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Outcome of Combined Use of Mifepristone and Misoprostol in Induction of Labour in IUFD with Previous History of LSCS at Chittagong Medical College Hospital

Akefa Jahan[1*] Sharmila Barua[2] Kamrun Nesa Begum[3]

Abstract

Background : Intrauterine Fetal Death (IUFD) is one of the most distressful condition in a woman's life. It causes emotional breakdown,psychological upset and time related risk like DIC compel to induce labour instead of waiting for spontaneous onset. Recently as LSCS rate is increasing,we find more cases of IUFD with previous history of LSCS. In IUFD journey of labour is fruitless,so we want to terminate the pregnanancy vaginally even in scarred uterus to reduce mental trauma, physical morbidity and to decrease repeat LSCS rate. But there is fear of scar dehiscence,scar rupture in induction of labour in scarred uterus. So we want to see outcome of combination of mifepristone and misoprostol in the management of IUFD as it is one of the major advances in modern clinical practice with safety and efficacy. Mifepristone causes decidual separation and increases the sensitivity of misoprostol to myometrium and misoprostol increases uterine contractility. Thus combined regimen shortens the induction to delivery interval which is very necessary in IUFD cases as women are often keen for a quick resolution and delivery.

To evaluate the outcome of combined use of Mifepristone and Misoprostol in induction of labour in IUFD with previous history of Lower Segment Caesarean Section (LSCS) at Chittagong Medical College Hospital (CMCH).

Materials and methods: This was prospective clinical trial study and was conducted in Department of Obstetrics & Gynecology of CMCH from April 2021 to September 2021. During the study period 50 patients presenting with IUFD with previous history of LSCS were taken as study subjects. After getting written informed consent Tab. Mifepristone (200mg) was given 8 hourly for 48 hours (6 doses). Then patient was being waited for another 48 hours. If labour pain not start, then Tab. Misoprostol (25 µg) was given per vaginally 6-8 hourly maximum 4 doses in 24 hours. All the information was recorded according to fixed protocol. Collected data were classified, edited, coded and entered into the computer for statistical analysis by using SPSS version 23.

Results: Out of 50 patients, the mean age was 28.3±6.4 years. Patients with previous history of 1 LSCS were 45 (90.0%) and 2 LSCS were 5 (10.0%). After combined use of mifepristone and misoprostol, majority 32(64.0%) patients need induction to delivery interval within 120 hrs, out of which most of the patients 23(46.0%) delivered within 96-110 hours. 96.0% patients gave vaginal birth and 4.0% patients needed caesarean section. Regarding maternal complication, PPH was found in 3(6.0%) cases and retained placenta 3(6.0%) cases which could be controlled effectively. No case of scar rupture was found.

Primary outcome: Induction to delivery interval, Secondary outcome: Assesment of complication of induction and Assesment of failure rate after induction.

Conclusion: Combination of mifepristone and misoprostol appeared to be more effective in comparison to existing regimens like misoprostol alone or oxytocin or mechanical balloon catheter for induction of labour in cases of IUFD with scarred uterus and the regimen was safe, easy to administer and affordable to the patients.

Kew words: IUFD; LSCS; Mifepristone; Misoprostol.

Introduction

Motherhood is one of the sweetest feeling in every woman's life which can be achieved by a difficult journey of labour pain. Every mother accepts the labour pain with a smile when she sees the face of a living baby.[1] Scenario is different in intrauterine fetal death cases. As in IUFD is a distressful condition, it is of utmost important to search the method that can lessen the duration of labour pain in IUFD cases.[2] 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 sign of life at or after 28 weeks of gestation.[3,4] 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.

1. Medical Officer
Upazila Health Complex Dohar, Dhaka.
2. Professor of Obstetrics & Gynecology (Retired)
Chittagong Medical College, Chattogram.
3. Associate Professor of Obstetrics & Gynecology
Chittagong Medical College, Chattogram.

***Correspondence: Dr. Akefa Jahan**
Cell : 01846 96 80 92
E-mail: akefajahan@gmail.com

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Intrauterine fetal demise is a common problem with 1 in 200 babies born dead.[5] Spontaneous expulsion of IUFD cases may take several weeks. In the meantime some maternal complications like psychological distress and risk of DIC may increase. So it is wise to induce fetal expulsion when possible. As the number of cesarean section is also on rise, there is increasing likelihood of medical indication for termination of pregnancy in patients with previous cesarean section. Induction of labour in women with previous history of LSCS is not easy as it can lead to life threatening events like rupture uterus, retained placenta and excessive bleeding. Hence, induction in these women requires tertiary setup for close monitoring, diagnosis and treatment of hyper stimulation and uterine rupture, availability of blood transfusion and surgical intervention.[6]

Oral misoprostol administration for labor induction with an IUFD was first described in Sao Paulo, Brazil in 1987. Since that time, misoprostol use for obstetrical purposes has grown widely. Repeated dose requirement and side effects such as uterine over activity (Hyper stimulation, hyper tonus and tachysystole) and systemic response (nausea, vomiting, diarrhea and shivering) always remains issue of concerns. Mifepristone is a steroid compound, which competes with progesterone at the receptor level and is widely used for first and second trimester termination of pregnancy.[7] The combination of mifepristone and misoprostol in the management of intrauterine fetal death is one of the major advances in modern clinical practice, with safety and efficacy reported by numerous observational and non-randomised controlled trials.[8-10]

Mifepristone and Misoprostol can be used safely and effectively for induction of labour with previous history of LSCS to avoid repeat CS rates with very good efficacy and less complications. The existing regimens are misoprostol alone or oxytocin or mechanical balloon catheter which causes infection, uterine hyperstimulation followed by scar rupture and lengthens induction to delivery interval (>72 hours).[11] The purpose of this study is to evaluate the outcome of combined use of Mifepristone and Misoprostol in induction of labour in IUFD with previous history of LSCS at CMCH.

Materials and methods

This prospective clinical trial study was conducted in the Department of Obstetrics & Gynaecology of Chittagong Medical College Hospital, Chattogram, Bangladesh during the period of April 2021 to September 2021. A total of 50 patients presenting with IUFD with previous history of LSCS were taken as study subjects. Patients with scar tenderness, presence of any clinical feature of imminent labour, big baby, multiple pregnancy and known hypersensitivity to mifepristone and misoprostol, any untreated bleeding or coagulation disorder were excluded from the study. Data was collected by interview and physical examination using a structured questionnaire and check list containing all the variables of interest (Antenatal history, Obstetric history, Socio-demographic differentials,General examination, Induction to delivery interval, Adverse effects, Complications).

All the patients presenting with IUFD with previous history of LSCS in the department of Obstetrics and Gynecology, CMCH giving consent was included in the study. Total 50 samples were selected according to inclusion and exclusion criteria by convenient sampling and thoroughly informed about the aims, objectives and procedure of the study. They were encouraged for voluntary participation and allowed freedom to withdraw from the study whenever they like even after participation. After getting written informed consent, Tab. Mifepristone (200 mg) was given 8 hourly for 48 hours (6 doses). Then patient was being waited for another 48 hours. If labour pain not start, then Tab. Misoprostol (25 µg) was given per vaginally 6-8 hourly maximum 4 doses in 24 hours. All data was collected and rechecked by the researcher own to avoid the errors. Data was entered, cleaned and analyzed using Statistical Package for Social Sciences (SPSS -23) software. Continuous variables were statistically described in terms of mean and standard deviations (± SD). Qualitative or categorical variables were described as frequencies and proportions. Proportions were compared using Chi-square test. Statistical significance was defined as $p \leq 0.05$.

Results

In this study more than one fourth (26.0%) patients belonged to age 26-30 years. The mean

age was found 28.3±6.4 years with range from 19 to 39 years (Table I). More than half 27(54.0%) patients had para 1, 16(32.0%) had para 2 and 7(14.0%) had para >2. Previous history of 1 LSCS was found in 45(90.0%) and previous history of 2 LSCS was 5(10.0%). More than three fourth 38(76.0%) patients preterm gestational age and 12(24.0%) had term gestational age, the mean age was 36.7±1.9 weeks. Regular antenatal check up was found in 28(56.0%), irregular 17(34.0%) and not done in 5(10.0%) (Table II). In this study majority 23(46.0%) patients had induction to delivery within 97-110 hrs followed by 11(22.0%) had 48-72 hrs, 9(18.0%) had 111-120 hrs and 5(10.0%) had 73-96 hours. Failed induction was found in 2(4.0%) (Table III). Most of the patients 96.0% delivered vaginally after induction and 4.0% patients needed caesarean section (Figure-1). Regarding maternal complication, it was observed that PPH was found in 3(6.0%), retained placenta was found in 3(6.0%) and no complication was found in 44(88.0%) cases.

Table I Distribution of the study patients by age (n=50)

Age (Years)	Frequency	Percentage (%)
≤20	6	12.0
21-25	12	24.0
26-30	13	26.0
31-35	11	22.0
>35	8	16.0
Mean ±SD	28.3	±6.4
Range (Min-max)	19	-39

Table II Distribution of the study patients by obstetric history (n=50)

Obstetric history	Frequency	Percentage (%)
Parity		
1	27	54.0
2	16	32.0
>2	7	14.0
Number of previous history of LSCS		
Previous history of 1 LSCS	45	90.0
Previous history of 2 LSCS	5	10.0
Gestational age (Weeks)		
<37 (Preterm)	38	76.0
37-40 (Term)	12	24.0
Mean±SD	36.7 ±1.9	
Antenatal check-up		
Regular	28	56.0
Irregular	17	34.0
Not done	5	10.0

Table III Distribution of the study patients according to time interval of induction to delivery (n=50)

Time interval of induction to delivery (Hours)	Frequency	Percentage (%)
48-72 hrs	11	22.0
73-96 hrs	5	10.0
97-110 hrs	23	46.0
111-120 hrs	9	18.0
Failed induction*	2	4.0

* 2 patients were failed induction due to scar tenderness and impending rupture.

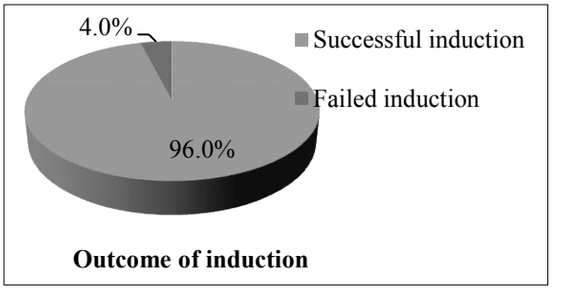

Figure 1 Pie chart showing outcome of induction of the study patients (n=50)

Table IV Distribution of the study patients according to maternal complication (n=50)

Maternal complication	Frequency	Percentage
PPH	3	6.0
Retained placenta	3	6.0
No complication	44	88.0

Discussion

Induction of labour in IUFD is a standard obstetric approach in properly selected patients. Achievement of vaginal delivery for a woman who requires induction of labour in intra uterine foetal death should be simple, safe, effective and non invasive.[12] With misoprostol being widely used, earlier reports indicate successful induction of labor using mifepristone. It was also observed in earlier studies that mifepristone misoprostol when used in a combination, proved to be a safe and effective regime to induce labor in IUFD.[13] The study was carried out to evaluate the outcome of combined use of Mifepristone and Misoprostol in induction of labour in IUFD with previous history of LSCS.

In this study more than one fourth (26.0%) patients belonged to age 26-30 years. The mean age was found 28.3±6.4 years with range from 19 to 39 years. Abbasi et al. reported that average age

of patient was 26.92±2.19 years.[12] Sindhuri et al. showed the mean age of patients was 24.1 ± 3.36 years and the majority of the patients were between the age group 21 and 30 years with 78.57%.[13] In a study done by Arora et al. observed that mean age of the women studied were 29.3 yrs.[14] Their study findings were also consisted with the study.

In this study previous history of 1 LSCS was found in 45(90.0%) and previous history of 2 LSCS was 5(10.0%). Arora et al. reported that previous 1 LSCS was found in 87.1% and previous 2 LSCS was 10.2%.[14] Ahuja and Dahiya described that previous 1 caesarean section was 16(53.33%) and previous 2 caesarean section was 3(10.0%).[15]

In this study majority 23(46.0%) patients had induction to delivery within 97-110 hrs followed by 11(22.0%) had 48-72 hrs, 9(18.0%) had 111-120 hrs and 5(10.0%) had 73-96 hours. Failed induction was found in 2(4.0%). Most of the patients 96.0% delivered vaginally after induction and 4.0% patients needed caesarean section. Arora et al. study also spontaneous labour occurred in 74.3% women which is quite close to the success rate in studies by Cabrol et al. Frydman et al. and Leiaidier et al. but very less compared to study by Ahuja et al.[14-18] Abbasi et al. reported most of the patients 100% in combined group and 97.4% in misoprostol group delivered vaginally after induction in both groups, 2.9% patients needed caesarean section.[12]

Modak et al. reported that successful delivery within 24 hours of commencement of the first dose of misoprostol without additional intervention occurred in 93.65 % (59/63) of women who received mifepristone prior to misoprostol and 80.71% (46/57) of women who received misoprostol only, the difference is statistically significant (p=0.0450). In women pre-treated with mifepristone, successful induction was 86%.[19] In study by Vayrynen et al. 73% of women delivered within 24 hours using 25 g of misoprostol after pre-treatment with mifepristone for women after 22 weeks of gestation.[8] Study by Wagaarachchi et al. reported success rate of 98.9% but has described successful induction - delivery within 72 hours of induction. In their study delivery within 24 hour was 87.5%.[20]

Pre-treatment with mifepristone decreased the number of dose of misoprostol required for women to go into labor. Vayrynen et al. showed total dose of misoprostol needed was lower in the group pre-treated with mifepristone, compared to misoprostol only.[8] Induction-delivery interval after pre-treatment with mifepristone is lower in women induced with misoprostol.[20] There was no significant difference in induction to delivery interval according to gestational age and parity in our study. Vayrynen et al. showed that in the group treated with misoprostol-only, the dose needed was significantly lower when the duration of pregnancy was 31 weeks.[8] Thus it seems that mifepristone converts the pregnant uterus into a prostaglandin sensitive organ at all gestation. Mifepristone increases uterine sensitivity to oxytocin when used for induction of term labor.[21]

Regarding adverse effects in this study observed that nausea/vomiting was found in 3(6.0%), 1 (2.0%) patient had hyperthermia and no side effects was found in 46(92.0%) cases. Sharma et al. documented that as far as the side effects are concerned, only two women experienced vomiting and diarrhea, one each with mifepristone. With misoprostol, the side effects like nausea, vomiting, headache, diarrhea and fever were experienced by 10.75%, 25%, 14.29%, 7.15%, and 17.86% of women, respectively.[22] Modak et al. had observed that both the groups are comparable in respect to adverse effects. In misoprostol alone group 5(8.77%) women suffered from shivering whereas it was noted only in 3.17% in women of combination group who received mifepristone prior to misoprostol.[19] Arora et al. also found 3.2% of patients had side effects while 70% of patients side effects in the form of nausea, vomiting, fever and shivering.[14]

Regarding maternal complication in this study observed that PPH was found in 3(6.0%), retained placenta was found in 3(6.0%) and no complication was found in 44(88.0%) cases. Abbasi et al. reported that PPH was found 1(2.9%) retained placenta was found in 1(2.5%) and no complication was found in 31(85.7%) cases.12 Another study conducted by Panda et al. showed incident rate of retained placenta was 3.8%.[23]

Limitations

The present study was conducted at a very short period of time. Small sample size was also a limitation of the present study. Therefore, in future further study may be under taken with large sample size.

Conclusion

Combination of mifepristone and misoprostol appeared to be more effective in comparison to existing regimens like misoprostol alone or oxytocin or mechanical balloon catheter for induction of labour in cases of IUFD with scarred uterus and the regimen was safe , easy to administer and affordable to the patients. In our study majority were delivered vaginally with strict supervision and only two patients were needed surgical intervention. Ultimately there was decrease in physical morbidity, less need for hospital stay and reducing the overall cost of patients. It will also have good impact on national economy of our country.

Recommendations

Further large-scale, multicenter randomized studies are needed for better treatment option, optimum dosage and dosing interval of the two drugs for a better management of IUFD cases.

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Contribution of authors

AJ-Conception, design, critical revision of the version, acquisition of data, data analysis, manuscript writing & final approval.

SB-Conception, critical revision & final approval.

KNB-Design, Interpretation of data, critical revision & final approval.

Disclosure

All the authors declared no competing interest.

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