended that surgical abortion should be the first line option and be the part of any strategy to improve first trimester pregnancy termination cares in Iran.



## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Acknowledgements

Our thanks go to the staffs of three hospitals affiliated to Iran University of Medical Sciences (Hazrate Rasool-e Akram, Firoozgar, and Shahid Akbar Abadi) that have been extremely helpful and supportive of this research and committed considerable amounts of time, expertise, and effort to improve this work. This study was financially supported by Iran University of Medical Sciences as a part of PhD thesis in Health Economics with research code in the university system: 17515 and with Ethical Code: [IR.IUMS.REC.1399.068].

## Financial support and sponsorship

This study was financially supported by Iran University of medical sciences as a part of PhD thesis in Health Economics with research code in the university system: 17515 and with Ethical Code: [IR.IUMS.REC.1399.068].

## Conflicts of interest

There are no conflicts of interest.

## References

- Coast E, Lattof SR, Meulen Rodgers YV, Moore B, Poss C. The microeconomics of abortion: A scoping review and analysis of the economic consequences for abortion care-seekers. *PLoS One* 2021;16:e0252005.
- Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. *Lancet GlobHealth* 2014;2:e323-33.
- Zalvand R, Tajvar M, Pourreza A, Asheghi H. Determinants and causes of maternal mortality in Iran based on ICD-MM: A systematic review. *Reprod Health* 2019;16:16.
- Bearak J, Popinchalk A, Ganatra B, Moller AB, Tunçalp Ö, Beavin C, et al. Unintended pregnancy and abortion by income, region, and the legal status of abortion: Estimates from a comprehensive model for 1990-2019. *Lancet GlobHealth* 2020;8:e1152-61.
- Soleimani Movahed M, Hussein Barghazan S, Askari F, Arab Zozani M. The economic burden of abortion and its complication treatment cares: A systematic review. *JFamily ReprodHealth* 2020;14:60-7.
- Nagendra D, Koelper N, Loza-Avalos SE, Sonalkar S, Chen M, Atrio J, et al. Cost-effectiveness of mifepristone pretreatment for the medical management of nonviable early pregnancy: Secondary analysis of a randomized clinical trial. *JAMA Network Open* 2020;3:e201594.
- Abubeker FA, Lavelanet A, Rodriguez MI, Kim C. Medical termination for pregnancy in early first trimester ( $\leq 63$  days) using combination of mifepristone and misoprostol or misoprostol alone: A systematic review. *BMC Womens Health* 2020;20:142.
- Moseson H, Jayaweera R, Raifman S, Keefe-Oates B, Filippa S, Motana R, et al. Self-managed medication abortion outcomes: Results from a prospective pilot study. *Reprod Health* 2020;17:164.
- Rausch M, Lorch S, Chung K, Frederick M, Zhang J, Barnhart K. A cost-effectiveness analysis of surgical versus medical management of early pregnancy loss. *FertilSteril* 2012;97:355-60.
- Barghazan SH, Hadian M, Rezapour A, Nassiri S. Economic evaluation of medical versus surgical strategies for first trimester therapeutic abortion: A systematic review. *J Educ Health Promot* 2022;11:184.
- Whitehouse KC, Kim CR, Ganatra B, Duffy JMN, Blum J, Brahmi D, et al. Standardizing abortion research outcomes (STAR): A protocol for developing, disseminating and implementing a core outcome set for medical and surgical abortion. *Contraception* 2017;95:437-41.
- Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian JPsychol Med* 2013;35:121-6.
- Zhang J, Gilles JM, Barnhart K, Creinin MD, Westhoff C, Frederick MM. A comparison of medical management with misoprostol and surgical management for early pregnancy failure. *New EnglJMed* 2005;353:761-9.
- Cubo AM, Soto ZM, Haro-Pérez A, Hernández Hernández ME, Doyague MJ, Sayagués JM. Medical versus surgical treatment of first trimester spontaneous abortion: A cost-minimization analysis. *PLoS One* 2019;14:e0210449.
- Nwafor JI, Agwu UM, Egbuji CC, Ekwedigwe KC. Misoprostol versus manual vacuum aspiration for treatment of first-trimester incomplete miscarriage in a low-resource setting: A randomized controlled trial. *NigerJ Clin Pract* 2020;23:638-46.
- Vallvé C, Artés M, Cobo E. Non-randomized evaluation studies (TREND). *MedClin* 2005;125(Suppl 1):38-42.
- Ireland LD, Gatter M, Chen AY. Medical compared with surgical abortion for effective pregnancy termination in the first trimester. *ObstetGynecol* 2015;126:22-8.
- Moodliar S, Bagratee JS, Moodley J. Medical vs. surgical evacuation of first-trimester spontaneous abortion. *Int J Gynecol Obstet* 2005;91:21-6.
- Westfall JM, Sophocles A, Burggraf H, Ellis S. Manual vacuum aspiration for first-trimester abortion. *ArchFamily Med* 1998;7:559-62.
- Kim HJ, Park SL, Sohn HSJYH. Comparison of clinical outcomes between medical abortion and surgical abortion: Systematic review and meta-analysis. *Yakhak Hoeji* 2021;65:228-36.
- Niinimäki M, Jouppila P, Martikainen H, Talvensaari-Mattila A. A randomized study comparing efficacy and patient satisfaction in medical or surgical treatment of miscarriage. *FertilSteril* 2006;86:367-72.
- Say L, Kulier R, Gülmezoglu M, Campana A. Medical versus surgical methods for first trimester termination of pregnancy. *Cochrane DatabaseSyst Rev* 2002;2002:Cd003037.
- Breitbart V. Counseling for medical abortion. *AmJObstet Gynecol* 2000;183:S26-33.
- Ely GE. The abortion counseling experience. *Best Pract Ment Health* 2007;3:62-74.
- Gandomi N, Sharifzadeh G, Torshizi M, Norozi E. The effect of educational intervention based on self-efficacy theory on pregnancy anxiety and childbirth outcomes among Iranian primiparous women. *J Educ Health Promot* 2022;11:14.
- Boryri T, Navidian A, Zehi FH. Assessing the effect of self-care education on anxiety and depression among pregnant women with a history of spontaneous abortion. *J Educ Health Promot* 2020;9:347.
- Sheerin MR, McDonald EM. Management of first trimester pregnancy loss: Mifepristone plus misoprostol versus misoprostol alone. *Br J Midwifery* 2019;27:711-4.
- Dunford A, Fyfe R. Combination therapy with mifepristone and

- misoprostol for the management of first trimester miscarriage: Improved success. *Aust N Z J Obstet Gynaecol* 2018;58:438-42.
29. Schreiber CA, Creinin MD, Atrio J, Sonalkar S, Ratcliffe SJ, Barnhart KT. Mifepristone pretreatment for the medical management of early pregnancy loss. *New Engl J Med* 2018;378:2161-70.
  30. Hamel CC, Snijders M, Coppus S, Vandenbussche F, Braat DDM, Adang EMM. Economic evaluation of a randomized controlled trial comparing mifepristone and misoprostol with misoprostol alone in the treatment of early pregnancy loss. *PLoS One* 2022;17:e0262894.
  31. Rogers J, Revesz A. Experimental and quasi-experimental designs. *The Routledge Handbook of Research Methods in Applied Linguistics*. Routledge; 2019. p. 133-43.