The Treatment Results Stillbirth in the Second and Third Trimesters by Misoprostol

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Abstract
The study carried out on 57 women with stillbirth in the second and third trimesters of pregnancy and was treatment by misoprostol at obstetrics and gynecology department in Vung Tay Nguyen General Hospital from 1/2024-12/2024. The success rate with medical abortion is 84,2%, of which the complete expulsion rate is 12,5%, incomplete is 87,5 %. The average total dose is 362,3 ± 290,3 mcg, which of 577,4 ± 227,6 mcg in second trimester and in third trimester is 105,8 ± 26,8 mcg ($p<0,05$). The average time to expulsion is 17,5 ± 7,9 hours, 81,3% case of study had vaginal birth achieved within 24 hours. In the cases had abdominal pain or vaginal bleeding, the average time to expulsion is shorter ($p<0,05$). There is no relationship between the number of previous pregnancies with expulsion results by misoprostol. Misoprostol is a safe and effective option for the management of intrauterine fetal demise in the second and third trimesters. But we need to consider dosage in the last third trimester to increase the treatment efficacy.

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Introduction

Stillbirth is defined as fetal death that remains in the uterine cavity at any gestational age. This condition causes significant psychological distress and may lead to severe complications that threaten maternal health [1]. The global average stillbirth rate is 13.9 per 1,000 births, predominantly occurring in low-income and developing countries [2].

Currently, various methods are available for the management of stillbirth in the second and third trimesters. However, medical induction with Misoprostol remains a preferred option due to its effectiveness in stimulating uterine contractions through selective binding to EP-2 and EP-3 receptors [3]. Multiple studies have demonstrated the efficacy of Misoprostol in expelling the fetus [4, 5]. Nevertheless, unlike first-trimester losses, the optimal regimen for managing stillbirth in the second and third trimesters has yet to be clearly established [6]. The dosage of Misoprostol varies widely, ranging from 25–400 mcg every 3–24 hours [7, 8]. Determining the standard dose, success rates, routes of administration, and potential complications continues to be a major concern in obstetrics and gynecology. Based on this context, we conducted the study titled: "The treatment results stillbirrth in the second and third trimesters by Misoprostol".

Methods

Study design and setting

Cross-sectional descriptive study on 57 cases of stillbirth at second and third trimester were treated by misoprostol at the Department of Obstetrics and Gynecology, Tay Nguyen Regional General Hospital from Jan 2024 to November 2024.

Disease selection criteria

Gestational at second and third trimester and the pregnancy has been diagnosed with stillbirth and were treated by misoprostol.

Exclusion criteria
Gestational age at first trimester or were treated by using other methods.

Procedure
Treat patients according to the department's protocol. Record and evaluate clinical progress based on the pre-designed data collection form.

Statistical analysis
The statistics were recorded, cleaned and statistically processed using IBM SPSS Statistics 20 software. Describe the data using descriptive statistics and analytical statistics. Qualitative variables will be described as numbers and percentages. Quantitative variables with normal distribution are described as mean ± standard deviation, without normal distribution are described as median and interquartile range. Use the "t" test and the Z formula to compare the average of two observations. With evaluation criteria: $p < 0.05$: statistically significant difference. Use the $\chi 2$ test to compare the difference between two ratios.

Results

Table 1: Misoprostol treatment outcomes

Results		Cases (n)	Rate (%)
Success		48	84.2
	No retained placenta	6	10.5
	Retained placenta	42	73.7
Failure		9	15.8
	Failed Expulsion	6	10.5
	Complications	3	5.3

The success rate was 84.2%, with retained placenta occurring in 87.5% of these cases. The failure rate was 15.8%, and there were 3 cases of complications (5.3%).

Table 2: Outcomes and total dosage by gestational age groups

	Second trimester		Third trimester		p
Results	**n**	**%**	**n**	**%**	
Success	29	93.5	19	73.1	0.065
Failure	2	6.5	7	26.9	
Total Dosage (mcg)	577.4 ± 227.6		105.8 ± 26.8		<0.001
Mean±SD	362.3 ± 290.3				

The success rates in the second and third trimester groups were 93.5% and 73.1%, respectively ($p < 0.05$). The mean total dose of Misoprostol was 362.3 ± 290.3 mcg, with 577.4 ± 227.6 mcg in the second trimester group and 105.8 ± 26.8 mcg in the third trimester group ($p < 0.05$).

Table 3: Relationship between expulsion time and gestational age

Expulsion Time (hour)	Second trimester		Third trimester		Total		p
	n	**%**	**n**	**%**	**n**	**%**	
≤ 24	24	82.8	15	78.9	39	81.3	1.0
> 24	5	17.2	4	21.1	9	18.8	
Mean ± SD	16.1 ± 8.1		19.7 ± 7.4		17.5 ± 7.9		0.127

A total of 81.3% of cases achieved successful expulsion within 24 hours. The mean expulsion time was 17.5 ± 7.9 hours, with no statistically significant difference observed ($p > 0.05$).

Table 4: Relationship between clinical symptoms and expulsion time

Abdominal Pain / Vaginal Bleeding	Cases (n)	Expulsion Time (hour)	p
Yes	11	12.7 ± 8.5	<0.001
No	37	19.9 ± 7.3	

Cases presenting with abdominal pain or vaginal bleeding had a shorter expulsion time compared to those without these symptoms ($p < 0.05$).

Table 5: Association between route of administration and treatment outcomes

Results	Buccal		Vaginal		p
	n	**%**	**n**	**%**	
Success	18	85.7	30	83.3	1
Failure	3	14.3	6	16.7	
Total dose (mcg)					
Second trimester	13	576.9 ± 265.1	16	587.5 ± 212.5	0.906
Third trimester	5	85.0 ± 22.4	14	107.1 ± 24.9	0.098
Mean ± SD	440.3 ± 318.0		363.3 ± 288.2		0.393

The rates of successful expulsion were 85.7% in the buccal group and 83.3% in the vaginal group, with no significant difference observed (p > 0.05). The mean total dose of Misoprostol administered was 440.3 ± 318.0 mcg in the buccal group and 363.3 ± 288.2 mcg in the vaginal group (p > 0.05).

Table 6: Association between parity and treatment outcomes

Parity	Success		Failure		p
	n	%	n	%	
0	19	39.6	2	22.2	0.452
1-2	21	43.8	4	44.4	
≥ 3	8	16.7	3	33.3	

No association was found between parity and the success of fetal expulsion with Misoprostol (p > 0.05).

Discussion

In this study of 57 cases, the overall success rate of fetal expulsion was 84.2%, with retained placenta observed in 87.5% of these cases. This success rate was lower than that reported by Amin (2019), who documented a 97% success rate, possibly due to the lower Misoprostol doses used in our protocol [6]. Specifically, the success rates in the second and third trimester groups were 93.5% and 73.1%, respectively, consistent with findings by Pham Thi Linh (2017) [9]. The lower success and higher retention rates observed in the third trimester highlight the question of whether higher doses might yield improved outcomes, as Sultana Z reported a 96% success rate using a 50 mcg regimen in late gestations [4]. Retained placenta primarily occurred in second-trimester cases, likely due to immature placental separation and lower uterine sensitivity to Misoprostol. However, this difference was not statistically significant, potentially because of the small sample size and exclusion of spontaneous or alternative management cases.

There were 9 failures (15.8%), including 6 cases with failed expulsion after five doses of Misoprostol and 3 complicated cases (2 suspected uterine ruptures, 1 prolonged fever suggesting infection), comparable to previous studies. Failure rates were 6.5% in the second trimester and 26.9% in the third trimester, possibly reflecting the limited number of doses and lower Misoprostol use. The high incidence of retained placenta underlines the need for careful postpartum monitoring to prevent complications. Compared to Palod (2016), who reported a 95.3% success rate with higher Misoprostol doses, our study noted fewer side effects such as abdominal pain, nausea, and vomiting [10].

Approximately 71.9% of cases required 2–3 doses of Misoprostol, similar to the 84% reported by Sultana Z (2020) [4], emphasizing the need for repeated dosing to maintain adequate uterine stimulation. The mean total Misoprostol dose was 362.3 ± 290.3 mcg, lower than that in Cetin (2016), which also reported two cases requiring hysterectomy [11]. El-Ghabit (2011) similarly showed lower Misoprostol doses associated with increased oxytocin supplementation, highlighting the importance of balancing dose efficacy with safety [12]. Notably, third trimester pregnancies required lower total Misoprostol doses than second trimester cases but achieved comparable efficacy, reflecting greater uterine sensitivity at advanced gestational ages.

Expulsion occurred within 24 hours in 81.3% of cases, aligning with previous studies (67–83%). The mean expulsion time was 17.5 ± 7.9 hours, with no significant difference between second and third trimester groups (p > 0.05), despite the greater sensitivity in later gestation, likely due to the lower Misoprostol dosing. Compared to Cetin (2016) and El-Ghabit (2011), expulsion times in our study varied depending on dose and adjunct protocols (such as additional oxytocin) [11, 12]. Amin (2019) also noted longer Misoprostol induction times compared to dinoprostone or Foley catheter, though without statistical significance, supporting Misoprostol's practicality and ease of use [6]. Moreover, patients presenting with abdominal pain or vaginal bleeding had significantly shorter expulsion times (p < 0.05), suggesting these symptoms indicate early labor onset.

Success rates were 85.7% with vaginal administration and 83.3% with buccal administration (p > 0.05), in line with previous studies and guidelines. Total Misoprostol doses did not differ significantly by route. Bracken (2014) showed that dose, rather than route, more strongly influenced outcomes, with 200 mcg outperforming 100 mcg buccally [13]. Similarly, Cleeve (2019) demonstrated comparable efficacy across buccal, vaginal, and sublingual routes, although vaginal administration maintained a more prolonged effect [14]. Therefore, route selection may be tailored to patient condition and preference.

Finally, there was no significant association between parity and the success of Misoprostol-induced expulsion (p > 0.05). Contrary to the hypothesis that multiparous women would expel more readily, our data showed no notable influence of obstetric history on Misoprostol efficacy. Nonetheless, given the small sample size and unequal group distribution, further studies with larger cohorts are needed to validate these findings.

Conclusion

Misoprostol is effective for the expulsion of stillbirrth demise at gestational at second and third trimesters. However, dosing in the third trimester should be carefully considered to enhance efficacy while reducing the incidence of retained placenta.

References

1. Gomez R, Wing D. Misoprostol for termination of pregnancy with intrauterine fetal demise in the second and third trimester of pregnancy - a systematic review. Contraception. 2009;79(4):259-71. doi:10.1016/j.contraception.2008.10.012.
2. Sultana Z, Rahman MM, Begum M, Akhter S, Nahar K. Induction by misoprostol in case of intrauterine fetal death: a cross-sectional study. Mymensingh Med J. 2020;29(3):616-22.
3. Amin KV, Chauhan AR, Goel A. Current practices of cervical ripening and induction of labour in intrauterine foetal demise: an observational study. J Obstet Gynaecol India. 2019;69(1):37-42. doi:10.1007/s13224-018-1113-9.
4. Das SR, Akhter S, Begum M, Nahar K. Safety and efficacy of different doses of misoprostol in termination

of intrauterine fetal death (IUFD) cases. Bangladesh J Obstet Gynaecol. 2016;28(1):15-20.
5. Gomez R, Wing D, Fiala C. Misoprostol for intrauterine fetal death. Int J Gynaecol Obstet. 2007;99 Suppl 2:S190-3. doi:10.1016/j.ijgo.2007.09.004.
6. Palod S, Nayak T. Use of misoprostol for termination of second and third trimester pregnancy with intrauterine foetal death. Int J Reprod Contracept Obstet Gynecol. 2016;5(4):1216-21. doi:10.18203/2320-1770.ijrcog20160931.
7. Cetin C, Yucel B, Ozdemir O, Cetin M. Comparison of two misoprostol regimens for mid-trimester pregnancy terminations after FIGO's misoprostol dosage recommendation in 2012. J Matern Fetal Neonatal Med. 2016;29(8):1314-7. doi:10.3109/14767058.2015.1046825.
8. El-Gharib MN, Elebyary MT. Low-dose vaginal misoprostol in the management of intrauterine fetal death. J Matern Fetal Neonatal Med. 2011;24(10):1239-42. doi:10.3109/14767058.2010.547963.
9. Bracken H, Dabash R, Tsertsvadze G, Posohova S, Shah M, Hajri S, *et al*. Buccal misoprostol for treatment of fetal death at 14-28 weeks of pregnancy: a double-blind randomized controlled trial. Contraception. 2014;89(3):187-92. doi:10.1016/j.contraception.2013.11.009.
10. Cleeve A, Fonhus MS, Lavelanet A. A systematic review of the effectiveness, safety, and acceptability of medical management of intrauterine fetal death at 14-28 weeks of gestation. Int J Gynaecol Obstet. 2019;147(3):301-12. doi:10.1002/ijgo.12951.
11. Ministry of Health. Stillbirth. In: National guidelines on reproductive health services. Ministry of Health; 2016. p. 125-7.
12. United Nations Inter-agency Group for Child Mortality Estimation. A neglected tragedy: the global burden of stillbirths. New York: UNICEF; 2020.
13. Vo Thi Thanh Huyen. Evaluation of the effectiveness of misoprostol in the management of first and second trimester intrauterine fetal death [Specialist Thesis Level II]. Hue University of Medicine and Pharmacy; 2024.
14. Pham Thi Linh, Truong My Ngoc, Le Thi My Tien. Evaluation of the outcomes of pregnancy termination with misoprostol at 13 to 22 weeks of gestation at Can Tho City Obstetrics Hospital [Institution-Level Research Project]. Can Tho City Obstetrics Hospital; 2018.