Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2023; 40(4): 710-714
doi: 10.52142/omujecm.40.4.8

Termination of pregnancy using vaginal misoprostol-only regimen: Analysis of number of doses needed for successful termination

Murat Aykut ÖZEK [1,*], Tuncay YÜCE[2]

[1]Department of Perinatology, School of Medicine, Koc University, İstanbul, Türkiye
[2]Department of Perinatology, Liv Hospital, Gaziantep, Türkiye

Received: 30.05.2023 • **Accepted/Published Online:** 05.09.2023 • **Final Version:** 29.10.2023

Abstract

The aim of this study was to determine course number of misoprostol to successfully terminate a pregnancy according to gestational age. We retrospectively analyzed 365 consecutive terminations of pregnancies from the hospital records and our Perinatology Unit registry. The study cohort was divided into three; according to the trimesters of the pregnancy. The course number of vaginal misoprostol, hemoglobin levels and indications of pregnancy terminations were compared. More than half of the medical terminations of pregnancies were due to fetal central nervous system anomalies (51,2%). The course number needed for successful termination of pregnancy was significantly higher in the second trimester of pregnancy, compared to the first trimester group (p=0.0002). There was no significant difference between first and third trimesters (p=0.652). Increased number of courses of misoprostol was directly associated with drop in hemoglobin levels, regardless of gestational week or parity. Vaginal misoprostol alone is still safe and effective method for termination of pregnancy. The number of courses needed for expulsion of the fetus is significantly higher during the second trimester of the pregnancy and as course number increased, the reduction in hemoglobin levels was more pronounced.

Keywords: termination, pregnancy, vaginal, misoprostol

1. Introduction

Termination of pregnancy (ToP) using medical methods emerged as alternatives to the surgical procedures and evolved substantially to enter the WHO model list of essential medicines (1-3). Despite being proven as the most effective and safe method of medical ToP, combination of mifepristone and misoprostol is not available in most of the countries (3). Turkey is also one of the countries that mifepristone is not available, so misoprostol as single agent is still the main option for medical ToPs. There have been reports about the indications and current medico legal climate in Turkey (4, 5). We think that there is a gap of knowledge on success rates, maternal morbidity and hospital stays, based on current misoprostol only ToP practices.

In this study, we aimed to analyze the procedure of medical ToP using vaginal misoprostol only, in regards with the complications and compare the course numbers needed to successfully terminate the pregnancy between first, second and third trimesters of pregnancy.

2. Materials and Methods

This is a retrospective analysis of 365 consecutive terminations of pregnancies between 2017 and 2019 at Cengiz Gokcek Maternity Hospital, Gaziantep. Gaziantep is located in the south-east of Turkey. It is a city of industry and is one of the most populated and wealthy cities of the country. In contrast with that, because it is located in the Syrian border, there are highly populated refugee camps around the city. The hospital in which this trial was conducted, there are 11.500 births per year of whom 40% percent are Syrian refugees.

All of the cases were evaluated and counselled by A.O. and T.Y. Fetal ultrasonographic examinations and the prenatal diagnostic tests (if considered as necessary), feticides (beyond 20 weeks of gestation, with intracardiac KCl injection) and inpatient follow up during the medical termination procedure were all done by the authors.

Data were extracted from electronic database of the hospital and special registry of the Perinatology Department for ToPs. Length of hospital stay, number of course and the

*Correspondence: aykut.spm@gmail.com

total dose of misoprostol, complete blood counts upon admission and discharge were also noted to calculate hemoglobin drop.

Vaginal misoprostol was used as single agent for all of the cases, as mifepristone is not available in Turkey. Vacuum aspiration or sharp curettage was performed after completion of medical abortion. Dosage and frequency of misoprostol were judged case by case and according to the clinical recommendations of FIGO for induced abortion (6). During the first trimester (<13 weeks) 800 µg vaginal misoprostol was every three hours. Between 13 and 26 weeks of gestation, 400 µg vaginal misoprostol was used every three hours. For the cases ≥27 weeks, 25 µg vaginal misoprostol was administered every six hours. Misoprostol dose was tapered to half if the patient had history of hysterotomy. Course number needed for expulsion of the fetus was recorded for each case. Cervical balloon was introduced when cervical ripening has not been achieved. Hysterotomy was reserved only for patients with suspected uterine dehiscence or rupture.

Indications of ToPs were grouped mainly as fetal (malformations by organ system, chromosomal abnormalities, genetic syndromes, etc.) and maternal (PPROM, maternal systemic disease e.g. malignancy) indications. Cases were also grouped as a function of gestational age according to trimesters (Group 1: <13 weeks of gestation, Group 2: 13-26 weeks of gestation, Group 3: ≥27 weeks of gestation. Association of number of misoprostol course needed with other clinical parameters such as gestational age, trimester of pregnancy, history of hysterotomy were assessed with Poisson regression analysis.

Multifetal pregnancy reductions, elective pregnancy terminations because of unwanted pregnancies and cases with intrauterine fetal demise were excluded from the analysis. All the patients gave informed consent and were counselled for every step of medical or surgical interventions. Ethical approval was taken from the institutional review board of our hospital (Decision No: 2023/02/A) in order to revise the patients' data. The study was conducted in compliance with the Helsinki declaration of 1975, which was revised in 2013.

3. Results

There were 364 cases with whom the option of ToP was discussed with. The demographic and maternal/obstetric characteristics are presented in Table 1.

Table 1. Demographic and maternal characteristics

	Median	Minimum	Maximum
Age	29	17	46
Gravida	3	1	11
Parity	1	0	10
Gestational age at ToP	18	10	31

Among 364 cases, 5 were lost to follow up. Remaining 359 women were hospitalized and their pregnancies were terminated in the same center under supervision of the authors. Regarding the ethnic origins of the cases, 94 (26,1%) of them were Syrian refugees and 265 (73,8%) were Turkish citizens.

Table 2 shows that majority of the cases were terminated between 13-26 weeks of gestation. First trimester and third trimester ToPs followed them.

Table 2. Distribution of cases regarding gestational age at ToP

Gestational Age at ToP	N	%
<13 weeks	32	9
13-26 weeks	303	84,4
≥ 27 weeks	24	6,6
Total	**359**	**100**

We present the fetal and maternal indications of ToPs as a function of gestational age in Table 3. The most frequent reason for ToP -more than half of the cases- among all gestational ages were fetal central nervous system abnormalities (n=184, 51,2%); followed by fetal chromosomal abnormalities (n=45, 12,5%), second trimester PPROM/anhydramniosis (n=34, 9,5%) and musculoskeletal system anomalies (n=23, 6,4%).

Misoprostol as a single agent was successful in the vast majority of the cases. Among 10 cases (8 women with previous cesarean section), cervical balloon was also performed for cervical ripening. Median days of hospitalization was 1 day (minimum 1 day-maximum 4 days). Median value for the total number of misoprostol course was 5 (minimum 2 courses, maximum 14 courses).

Table 4 shows the association of course number of misoprostol and the gestational age at termination, history of hysterotomy and the hemoglobin drop. Our analysis revealed that, the course number needed for successful termination of pregnancy was significantly higher in the second trimester of pregnancy, compared to the first trimester group (p:0.0002). Number of courses for expulsion of the fetus was increased by 50% in the second trimester. There was no statistically significant difference between the first and third trimesters. The quadratic distribution of course number is presented in the Fig 1. Besides, among the cases with a uterine scar, the course number was significantly high (p<0.0001).

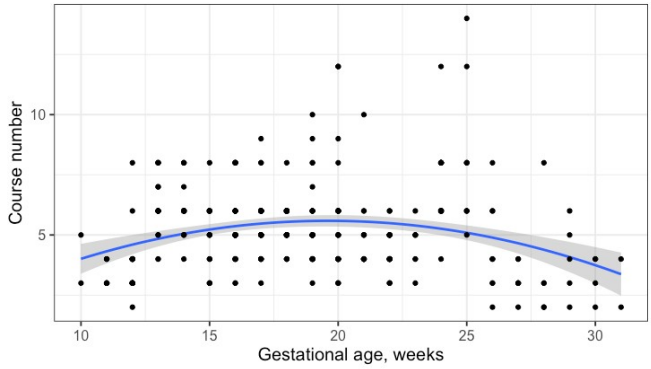

Fig. 1. Association of course number needed and gestational age

Moreover, we found that as the course number increased, the fall in hemoglobin levels were more prominent (p:0.002). Linear regression analysis revealed that this relation was not affected by neither gestational week nor parity.

There were two cases with suspected uterine rupture which ended up with laparotomy. Uterine dehiscence was detected in one of the cases (18 weeks of gestation) and uterine rupture (20 weeks of gestation) in the other. Both of the cases had history of hysteromoty. Maternal transfusion of red blood cells was required for only one case, because of low hemoglobin level upon admission (Hb 6,8 g/dL).

Table 3. Indications of ToPs according to gestational weeks

		Number of Cases			Total
		<13 weeks	13-26 weeks	≥27 weeks	
Diagnosis	Anencephaly	19	59	5	83
	Spina Bifida	1	37	5	43
	Encephalocele	4	13	1	18
	Hydrocephaly	0	18	2	20
	Other CNS Anomalies	4	14	2	20
	Cardiovascular System	0	5	2	7
	Respiratory System	0	3	0	3
	Urinary System	0	18	1	19
	Musculoskeletal System	0	22	1	23
	Other Fetal Systemic Disorder	1	8	0	9
	Trisomy 21	1	15	2	18
	Trisomy 18	0	11	2	13
	Trisomy 13	0	7	0	7
	Monosomy X	1	4	0	5
	Other Chromosomal Disorders	0	2	0	2
	Non-immune Hydrops Fetalis	0	19	0	19
	Heritable Disease/Genetic Syndromes	0	12	1	13
	PPROM/Anhydramnios	0	34	0	34
	Other Causes	1	2	0	3
Total		32	303	24	359

Table 4. Analysis of course number needed according to different variables

Variables	RR (95%CI)	P
Gestational age at termination		
- Linear term	1.03 (0.98 – 1.08)	0.274
- Quadratic term	0.93 (0.89 – 0.96)	0.0002
Trimester at termination		
- First trimester	Reference	
- Second trimester	1.50 (1.26 – 1.82)	<0.0001
- Third trimester	0.94 (0.70 – 1.24)	0.652
Previous caesarean delivery	1.36 (1.16 – 1.58)	<0.0001
Hemoglobin drop	1.07 (1.02 – 1.11)	0.002

4. Discussion

Termination of pregnancy is a multifaceted procedure complicated by medical (healthcare access, timely diagnosis e.g.), ethical (limit of gestational age to perform ToP, decision making) and legal issues. It has always been debated across the globe with ups and downs in terms of women's rights; which has been greatly influenced by political environment of the countries.

According to World Health Organization, 73,3 million abortions are performed each year, globally (7). It is estimated that one third of those abortions takes place in unsafe circumstances (8) and between 2003 and 2009, 4.7 to 13.2 % of maternal deaths were due to abortion, worldwide (9). Around 1 million live births occur in Turkey, each year. The 2019 report of Hacettepe University Institute of Population Studies revealed that the rate of medical abortus (including unwanted pregnancies and ToPs) was 5,9% in 2018 (10). According to this report, the proportion of ToPs was 62%. In addition to that, the official report of Ministry of Health revealed that the rate of maternal death was 13,1 women/100.000 live birth in 2019, in Turkey (11). Unfortunately, the exact rate of maternal deaths related to abortion is not known.

Termination of pregnancy is regulated under the Code of

Population Planning which was enacted in 1983. According to this law, unwanted pregnancies can be terminated up to 10 gestational weeks. After ten weeks, ToP can be performed only under circumstances that endanger wellbeing of the mother or if it was considered that the fetus would have serious disability; without any limit of gestational age (12).

Most of the cases in our study population were fetal CNS abnormalities during all trimesters, which is consistent with literature (5, 13). They were followed by fetal chromosomal aneuploidies, second trimester PPROM/anhydramniosis cases and lethal musculoskeletal dysplasias in the fetus. The reason for the latter may be the relatively high rate of consanguineous marriages in the study population area.

Although it has been demonstrated that sequential use of mifepristone and misoprostol is the most efficient and safe way of terminating pregnancy, mifepristone is not available in most of the countries, including Turkey (3). It has been shown that the dose and days of hospitalization is lower with combined mifepristone+misoprostol protocol, compared with other medical methods (14). That said, other than 2 cases out of 359 ToPs, none of the cases needed laparotomy. In addition to that, only one case needed transfusion and that was before ToP. We are in the opinion that vaginal misoprostol as a single agent is still a safe and efficient choice, among all trimesters.

This is the first study that evaluated the state of medical ToP in Turkey; "from number of doses of misoprostol" point of view, to the best of our knowledge. The course number needed for successful expulsion was significantly higher in the second trimester termination group when compared with first trimester cases. The main reason would be the higher doses used in the first trimester than other trimesters. There was no statistically significant difference between first and third trimester groups. We are in the opinion that this could be explained with the increased receptiveness of the gravid uterus to the prostaglandin analogues during the third trimester. As expected, among cases with a history of hysterotomy, the course number of misoprostol was again higher than the cases without a uterine scar, obviously this group had lowered doses. More importantly, we detected that the cases who needed more courses of misoprostol had significant decline of hemoglobin which indicates higher blood loss. This effect was independent from parity or gestational age at ToP.

We believe that the main strength of this study is the standard evaluation and follow up of all cases from decision to perform ToP to successful termination of pregnancy and discharge from hospital, by the two authors. The major limitation of our study is its retrospective design and that we did not record blood loss during the ToP procedure routinely.

In conclusion, the present study showed that the misoprostol only medical ToP is still an effective and safe procedure. Second trimester ToPs needed more course numbers of misoprostol, which was associated with statistically significant reduction in maternal hemoglobin levels.

Conflict of interest

The authors report no conflicts of interest.

Funding

No funding was used for the study.

Ethical statement

Ethical approval was taken from the institutional review board of our hospital (Decision No: 2023/02/A) in order to revise the patients' data. The study was conducted in compliance with the Helsinki declaration of 1975, which was revised in 2013.

Acknowledgments

None.

Authors' contributions

Concept: M.A.O., Design: M.A.O., Data Collection or Processing: M.A.O., Analysis or Interpretation: M.A.O., T.Y., Literature Search: M.A.O., T.Y., Writing: M.A.O., T.Y.

References

1. World Health Organization Model List of Essential Medicines – 22nd List, 2021. Geneva. World Health Organization; 2021 (WHO/MHP/HPS/EML/202102).
2. Abubeker FA, Lavelanet A, Rodriguez MI, Kim C. Medical termination for pregnancy in early first trimester (</= 63 days) using combination of mifepristone and misoprostol or misoprostol alone: a systematic review. BMC Womens Health. 2020;20(1):142. Epub 2020/07/09. doi: 10.1186/s12905-020-01003-8. PubMed PMID: 32635921; PubMed Central PMCID: PMCPMC7339463.
3. Ho PC. Development of medical termination of pregnancy: a review. BJOG. 2017;124(13):1942-7. Epub 2017/09/01. doi: 10.1111/1471-0528.14905. PubMed PMID: 28856795.
4. Aslan H, Yildirim G, Ongut C, Ceylan Y. Termination of pregnancy for fetal anomaly. Int J Gynaecol Obstet. 2007;99(3):221-4. Epub 2007/09/25. doi: 10.1016/j.ijgo.2007.05.047. PubMed PMID: 17889880.
5. Ozyuncu O, Orgul G, Tanacan A, Aktoz F, Guleray N, Fadiloglu E, et al. Retrospective analysis of indications for termination of pregnancy. J Obstet Gynaecol. 2019;39(3):355-8. Epub 2018/11/16. doi: 10.1080/01443615.2018.1506427. PubMed PMID: 30428730.
6. Morris JL, Winikoff B, Dabash R, Weeks A, Faundes A, Gemzell-Danielsson K, et al. FIGO's updated recommendations for misoprostol used alone in gynecology and obstetrics. Int J Gynaecol Obstet. 2017;138(3):363-6. Epub 2017/06/24. doi: 10.1002/ijgo.12181. PubMed PMID: 28643396.
7. Bearak J, Popinchalk A, Ganatra B, Moller AB, Tuncalp O, 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 Glob Health. 2020;8(9):e1152-e61. Epub 2020/07/28. doi: 10.1016/S2214-109X(20)30315-6. PubMed PMID: 32710833.
8. Ganatra B, Gerdts C, Rossier C, Johnson BR, Jr., Tuncalp O, Assifi A, et al. Global, regional, and subregional classification of abortions by safety, 2010-14: estimates from a Bayesian hierarchical model. Lancet. 2017;390(10110):2372-81. Epub 2017/10/02. doi: 10.1016/S0140-6736(17)31794-4. PubMed PMID: 28964589; PubMed Central PMCID: PMCPMC5711001.

9. Say L, Chou D, Gemmill A, Tuncalp O, Moller AB, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. Lancet Glob Health. 2014;2(6):e323-33. Epub 2014/08/12. doi: 10.1016/S2214-109X(14)70227-X. PubMed PMID: 25103301.

10. Hacettepe University Institute of Population Studies TRPoTDoSaBaT, Ankara, Turkey. 2018 Turkey Demographic and Health Survey. 2019.

11. S B. The Ministry of Health of Turkey, Health Statistics Yearbook, 2019. General Directorate of Health Information Systems, Ministry of Health, Turkey, 2021. 2021.

12. Turkey: Law No. 2827 of 1983 Population Planning Law [Turkey], 24 May 1983, available at: https://www.refworld.org/docid/4c4476752.html [accessed 22 December 2021].

13. Baumann S, Darquy S, Miry C, Duchange N, Moutel G. Termination of pregnancy for foetal indication in the French context analysis of decision-making in a Multidisciplinary Centre For Prenatal Diagnosis. J Gynecol Obstet Hum Reprod. 2021;50(8):102067. Epub 2021/01/24. doi: 10.1016/j.jogoh.2021.102067. PubMed PMID: 33484935.

14. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. Cochrane Database Syst Rev. 2011(1):CD005216. Epub 2011/01/21. doi: 10.1002/14651858.CD005216.pub2. PubMed PMID: 21249669; PubMed Central PMCID: PMCPMC8557267.