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The impact of misoprostol in inducing labor in patients having intrauterine foetal death

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Abstract---Background: The most detrimental outcome of pregnancy, intrauterine foetal death (IUFD), causes psychological suffering to the expectant mother and the entire family. Objective: The purpose of this study was to evaluate the effectiveness as well as safety of misoprostol for labour induction in IUFD. Methods: The Department of Obstetrics and Gynecology at the MTI-HMC, Peshawar, conducted this clinical research on 120 women who had IUFD from 09 September 2020 to 09 March 2021. With the patient's informed agreement, labour was induced with vaginal misoprostol pills at a dose of 50 mcg four times per day. Results: In research including 120 women, the majority of the women (n=55; 45.83%) were between the ages of 21 and 30, with a median gestational age of 37.61 ± 4.17 weeks. The majority of patients (n=83; 69.17%) did not have appointments, were from rural areas (n=79; 65.83%), and had no formal education (n=91; 75.83%). In our study, 49 women (40.83%) were primigravidas, whereas 71 women (59.17%) were multigravidas. Following misoprostol introduction, the average Bishop's score increased to 6.89 ± 2.3 from 2.32 ± 1.28 at baseline, a difference of 4.57 on average. The average time from when labour began to when delivery occurred was 9 ± 6.56 hours, and 44.17 % of the women (n=53) delivered their babies within 12 hours. The average amount of misoprostol needed was 149.5 ± 85.8 mcg. All of the ladies underwent effective inductions, however two of them required laparotomies due to uterine rupture. The following adverse events were reported: fever (n=7; 5.83%), diarrhea (n=5; 4.17%), vomiting (n=4; 3.3%), ruptured uterus (n=2; 1.67%), uterine hyper

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stimulation (n=8; 6.67%), retained placenta and atonic post-partum hemorrhage (n=3; 2.5% respectively). Conclusion: Misoprostol is an affordable, efficient, and secure medication that could be utilized to create labour and mature the cervical cervix in cases of IUFD. Clinical relevance: The women's parity, Bishop's score, and gestational age all affect how misoprostol responds in patients.

Keywords---misoprostol, labour, pregnancy, induction, intrauterine foetal death.

Introduction

A prostaglandin E1 (PGE1) analogue called misoprostol is employed to manage and avoid duodenal and stomach ulcers that are brought on by non-steroidal anti-inflammatory medicines. Misoprostol is a crucial medication for female reproductive health yet the United States Food and Drug Administration (FDA) has not licensed it to be administered during pregnancy. Misoprostol works wonderfully for inducing labour in the 2nd and 3rd trimester pregnancy, according to studies published in the last five years [1-5]. When combined with mifepristone or administered alone, misoprostol is also successful for premature termination of pregnancy. It also shows assure for a number of other signs, such as cervical priming, the management and inhibition of hemorrhaging after delivery, and the treatment of spontaneous abortion [6-10].

Initially it is a reliable analogue of PGE1which makes it fewer subject to rigid preservation rules - a clear benefit in tropical climates - secondly, it is inexpensive and readily accessible, and thirdly, it is capable of being taken by mouth in alongside intravaginal management, making misoprostol a natural option over traditional oxytocics for abortion and labour stimulation. In our circumstances, where traditional PGE2 is extremely limited but also excessively costly, these benefits made misoprostol a beneficial agent. Additionally, oxytocin, the only medication that is widely accessible and within the means of most patients, is not highly successful in ending midtrimester pregnancy [11-13]. The importance of misoprostol in the stimulation of birth in our situation is not well understood. According to information from South Africa, Uganda and Egypt, misoprostol can be employed to induce delivery and end second-trimester pregnancies. Misoprostol has been shown to be useful in managing embryonic mortality and inducing childbirth in term pregnancy [14-15]. This study's goal was to assess the effectiveness and safety of vaginal misoprostol pills for labour induction in cases of IUFD.

Material and Methods

The Peshawar MTI-HMC's Department of Obstetrics and Gynecology conducted this study over a time frame of six months, from 09 September 2020 to 09 March 2021, with the local Institute of Ethical Committee's approval. The study comprised 120 women, comprising primigravida and multigravida, between the ages of 18 and 40 years who had singleton deceased fetus with a cephalic appearance with undamaged or rupturing membranes and gestational months

that were more than 28 weeks. Women with previous history of liver illness, prostaglandin hypersensitivity, a scarred uterus from a prior caesarean section, convulsive disorder, glaucoma and women with placenta praevia were all disqualified from the trial.

A thorough history was taken for every client, and a medical examination was performed. The IUFD was confirmed by ultrasound. Following patient discussion, consent was obtained. The Bishop's score was evaluated after a thorough investigation of each case. Misoprostol 50 mg was given to the patients in the posterior fornix. If Bishop's score and contractions in the uterus change, the dosage is repeated every six hours. No more prescriptions of misoprostol were given if the Bishop's score was eight or higher or if there were more than two contractions in 10 minutes that lasted less than 40 seconds. There was a limit of six dosages that may be given. The adverse effects suffered during induction, such as digestive problems, shaking, and fever, were documented. Also noticed were problems such uterus retention, PPH, and placental abruptions. Any further medicinal interventions or the requirement for surgical surgery to remove the placenta were reported. If this approach did not result in delivery, then a suitable strategy for ceasing pregnancy was utilised depending on the clinical condition. There were reports of any difficulties during the induction phase and up to 24 hours following birth.

During the delivery process and after birth, routine medicines were administered. After a day of birth or afterwards, depending on the patient's clinical status, patients were released from the hospital. The SPSS 20 for Windows statistical program was used for analyzing the data, including the age of the mother, parity, duration of gestation, Bishop's score, birth weight of the baby, and the time between induction and delivery. The unpaired student's t test was employed to analyze the data, and the normally distributed variables are displayed as means with standard deviations and ranges. If the P value was less than 0.05, differences were considered statistically significant.

Results

The study included a total of 120 females who had been hospitalized to the Department of Obstetrics and Gynecology at the MTI-HMC in Peshawar with IUFD. The group's age varied from 18 to 40 years old. The majority of the women (n=55; 45.83%) were in the 21–30 age range, with a median gestational age of 37.61 ± 4.17 weeks. The majority of patients (n=83; 69.17%) did not have appointments, were from rural areas (n=79; 65.83%), and had no formal education (n=91; 75.83%). 49 women in our research were primigravidas (40.83%), while 71 women (59.17%) were multigravidas (Table 1). Baseline Most women (n=83; 69.17%) had a Bishop's value (0-2), and there was a substantial shift in Bishop's value after labour initiation. Bishop's scores varied from 0 to 6 (Table 2).

Table 1
All Cases' Demographic Information

Variables	Frequency	Percentage
Age Group		
Up to 20 years	42	35
21 - 30 years	55	45.83
31 – 40 years	23	19.17
Socio-economic status		
Had Appointments	37	30.83
Had No Appointments	83	69.17
Urban	41	34.17
Rural	79	65.83
Well-educated	29	24.17
Uneducated	91	75.83
Obstetrics score		
Primi gravida	49	40.83
Multi gravida	71	59.17

Table 2
Adjustment to Bishop's Score

Average Bishop's score		The mean variation	P value
Prior of Induction	After Induction		
2.32 ± 1.28	6.89 ± 2.3	4.57	0.001
P value has significance. Data displayed as mean ± S.D. for the Student's t test			

The total amount of misoprostol medicine needed fluctuated from 50 - 350 mcg. The average dosage needed overall was 149.5 ± 85.8 mcg. The time between labour beginning after induction varied from 2 hours to 25 hours, with 9 ± 6.56 hours being the norm. The average induced delivery period was 13.56 hours, and the range was 3 hours 30 minutes to 36 hours 30 minutes. With growing pregnancy time frame, parity, and growing Bishop's score, it was discovered that the average total dosage needed, the average time between induction and the start of labor, as well as the average time between induction and delivery, both fell. Bishop's score, parity, and gestational age all had an inverse relationship with the length of the first stage of labor, whereas the pace of cervical dilation was directly connected to both (table 3). All of the inductions were successful. However, 118 instances (98.33%) of deliveries were vaginal, and two (1.67%) required laparotomies as a result of uterine rupture (figure 1). The following adverse events were reported due to higher doses of misoprostol: fever (n=7; 5.83%), diarrhea (n=5; 4.17%), vomiting (n=4; 3.3%), ruptured uterus (n=2; 1.67%), uterine hyper stimulation (n=8; 6.67%), retained placenta and atonic post-partum hemorrhage (n=3; 2.5% respectively) (figure 2).

Table 3
The patients' perinatal characteristics

Outcome	Range/Frequency
beginning of labour after induction (hours)	9 ± 6.56 (2-25 hours)
initiation-delivery interval (hours)	13.56 (3 hours 30 minutes – 36 hours 30 minutes)
Less than 12 hours	53 (44.17)
Between 12 to 24 hours	46 (38.33)
Greater than 24 hours	21 (17.5)
Misoprostol dose (mcg)	149.5 ± 85.8 (50 mcg – 350 mcg)
50 mcg	21 (17.5)
100 mcg	32 (26.67)
150 mcg	25 (20.83)
≥ 200 mcg	42 (35)
Requirement for oxytocin augmentation (%)	39 (32.5)
Analgesia requirement (%)	35 (29.17)
Labour Duration	
First stage	3.4 ± 1.9 (1 hour 26 minutes – 13 hours 54 minutes)
Second stage	38.92 ± 18.65 (10 – 100 minutes)
Third stage	6.73 (30 minutes)
P value has significance. Data displayed as mean ± S.D. for the Student's t test	
Frequency of cervical dilatation (cm/ hour)	2.21 ± 0.39 (0.45 -5.06)

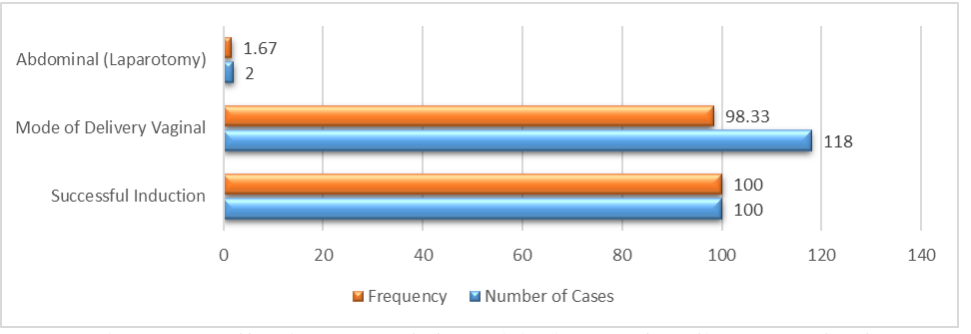

Figure 1. Effectiveness of the Initiation and Delivery Method

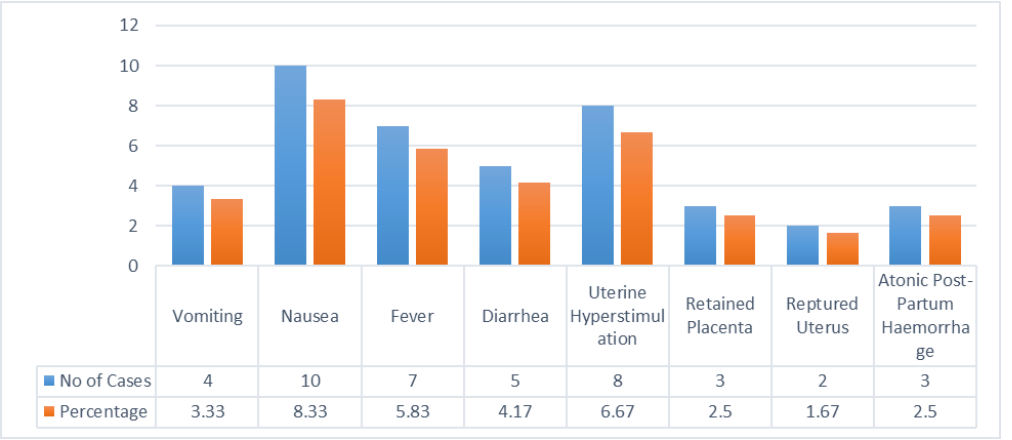

Figure 2. Consequences and complications for the mother

Discussion

In our research, 40.83% of the women (n=49) were primigravida, while the remaining women (n=71; 59.17%) were multigravida. These women ranged in age from 21 to 30 years, with average gestational age of 37.61 ± 4.17 weeks. Women (n=83; 69.17%) received a score of 0 to 2 on the first Bishop's scale, which had a range of 0-6. In the research conducted by Easmin S *et al.,* (2011), 47% belongs to the age range of 20 to 30 years, 78% had a gestational age of 27 to 36 weeks, 63% had an early Bishop's value (0-2), and the remaining 3 to 6 percent had a Bishop's score of 3 to 6 [16]. In our trial, a mean total dosage of 149.5 ± 85.8 mcg of misoprostol was administered vaginally every four hours until the commencement of early delivery or a maximal dose of 350 mcg. Misoprostol dose and frequency dosage guidelines have not established. El Gharib *et al.,* (2011) utilized 25 mcg three times per hour for a total of 24 hours, resulting in a mean dosage of 119 ± 27.98 mcg. Panda S *et al.,* (2013) employed 150 mcg every four hours, with a daily limit of 600 mcg [17,18].

Our investigation revealed that induction had a complete success. El Gharib *et al.,* (2011) found that the third trimester and the second trimester of foetal fatalities had success rates of 92% and 47%, respectively [17]. The rate of efficacy for Chaudhari P *et al.,* (2015) study comparing the use of misoprostol alongside or without mifepristone were 91.7% and 72.1%, respectively [19]. The length of the becoming pregnant, parity, and initial Bishop's score were observed to adversely interact with the average induction-delivery delay recorded in our research, which was 13.56 hours. According to El Gharib et al. (2011), the initial delivery interval was 8.59 ± 2.36 hours, and it got shorter as the gestational period got longer [17]. In their study, Chaudhari P et al. (2015) discovered that the initiation delivery duration was 8.9 ± 3.4 hours and 15.4 ± 5.6 hours, respectively, depending on whether mifepristone and misoprostol were used. While El Gharib et al. (2011) found oxygen need in 45% of women receiving induction for third trimester foetal loss [19,17] while the oxygen augmentation was necessary for 32.5% (n=39) of the study participants in our research.

Analgesic need was identified in 29.17% (n=35) of women, which was close to research by Nyende *et al.,* (2004) and De Heus *et al.,* (2004) that were 34.3% and 32.8%, respectively [20,21]. In the current study and prior investigations, vaginal misoprostol side effects and problems like Nyende *et al.,* (2004), De Hues *et al.,* (2004), Easmin et al., (2011) included postpartum hemorrhage, retained placenta, nausea, diarrhea, and vomiting. However, the present study and earlier studies indicated that nausea and fever rose with higher doses of misoprostol [16, 20, 21].

Conclusion

IUFD is a pretty unpleasant yet frequently occurring circumstance. Misoprostol, which may be administered regardless of gestational ages and has the twin properties of softening the cervical cervix and starting contractions in the uterus, is a very successful medication for inducing labour. Although the ideal dosage has not yet been established, cases with a shorter gestational period, a lower cervical score, or less parity should typically benefit from using higher doses more frequently, which will also help to prevent complications. considering the potential risks associated with labour induction, particular signed informed permission should be required for all misoprostol administrations. Institution-specific practise standards and procedures should also be in place, along with careful chart documentation of all pertinent outcomes.

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