International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Rajkumar et al. Int J Reprod Contracept Obstet Gynecol. 2024 Sep;13(9):2351-2354
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20242481

Original Research Article

Comparison of combination of mifepristone and misoprostol with misoprostol alone in management of intrauterine death

Rajkumar*, Mamta Sharma

Department of Obstetrics and Gynecology, Government Medical College, Kota, Rajasthan, India

Received: 25 June 2024
Revised: 27 July 2024
Accepted: 31 July 2024

***Correspondence:**
Dr. Rajkumar,
E-mail: rajkumar020994@gmail.com

ABSTRACT

Background: Intrauterine fetal death is one of the most devastating obstetric complications. A clinically accepted definition of IUFD is the death of fetus at or after 20 weeks of pregnancy, but for international comparison WHO has now recommended IUFD as a baby born with no signs of life at or after 28 weeks of gestation.
Methods: The prospective analytical study was be conducted in the department of obstetrics and gynecology at government medical college and J. K. Loan Hospital Kota over a 1 June 2021 to 30 November 2022 year women with intrauterine death after 28 weeks of gestation are studied. 120 pregnant women were divided randomly, alternatively into two groups of 60 each. Group I (combination regimen)- women received 200 mg mifepristone orally and misoprostol after 24 hours. Group II (misoprostol group).
Results: We included 120 patients with late IUD and found that the mean induction to delivery interval was 9.98 hours in combination group where as it was 14.2 hours in misoprostol only group. This provides a good alternate regimen in the management of late intrauterine deaths.
Conclusions: The combination of mifepristone and misoprostol for induction of labour in IUFD has shorter induction to delivery interval and lesser number of misoprostol doses usage when compared to only-misoprostol group. However, conventional regimen with misoprostol alone may be appropriate in settings where cost is a prohibitive factor.

Keywords: Intrauterine fetal death, Mifepristone, Misoprostol

INTRODUCTION

IUFD is the death of fetus at or after 20 weeks of pregnancy, but for international comparison WHO has now recommended IUFD as a baby born with no signs of life at or after 28 weeks of gestation.[1,2] Common causes of IUFD include maternal causes such as diabetes mellitus and hypertension and fetal causes such as infection, immune haemolytic disease, cord accidents, metabolic disorders, malformation and placental dysfunction.[3] Almost 90% of women with IUFD deliver spontaneously within 3 weeks of the event. Until then the retention of dead fetus could cause emotional distress and intrauterine infection following rupture of membrane.[4] About one in four women with a dead fetus retained for 4 weeks or more may develop consumptive coagulopathy.[3] WHO recommends oral or vaginal misoprostol for induction of labor in the third trimester of pregnancy in women with dead or malformed fetus.[5]

Aim of our study was to compare the efficacies of different regimen for induction of labour in late IUFD.

METHODS

The prospective analytical study was conducted in the department of obstetrics and gynaecology at government medical college and J. K. Loan Hospital Kota over a 1 June 2021 to 30 November 2022 year women with intrauterine death after 28 weeks of gestation are studied.

Inclusion criteria

The woman with intrauterine death confirmed by ultrasound (absent fetal heart pulsations). Women who were not in labor (no regular contractions or unfavorable cervix). Those patients who understood the medical regimen and gave informed written consent for induction with combined regimen were included in the study.

Exclusion criteria

Women who were in labor, multiple pregnancy with one intrauterine death, major degree of cephalo-pelvic disproportion (for big baby with intra uterine death), previous two/one cesarean deliveries. Woman who did not give consent. Patients with glaucoma, asthma, epilepsy, heart disease, jaundice, renal and hepatic dysfunction. Grand multipara.

120 pregnant women were divided randomly, alternatively into two groups of 60 each. Group I (combination regimen)- women received 200 mg mifepristone orally and misoprostol after 24 hours. Dose of misoprostol was 1) for 28 to 32 weeks- induction with 100 µg of intravaginally misoprostol every four hourly for a maximum of six doses. 2) for 32 to 40 weeks- a lower dose 50/25 µg of misoprostol was given. If the cervix was unripe (Bishop score below 6), 50/25 µg was given every four hourly upto six doses. Group II (misoprostol group)- women received 1) 28 to 32 weeks- induction with 100 µg of intravaginally misoprostol every four hourly for a maximum of six doses. 2) 32 to 40 weeks- a lower dose 50/25 µg of misoprostol were given. If the cervix was unripe (Bishop score below 6), 50/25 µg was given every four hourly upto six doses.

Successful treatment was defined as delivery within 72 hours of first misoprostol dose.

SPSS 3.0 software was used for all statistical calculation.

RESULTS

In group 1, 15 patients were booked and 45 were unbooked. In group 2, 12 patients were booked and 48 were unbooked (Table 1).

Table 1: Booking status.

Book/ unbook	Group-1		Group-2	
	N	%	N	%
Booked	15	25	12	20
Unbooked	45	75	48	80
Total	60	100	60	100

The mean age of patients in group 1 was 24.56 years and in group 2 was 24.26 years respectively. P value- 0.6231 (not significant) (Table 2).

Table 2: Distribution of patients according to age groups.

Age distribution	Group-1	Group-2	P value
20-24	33	32	0.6231
25-29	21	26	
30-34	5	2	
35-40	1	0	
Total	60	60	
Mean±SD	24.56±3.63	24.26±3.0	

Table 3: Distribution of patients according to parity.

Para	Group-1		Group-2	
	N	%	N	%
P0	32	53.33	33	55
P1	21	35	19	31.66
P2	7	11.66	8	13.33
Total	60	100	60	100

In group I percentage of parity among patients was P0-53.33%, P1-35%, P2-11.66% respectively. In group II percentage of parity among patients is P0-55% P1-31.66% P2-13.33% respectively (Table 3).

Table 4: Distribution of patients according to gestational age.

Gestational age	Group-1		Group-2		P value
	N	%	N	%	
28-32	27	45	28	46.66	0.5949
33-36	25	41.66	26	43.33	
37-42	8	13.33	6	10	
Total	60	100	60	100	
Mean±SD	33.46±3.24		33.15±3.26		

In group I percentage of patients in gestational age between 28-32 weeks was 45%, 33-36 weeks was 41.66%, 37-42 weeks was 13.33%. In group II percentage of patients in gestational age between 28-32 weeks was 46.66%, 33-36 weeks was 43.33%, 37-42 weeks was 10%.

Table 5: Bishop score (modified) at the time of induction.

Bishops score	Group-1		Group-2		P value
	N	%	N	%	
0	8	13.33	9	15	0.5915
1	4	6.66	4	6.66	
2	16	26.66	17	28.33	
3	15	25	16	26.66	
4	12	20	10	16.66	
5	2	3.33	2	3.33	
6	3	5	2	3.33	
Total	60	100	60	100	
Mean±SD	2.61±1.55		2.46±1.50		

Group I patients with Bishop score 0- 13.33%, 1- 6.66%, 2- 26.66%, 3- 25%, 4- 20%, 5- 3.33%,6- 5%. Group 2 patients with Bishop score 0- 15%, 1- 6.66%, 2- 28.33%, 3- 26.66%, 4- 16.66%, 5- 3.33%, 6- 3.33% (Table 5).

Table 6: Induction delivery interval.

induction delivery (hours)	Group-1		Group-2		P value
	N	%	N	%	
0-5	9	15	0	0	0.0001
6-10	28	46.66	15	25	
11-15	14	23.33	22	36.66	
16-20	5	8.33	14	23.33	
21-25	4	6.66	8	13.33	
26-30	0	0	1	1.66	
Total	60	100	60	100	
Mean±SD	9.98±5.27		14.2±5.32		

Mean induction to delivery interval in group 1 was 9.98. Mean induction to delivery interval in group 2 was 14.2 (Table 6).

DISCUSSION

In this study Table 1 showed booked patients 25% (in group 1) and 20% (in group 2) and unbooked patients were 75% in group 1 and 80% in group 2. Majority of patients were unbooked because our centre is tertiary centre so referred patients were more.

In this study Table 2 showed mean age of patients of distribution in group 1 24.56 years and group 2- 24.26 years respectively (p value was not significant).

Table 7: Comparison of our study with similar other studies mean age of patients of distribution in group 1 and group 2.

Study	Mean age (years) in group 1	Mean age (years) in group 2
Our study	24.56	24.26
Sharma et al[6]	22.85	23.6
Gupta et al[7]	28.4	27.5
Maheshwari et al[8]	26.53	27.13
Panda et al[9]	27.9	26.8
Modak et al[10]	20.86	20.84
Vayrynen et al[11]	32	30

Bugalho et al also found a quicker uterine response in women with more advanced gestation (over 34 weeks) and higher Bishop's score (>5).[12] Uterine sensitivity to PGs is known to increase with advancing gestation. As Bugalho et al our study shown that induction to delivery interval decreased with advanced gestation (p value- 0.032) in both the groups.[12]

In this study, Table 3 showed maximum patients belong to P0- 53.33% in group 1 and 55% in group 2 respectively. In group 1 and 2, para 1 were 35% and 31.66%, para 2 were 11.66% and 13.33% respectively.

In this study, Table 4 showed mean gestational age 33.46 weeks in group 1 and 33.15 weeks in group 2 respectively.

Table 8: Comparison of our study with similar other studies mean gestational age in group 1 and group 2.

Study	Mean gest. age (weeks) in group 1	Mean gest. age (weeks) in group 2
Our study	33.46	33.15
Sharma et al[6]	33.35	34.60
Gupta et al[7]	32.4	31.2
Maheshwari et al[8]	34.47	34.58
Panda et al[9]	34.63	35
Modak et al[10]	32.95	33.14
Vayrynen et al[11]	32	30

In this study, Table 5 showed mean Bishop score at the time of induction 2.61 in group 1 and 2.46 in group 2 respectively.

Table 9: Comparison of our study with similar other studies mean Bishop score in group 1 and group 2.

Study	Mean Bishop score in group 1	Mean Bishop score in group 2
Our study	2.61	2.46
Sharma et al[6]	1.45	2.1
Gupta et al[7]	3	2.6
Maheshwari et al[8]	3.4	3.24
Vayrynen et al[11]	2	2

Table 10: Comparison of our study with similar other studies mean induction to delivery interval in group 1 and group 2.

Study	Mean induction to delivery interval (hours) in group 1	Mean induction to delivery interval (hours) in group 2
Our study	9.98	14.2
Sharma et al[6]	6.72	11.81
Gupta et al[7]	9.6	16.2
Maheshwari et al[8]	13.41	21.13
Panda et al[9]	8.46	15
Modak et al[10]	12.45	20.25
Vayrynen et al[11]	12.8	13.3

Our study was comparable to above mentioned studies. Although P values was insignificant in two groups. A multipara responds to induction more favourble than a

primipara. The initial score of cervices prior to induction largely determines successful induction.

Table 6 showed mean induction to delivery interval 9.98 in group 1 and 14.2 in group 2 respectively.

This study was in affirmation with the studies of the Wagaarachchi et al where mean induction to delivery interval with the use of mifepristone and misoprostol combination is 8.5 hours.[13]

Limitation of our study was sample size was small.

CONCLUSION

The loss of a wanted baby at any gestational age is distressing not only to the expectant parents, but also to their relatives and attending obstetrician. We included 120 patients with late IUD and found that the mean induction to delivery interval was 9.98 hours in combination group where as it was 14.2 hours in misoprostol only group. This provides a good alternate regimen in the management of late intrauterine deaths. The combination of mifepristone and misoprostol for induction of labour in IUFD has shorter induction to delivery interval and lesser number of misoprostol doses usage when compared to only-misoprostol group. However, conventional regimen with misoprostol alone may be appropriate in settings where cost is a prohibitive factor.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. ACOG Practice bulletin No.102: Management of stillbirth. Obstet gynecol. 2009;113:748-61.
2. WHO. Maternal, newborn, child and adolescent health. Available at: http://www.who.int/maternal_child_adolescent/epidemiology/stillbirth/en/. Accessed on 15 June 2016.
3. Silver RM. Fetal death. Obstet Gynecol. 2007;109:153-67.
4. Wagaarachchi PT, Ashok PW, Narvekar NN, Smith NC, Templeton A. Medical management of late intrauterine death using a combination of mifepristone and misoprostol. Br J Obstet Gynecol. 2002;109(4):443-7.
5. WHO recommendation for induction of labor. WHO 2011. Available at: https://www.who.int/publications/i/item/9789241501156. Accessed on 15 June 2016.
6. Sharma D, Singhal SR, Poonam, Paul A, Kunika. Comparison of mifepristone combination with misoprostol and misoprostol alone in the management of intrauterine death: condensation - misoprostol and mifepristone combination is more effective than misoprostol alone in the management of intrauterine death. Taiwan J Obstet Gynecol. 2011;50(3):322-5.
7. Gupta S, Kagathra B, Desai A. Mifepristone and misoprostol versus misoprostol alone in management of late intrauterine fetal death. Int J Reprod Contracept Obstet Gynecol. 2016;5(9):2935-9.
8. Maheshwari S, Borgohain D. Methods of induction of labor in intrauterine fetal demise: A comparative study. Int J Reprod Contracept Obstet Gynecol. 2017;6(9):3911-5.
9. Panda S, Jha V, Singh S. Role of a combination of mifepristone and misoprostol versus misoprostol alone in induction of labor in late intrauterine fetal death. J Fam Reprod Health. 2013;7(4):177-9.
10. Modak R, Roy S, Biswas DK, Pal A, Mandal TK. Role of combination of mifepristone and misoprostol versus misoprostol alone in induction of labor in late intrauterine fetal death: a randomized trial. Int J Clin Obstet Gynecol. 2018;2(6):78-82.
11. Väyrynen W, Heikinheimo O, Muutila A. Misoprostol only versus mifepristone plus misoprostol in the induction of labor following intrauterine fetal death. Acta Obstet Gynecol Scand. 2007;86(6):701-5.
12. Pritchard JA. Fetal death in utero. Obstet Gynecol. 1959;14:573-80.
13. Operational guidelines for establishing sentinel stillbirth surveillance system, child health division ministry of health and family welfare government of India. 2016. Available at: https://nhm.gov.in/images/pdf/programmes/RBSK/Operational_Guidelines/Operational_Guidelines_for_establishing_Sentinel_Stillbirth_Surveillance_System.pdf. Accessed on 15 March 2020.

Cite this article as: Rajkumar, Sharma M. Comparison of combination of mifepristone and misoprostol with misoprostol alone in management of intrauterine death. Int J Reprod Contracept Obstet Gynecol 2024;13:2351-4.