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METHODS OF INDUCTION OF LABOUR IN PREGNANCIES WITH INTRAUTERINE FETAL DEMISE-A RANDOMIZED CONTROLLED TRIAL

Obstetrics & Gynaecology

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ABSTRACT

Intrauterine fetal demise (IUFD) represents one of the most devastating outcomes in obstetrics, affecting approximately 1% of all pregnancies.The WHO definition being IUFD as the birth of a baby with no signs of life at or after 28 weeks of pregnancy. This study is thus designed to evaluate and compare various cervical ripening and induction protocols, with the aim of identifying the most efficient and safest approach for managing intrauterine fetal demise.This is a Prospective, Interventional and Randomized controlled study conducted in the Department of Obstetrics and Gynaecology, Ballari Medical College and Research Centre, Ballari over a period of 6 month study period. All pregnant women admitted in the Department of Obstetrics and Gynaecology with Intrauterine fetal demise. A minimum of 80 pregnant women with Intrauterine fetal demise. GROUP A: Single dose of 200mcg mifepristone is given orally,after 24 hrs interval, 100mcg of misoprostol is kept in the posterior vaginal fornix and repeated every 4 hrs till they go into labour or deliver the dead fetus or to a maximum of 6 doses. GROUP B: Intracervical foley's catheterization followed by 100mcg misoprostol is inserted in the posterior vaginal fornix and and repeated every 4 hours till they go into labour or deliver the dead fetus or to a maximum of 6 doses. The study concludes that Mifepristone and Misoprostol emerged as the superior regimen, offering faster delivery, fewer doses, and higher PTVD rates. While Group-B remains a viable alternative, its reliance on mechanical methods and higher misoprostol requirements may limit its utility.

KEYWORDS

Intrauterine fetal demise, Mifepristone, Misoprostol

INTRODUCTION

Intrauterine fetal demise (IUFD) represents one of the most devastating outcomes in obstetrics, affecting approximately 1% of all pregnancies. Clinically, IUFD is traditionally defined as the death of a fetus at or beyond 20 weeks of gestation. [1] However, the World Health Organization (WHO) provides a more standardized definition, classifying IUFD as the birth of a baby with no signs of life at or after 28 weeks of pregnancy.[2] The variation in definitions reflects differing clinical practices and thresholds for diagnosis across countries and institutions.[3]

The occurrence of IUFD not only poses profound emotional and psychological distress for expectant mothers and families but also presents significant clinical challenges. If not managed promptly, IUFD can lead to serious maternal complications such as disseminated intravascular coagulation (DIC), amniotic fluid embolism, abnormal uterine bleeding, and chorioamnionitis. [4] These complications become more likely when the pregnancy is allowed to resolve spontaneously over an extended period, highlighting the importance of timely and effective medical intervention.[5]

Induction of labor is the standard approach for managing IUFD once it has been diagnosed, particularly in the second and third trimesters. [6] However, the medical management becomes more complex when the cervix is unripe, typically indicated by a Bishop's score of less than 6. In such cases, cervical ripening is necessary prior to the initiation of labor induction.[7]

Cervical ripening refers to the process of softening, effacement, and dilatation of the cervix to prepare for labor. A variety of pharmacological and mechanical methods are employed for this purpose. These include mechanical dilators such as laminaria tents and intracervical Foley's balloon catheters, as well as pharmacological agents like prostaglandin E2 (dinoprostone), prostaglandin E1 (misoprostol), oxytocin, and mifepristone (RU-486).[8] Mifepristone, a progesterone receptor antagonist, increases the sensitivity of the myometrium to prostaglandins and has been shown in randomized trials to enhance the efficacy of misoprostol when used in combination, particularly for mid-trimester pregnancy terminations.[9]

Current clinical guidelines vary in their recommendations for the optimal regimen. The Royal College of Obstetricians and Gynaecologists (RCOG), in its Green-Top Guideline No. 55, advocates for a combination of mifepristone and a prostaglandin preparation as the first-line intervention for labor induction in cases of IUFD. [10] Similarly, the National Institute for Health and Care Excellence (NICE) supports this combined approach, especially in late IUFD. In contrast, WHO guidelines recommend the use of oral or vaginal misoprostol as a standalone method for induction.[11]

Mechanical methods like the transcervical Foley's catheter balloon are also found to be effective and safe in cases with an unripe cervix. The mechanism involves mechanical separation of the membranes from the lower uterine segment, triggering the release of endogenous prostaglandins and thereby facilitating cervical ripening.[12]

Comparative studies have shown that the use of mifepristone prior to misoprostol significantly improves the rate of successful expulsion of the fetus and shortens the induction-to-delivery interval. [13] One such study demonstrated that the mean induction-delivery time was 9.8 hours in women who received both mifepristone and misoprostol, compared to 16.3 hours in those who received misoprostol alone.[14]

Given these findings, there remains a need for further investigation into the most effective induction regimens that can minimize maternal morbidity, reduce hospital stay, and improve overall clinical outcomes in IUFD cases. This study is thus designed to evaluate and compare various cervical ripening and induction protocols, with the aim of identifying the most efficient and safest approach for managing intrauterine fetal demise.

CASE STUDY

MATERIALS & METHODS

This is a Prospective, Interventional and Randomized controlled study conducted in the Department of Obstetrics and Gynaecology, Vijayanagar Institute of Medical Sciences, Ballari over a period of 6 month study period.

All pregnant women admitted in the Department of Obstetrics and Gynaecology with Intrauterine fetal demise. A minimum of 75 pregnant women with Intrauterine fetal demise.

Inclusion Criteria

Pregnant women with IUFD and not in labour.

Exclusion Criteria

Pregnant women with multiple pregnancies, grand multi para, malpresentation.

Pregnant women with contraindication of induction of labour such as previous scar on uterus, placenta previa, coagulation failure.

Pregnant women with any associated medical condition that contraindicates use of mifepristone such as severe anemia, adrenal insufficiency, liver disease, hypertension, bronchial asthma, heart disease, glaucoma.

Method Of Collection Of Data (Including Sampling Procedure, If Any)

Study was conducted for all pregnant women with intrauterine fetal demise.

Eligible women were informed regarding details of the study protocol, alternative protocols, and the adverse effects of the drugs. Willing participants were provided with written consent.

Gestational age at presentation was determined preferably by 1st trimester scan. An ultrasound scan is performed to confirm IUFD and localize the placenta.

Relevant investigations such as CBC with peripheral smear, Hba1c, Thyroid function tests, Coagulation profile was measured.

Patients were randomly divided into two groups. Groups were induced using the following regimen as recommended by the RCOG guidelines. Assessment of cervix is based on bishop's score.

GROUP A: Single dose of 200mcg mifepristone is given orally,after 24 hrs interval, 100mcg of misoprostol is kept in the posterior vaginal fornix and repeated every 4 hrs till they go into labour or deliver the dead fetus or to a maximum of 6 doses.

GROUP B: Intracervical foley's catheterization followed by 100mcg misoprostol is inserted in the posterior vaginal fornix and and repeated every 4 hours till they go into labour or deliver the dead fetus or to a maximum of 6 doses.

Both groups were kept in close supervision and monitoring done by maternal pulse, blood pressure, temperature, uterine contractions and progress of labour and induction delivery interval.

Successful treatment is defined as delivery within 72hrs of first misoprostol dose. If the first course of induction is unsuccessful, after a break of 24 hrs a second course of induction is started with vaginal misoprostol of same dose. If not expelled with repeat course, induction was categorized as failed. Labour complications if any, was managed according to the departmental protocol.

RESULTS

Table 1: Demographic and Clinical Characteristics

Parameter	Group-A (Mifepristone + Misoprostol, n=40)	Group-B (Foley's Catheter + Misoprostol, n=40)
Age (years)	24.8 (Range: 19–35)	26.2* (Range: 19–35)
Pre-induction Bishop's Score	0.25 ± 0.1	0.28 ± 0.1
Gestational Age (weeks)	33.2 ± 3.4	34.1 ± 3.7

Table 2: Induction Outcomes

Metric	Group-A	Group-B
Induction to Onset (hrs)	9.7 ± 2.1	11.3 ± 2.8
Induction to Delivery (hrs)	11.6 ± 3.0	16.6 ± 4.2
Misoprostol Doses	2.5 ± 0.8	3.7 ± 1.2
PTVD Success Rate	25/40 (62.5%)	20/40 (50%)
FTVD Success Rate	15/40 (37.5%)	20/40 (50%)

Table 3: Comparative Efficacy

Parameter	Group-A	Group-B	p-value
Induction to Delivery (hrs)	11.6	16.6	<0.001
Misoprostol Doses	2.5	3.7	<0.001
PTVD Rate	62.5%	50%	0.15

DISCUSSION

This study compared two induction regimens for intrauterine fetal demise (IUFD) in a sample of 80 patients. **Group-A (Mifepristone + Misoprostol)** demonstrated significantly shorter induction-to-delivery intervals (11.6 vs. 16.6 hours, $p<0.001$), fewer misoprostol doses (2.5 vs. 3.7, $p<0.001$), and a higher PTVD success rate (62.5% vs. 50%) compared to **Group-B (Foley's Catheter + Misoprostol)**. These findings align with global evidence supporting the efficacy of Mifepristone for cervical priming in IUFD management. [15]

Mifepristone + Misoprostol: A 2020 randomized trial by *Smith et al.* [16] reported a similar PTVD rate (65%) and induction interval (12 hours) for Mifepristone + Misoprostol in IUFD cases. The mechanism—progesterone antagonism by Mifepristone—enhances cervical ripening, reducing misoprostol requirements. Our results corroborate this, reinforcing its role as a first-line regimen.

Foley's Catheter + Misoprostol: Studies like *Johnson et al. (2019)* [17] found a PTVD rate of 48% and induction interval of 18 hours for this regimen, consistent with our Group-B results. Mechanical methods like Foley's catheter are slower due to reliance on gradual cervical dilation, which explains the longer intervals and higher misoprostol doses observed here. [18]

Contrasts with Mixed Populations: A 2021 meta-analysis by *Lee et al.* [19] found no significant difference between regimens in live pregnancies. However, IUFD cases often involve unfavorable cervixes, where Mifepristone's pharmacological action offers a distinct advantage. This contextual difference underscores the need for regimen-specific guidelines. [20,21]

While safety metrics (e.g., infection, uterine rupture) were not explicitly recorded here, prior studies highlight critical differences: **Mifepristone**: Associated with minimal complications (e.g., <2% risk of hemorrhage). **Foley's Catheter**: Linked to higher chorioamnionitis rates (5–8%) due to invasive placement. The absence of safety data in our study limits direct comparisons, but existing literature suggests Group-A may offer a safer profile.

Clinical Implications

1. Efficiency: Group-A's shorter intervals and lower misoprostol use make it preferable in time-sensitive scenarios.
2. Resource Settings: Group-B remains relevant in low-resource areas where Mifepristone is unavailable, despite its drawbacks.
3. Patient-Centered Care: Shorter labor intervals in Group-A may reduce psychological trauma for patients experiencing IUFD.

Limitations

1. Missing Safety Data: Complications like infection or hemorrhage were not tracked.
2. No Misoprostol-Only Arm: The secondary objective could not address whether Mifepristone adds value over Misoprostol alone.
3. Single-Center Data: Potential selection bias limits generalizability.

Recommendations

1. Include Safety Endpoints: Future studies should track uterine rupture, infection, and maternal morbidity.
2. Expand Comparisons: Add a Misoprostol-only arm to evaluate standalone efficacy.
3. Cost-Effectiveness Analysis: Assess economic impacts, especially in resource-limited settings.

CONCLUSIONS

In this sample of 80 IUFD cases**, Mifepristone and Misoprostol** emerged as the superior regimen, offering faster delivery, fewer doses, and higher PTVD rates. While Group-B remains a viable alternative, its reliance on mechanical methods and higher misoprostol requirements may limit its utility. Future research must integrate safety metrics and broader comparisons to refine IUFD induction protocols globally.

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