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Research Article

Retrospective Analysis of Mifepristone for the Cervical Preparation of Labour Induction in Live Births

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Abstract

Background: Mifepristone is a synthetic antagonist of progesterone and glucocorticoid receptors that is sometimes used for the induction of labour. However, because it is licensed as an abortive agent, its safety profile in healthy deliveries may be of concern. Therefore, this study aimed to evaluate the maternal and neonatal safety of mifepristone for the preparation of labour induction.

Methods: This was a retrospective cohort study of 105 women with singleton pregnancies who received 600mg mifepristone for preparation for induction of labour between 24 and 42 weeks of gestation in the Department of Gynaecology and Obstetrics of the Klinic Donaustadt, Austria, from April 2017 until March 2022. Maternal, pregnancy, induction, delivery, and foetal characteristics were collected and compared between very preterm (24-31 weeks of gestation, n=10), moderate/late preterm (32-36 weeks of gestation, *n* = 45), and term (37-42 weeks of gestation, *n* = 50) groups.

Results: The women were aged 31.3±5.6 years, the mean gestational age at delivery was 35.9±3.3 weeks, and all deliveries resulted in a live birth. Fifty-three (50%) of women in the cohort required no other agent for the inductiosn of labour. Spontaneous delivery was possible for 48 (46%) women, 12 (11%) required vacuum delivery, and 45 (43%) Caesarean section. The very preterm group had 100% admission to NICU, the moderate/late preterm group had 43% admission, and the term group had 16% admission (P<0.001). Two women were admitted to the ICU in the term group. Hospital stay in the very preterm group was 57 (32-160) days compared to 10 (1-49) days in the moderate/late preterm group and 4 (2-60) days in the term group (P<0.001). There were no cases of uterine hyperstimulation, abnormal foetal heart rate patterns, neonatal hypoglycaemia, or polysytole. There were two cases of neonatal death after live birth, one in the early preterm group and one in the moderate/late preterm group.

Conclusions: This analysis of women and newborn infants who received 600mg mifepristone for induction of labour identified no safety concerns for mother or newborn infant and could be a new strategy to reduce the number of caesarean sections.

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Introduction

The World Health Organization (WHO) defines Induction of labour as the process of artificially stimulating the uterus to start labour [1]. The aim of labour induction in term and post-term pregnancy is to achieve a successful vaginal delivery that is as natural as possible [2]. Ripening the cervix, so it becomes softened and ready for the onset of labour, is one key to successful induction of labour [3]. In many cases, this ripening process occurs with expectant management of the pregnancy, awaiting spontaneous labour. However, labour induction is one of the most common obstetric interventions, occurring in approximately one in four term pregnancies [4,5]. Studies into labour induction indicate that between 83 and 85 percent of women with an indication for labour induction require cervical ripening due to an unfavourable cervix, defined as a Bishop score of less than six [6,7]. This high level of intervention is in part due to the increased number of women at term who choose elective labour induction, but approximately 77 to 85 percent are due to medical indications [4,8].

Another important consideration for the induction of labour is when healthy pregnancies go beyond term. From 39 weeks of gestation onwards, the risk of stillbirth increases with a sharp rise after 40 weeks [9]. Therefore, induction of labour by 40 weeks of gestation has the potential to reduce the incidence of stillbirths by 50% [10]. Current guidelines by the WHO recommend labour induction for women who are known with certainty to have reached 41 weeks of gestation [11]. Evidence suggests that induction of labour at or beyond term, compared to expectant management, results in fewer perinatal deaths and lower Caesarean delivery rates but higher rates of operative vaginal births [4,12,13].

There are many approaches for labour induction, including mechanical methods such as the use of an intracervical balloon catheter and amniotic membrane sweeping or stripping and pharmacological methods, such as administration of prostaglandins or oxytocin [14]. Their selection is based on clinical assessment of the cervix, and methods and doses can vary widely depending on the clinic [3]. However, risks from oxytocin and prostaglandin interventions for labour induction mean that current pharmacological approaches require hospital administration and monitoring [15,16]. Consequently, women can experience extended stays in hospital and often have a poor experience during induction, requiring increased levels of pain relief [17-19]. In addition, despite the widespread availability of several labour induction methods, there is around a 10-20 percent failure rate [12,20]. This suggests we need to rethink methods to promote the onset of labour and improve the chance of a successful induction.

Mifepristone was developed as an abortion inducing drug in gestation of less than 63 days of amenorrhoea [21]. It is currently also indicated for softening and dilatation of the cervix uteri before surgical termination of pregnancy during the first trimester, preparation for the action of prostaglandin analogues in the termination of pregnancy beyond the first trimester for medical reasons, and labour induction in foetal death in utero [22]. Mifepristone is a synthetic antagonist of the progesterone and glucocorticoid receptors [21]. It acts on the entire process of cervical maturation, from softening to dilatation. It also sensitises the myometrium to prostaglandins or analogues [23,24]. Therefore, this has led to some clinics using mifepristone for labour induction at term [25-36]. These previous studies have found that mifepristone successfully induces labour in about 30% of cases [28,34]. In those who do not give birth, mifepristone ripens the cervix and sensitizes the uterus to the effects of prostaglandins and oxytocin, making subsequent labour induction shorter and more successful while reducing the risk of Caesarean section [36-38]. This is of special importance as Caesarean sections are currently the most common surgical procedure performed on women of childbearing age [39]. The World Health Organization, however, warned as early as 1985 against excessive use of Caesarean section and recommended a Caesarean section rate of between 10% and 15% [40]. Therefore, any option, such as Mifepristone, that promotes the birth process and thus prevents Cs should be given special attention.

However, because of its established role as an abortive agent, mifepristone is often disregarded for assisting delivery in healthy pregnancies [22]. The established safety profile of mifepristone suggests it would not require hospital admission for continuous monitoring, as currently required for other pharmacological agents, and it might be suitable for outpatient administration [22,41]. Nevertheless, some concerns have been raised that the safety profile of mifepristone in healthy deliveries is not well established, in particular about its effects on the foetus because it can cross the placenta [37,42]. In our department, mifepristone has been used since 2010 in special indications for the preparation of the cervix. Therefore, this study aimed to evaluate the safety and efficacy of mifepristone administration in preparation of the cervix for both the mother and child [43,44].

Patients and methods

This is a retrospective cohort study carried out in the department of gynaecology and obstetrics of the Clinic Donaustadt, Austria. The study included all women admitted to the hospital between April 2017 and March 2022 who fulfilled the inclusion criteria.

The inclusion criteria were as follows: 1) Singleton pregnancies; 2) between 24- and 42-weeks of gestation; 3) with a medical indication of termination of the pregnancy due to maternal factors or fetal growth restriction; 4) the women were admitted to the Department of gynaecology and obstetrics of the Klinic Donaustadt; 5) and received 600 mg doses of mifepristone for preparation for labour induction. Women who did not receive at least one dose of 600 mg mifepristone or with twin or multiple pregnancies were excluded. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Vienna (responsible for Public Hospitals) (Protocol number: EK 19-274-VK).

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Mifepristone administration

The women received standard care within the department of gynaecology and obstetrics according to the local guidelines. Those women with indications for induction were informed about the need for induction and given written informed consent to receive 600 mg of mifepristone (Mifegyne). In most cases, this was administered at the hospital, but in some low-risk pregnancies, this was administered at home. The Bishop score was calculated to evaluate cervical ripening before and after mifepristone administration.

The patients received cardiotocography (CTG) to monitor foetal condition and uterine activity twice a day or when contractions started. If necessary, after 48 hours, they received Propess or another secondary agent for labour induction.

Data collection

Information on the characteristics of the mother, including the mother's birth year, weight before pregnancy and before giving birth, height, body mass index (BMI) before pregnancy, number of deliveries, and number of pregnancies, was collected from the patient's medical records. Details about the pregnancy including weeks of pregnancy, indication for labour induction, mifepristone administration, secondary labour induction agents, time of delivery, mode of delivery, whether it was a live birth, and length of hospital stay and details of the new-born infant including date of birth, calculated due date, length, head circumference, gender, and genetic abnormalities were also collected from the hospital medical records.

Safety analysis

Safety data were collected for both the mother and newborn infant. This included intensive care unit (ICU) admission for the mother, uterine hyperstimulation, abnormal foetal heart rate (FHR) patterns [41], Apgar Score, neonatal intensive care unit (NICU) admission, neonatal hypoglycaemia, umbilical cord venous and artery pH, polysystole, birth abnormalities, and complications, including neonatal mortality.

Uterine hyperstimulation was defined as uterine tachysytole or contractions exceeding two minutes. Tachysystole is five or more contractions in ten minutes. Polysystole was defined as six or more uterine contractions within ten minutes. Neonatal hypoglycaemia was defined as a glucose concentration of <47 mg/dl (2.6 mmol/l).

Statistical analysis

Data were collected and analysed through Excel using the Data Analysis Toolpak (Office 365, Microsoft Corp., US). The numerical data were first tested for normal distribution, and those that followed a normal distribution are presented as mean ± standard deviation (SD), those with skewed distribution are presented as median and range. Categorical data are presented as numbers and percentages. The whole cohort was divided into very preterm (24-31weeks of gestation), moderate/late preterm (32-36 weeks of gestation), and term (37-42weeks of gestation) groups with analysis of variance (ANOVA) used for comparison between groups with normal distribution, Kruskal-Wallis analysis for skewed data, and chi-square test for categorical data. A P value of < 0.05 was considered significant.

Results

Baseline characteristics

This study included 105 patients. The mean age of the women based on their birth year was 31.3±5.6 years, the mean gestational age at delivery was 35.9±3.3 weeks, and all deliveries resulted in a live birth. For 15 (14%) of the women, there was a record of a previous Caesarean section. Fifty-three (50%) of women in the cohort required no other agent for the induction of labour after mifepristone administration.

The cohort was split into three groups based on gestational age at delivery. There were 10 women in the very preterm group (24-31weeks), 45 women in the moderate/late preterm group (32-36 weeks), and 50 women in the term group (37-42weeks). There was no significant difference in baseline characteristics between the groups, including age, BMI, para, or gravida, as shown in Table 1.

Preparation for labour

As might be expected, there were differences between the groups in terms of the reasons for induction (P<0.001, Table 2). In the very preterm group, the most common reason for induction was premature rupture of membranes, which was identified in 70% of cases. In the moderate/late preterm group, the most common reasons for induction were intrauterine growth restriction or being small for gestational age and a maternal hypertensive disorder, both of which were identified in 44% of cases. In the term group, the most common reason for induction was a maternal hypertensive disorder; however, this was identified in just 24% cases, and the reasons for induction in this group were spread over all indications except premature rupture of membranes.

Most women were administered mifepristone as inpatients, but in the moderate/late preterm group, 13% were administered

Table 1: Demographic and baseline characteristics.

Parameter	Very preterm (n=10)	Moderate/late preterm (n=45)	Term (n=50)	P value
Age	30.8 ± 6.9 years	31.8 ± 5.8 years	31.0 ± 5.2 years	0.725
Weight before pregnancy	70.1 ± 19.1 kg	68.1 ± 13.7 kg	70.7 ± 17.1 kg	0.726
Weight before giving birth	84.8 ± 20.9 kg	82.2 ± 15.6 kg	84.9 ± 17.4 kg	0.746
BMI before pregnancy	25.8 ± 6.9	25.2 ± 4.8	26.7 ± 5.6	0.406
Para	1.5 (1-5)	1.0 (1-8)	1.0 (1-6)	0.571
Gravida	1.5 (1-6)	2.0 (1-11)	2.0 (1-7)	0.835

Note: BMI body mass index
Data are presented as mean±SD, and comparison between the groups was by ANOVA, except for Para and Gravida, which are presented as median and range and compared with the Kruskal-Wallis test.

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Table 2: Preparation for labour and delivery information.

Parameter	Very preterm (n=10)	Moderate/late preterm (n=45)	Term (n=50)	P value
Indication for induction *				
- IGR/small for gestational age	40% (4)	44% (20)	22% (11)	
- Oligohydramnios/anhydramnios	30% (3)	2% (1)	4% (2)	
- Hypertensive disorder	30% (3)	44% (20)	24% (12)	
- PPROM/membrane rupture	70% (7)	16% (7)	0% (0)	<0.001
- Post-term	0% (0)	0% (0)	8% (4)	
- Diabetes	0% (0)	4% (2)	14% (7)	
- Other maternal medical condition	0% (0)	2% (1)	8% (4)	
- Fetal anomaly	10% (1)	7% (3)	4% (2)	
- Non-reassuring fetal status	0% (0)	7% (3)	18% (9)	
Mifepristone administration #				
- Outpatient	0% (0)	13% (6)	34% (17)	0.009
- Inpatient	100% (10)	87% (39)	64% (32)	
Bishop score				
- Before mifepristone	2.7 ± 1.6	3.4 ± 1.3	3.3 ± 1.2	0.270
- After mifepristone	3.2 ± 1.8	3.9 ± 1.4	3.7 ± 1.0	0.270
Bishop score gain	0.5 ± 0.8	0.5 ± 1.0	0.5 ± 1.0	0.993
Secondary agent *				
- None	60% (6)	60% (27)	40% (20)	
- Balloon catheter	0% (0)	0% (0)	2% (1)	0.304
- Prostaglandins E2	40% (4)	38% (17)	54% (27)	
- Prostaglandins E1	0% (0)	4% (2)	8% (4)	
Mode of delivery				
- Spontaneous delivery	60% (6)	38% (17)	50% (25)	0.082
- Vacuum	0% (0)	7% (3)	18% (9)	
- C-section	40% (4)	56% (25)	32% (16)	

Note: * Some women had more than one indication for induction or had more than one secondary agent
In one case in the term group, it was unclear where mifepristone was administered.
IGR intrauterine growth restriction; PPROM preterm premature rupture of the membranes.
Categorical data is presented as percentages and numbers. Comparison between the groups was by Chi chi-squared test, except for the Bishop score, that are presented as mean±SD and was compared with ANOVA.

mifepristone as outpatients, and this increased to 34% in the term group (P=0.009). There were no differences identified in the use of secondary agents for induction, Bishop score before or after mifepristone administration, Bishop score gain between the groups, or mode of delivery between the three groups (all P>0.05).

Comparison of Bishop Score change showed that the gain in score was 0.5 for each of the groups after mifepristone administration. This reflects that five (50%) of the women in the very preterm group increased their score, four (40%) maintained their score, and one (10%) case reduced their score. In the moderate/late preterm group, 21 (47%) of women increased their score, 16 (36%) maintained their score, and eight (18%) cases reduced their score. In the term group 27 (54%) of women increased their score, 13 (26%) maintained their score, and 10 (20%) cases reduced their score. In total, 53 (50%) cases increased their score.

Overall, 48 (46%) of the women had spontaneous delivery, 12 (11%) required vacuum delivery, and 45 (43%) women were delivered through Caesarean section.

Outcome and complications

The pregnancy outcome and complications are shown in Table 3. There were expected differences in birth weight, birth length, and head circumference of the newborn infants between the three groups (all P<0.001) that reflect the different stages of development at delivery. The rate of admission to NICU decreased with term; the very preterm group had 100% admission, the moderate/late preterm group had 43% admission, and the term group had 16% admission (P<0.001). The opposite was found with maternal ICU admission, with no cases in the very preterm or moderate/late preterm groups but 4% admission in the term group; however, this was not significantly different between the groups (P = 0.353).

The Apgar scores were significantly different between the three groups at 1 min (P = 0.002), 5 min, and 10 min. Again, this was to be expected as the very preterm infants had lower scores at all stages, which increased in the moderate/late preterm infants, and again in the term infants. Most studies consider an Apgar score at 5 min of less than seven as an indicator of adverse foetal outcome. In this study, four (4%) cases in the entire cohort were of concern in this regard.

There seemed to be a difference in both arterial and venous umbilical cord pH between the groups (P=0.016 and P=0.013, respectively), but these were within the normal range, and a stepwise reduction in mean umbilical arterial pH has previously been shown for infants born preterm, term, and post-term [42]. When a cut-off value of less than 7.2 was used to highlight cases of concern, there were 0, 8, and 12 cases in the very preterm, moderate/late preterm, and term groups for umbilical cord artery pH, and 0, 4, and 3 for the respective

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Table 3: Outcomes and complications

Parameter	Very preterm (n=10)	Moderate/ late preterm (n=45)	Term (n=50)	*P* value
Newborn infant weight	1.3 ± 0.2 kg	2.1 ± 0.5 kg	3.2 ± 0.7 kg	<0.001
Newborn infant length	39.0 ± 3.1 cm	44.7 ± 3.3 cm	50.4 2.9 ± cm	<0.001
Newborn infant head circumference	26.3 ± 1.4 cm	31.1 ± 2.2 cm	34.2 ± 1.6 cm	<0.001
Infant NICU admission	100% (10)	43% (20)	16% (8)	<0.001
Maternal ICU admission	0% (0)	0% (0)	4% (2)	0.353
Uterine hyperstimulation	0% (0)	0% (0)	0% (0)	-
FHR patterns	0% (0)	0% (0)	0% (0)	-
Apgar score median (range) - 1 min - 5 min - 10 min	 7.5 (5-8) 8.5 (6-10) 9.0 (8-10)	 9.0 (1-10) 9.0 (6-10) 10 (8-10)	 9.0 (3-10) 10 (4-10) 10 (8-10)	 0.002 <0.001 <0.001
Neonatal hypoglycaemia	0% (0)	0% (0)	0% (0)	-
Umbilical cord artery pH	7.32 ± 0.05	7.26 ± 0.07	7.25 ± 0.08	0.016
Umbilical cord venous pH	7.37 ± 0.05	7.30 ± 0.05	7.30 ± 0.07	0.013
Polysystole	0% (0)	0% (0)	0% (0)	-
Length of hospital stay	57 (32-160) days	10 (1-49) days	4 (2-60) days	<0.001
Birth abnormalities/ complications * - None - RDS - BPD - Jaundice/Hyperbilirubinemia - Sepsis - Retinopathy - Premature - Anaemia - Infection - Hypoglycaemia - Rh incompatibility - Blocked tear duct - VACTERL association - Trisomy 18 - Trisomy 21 - Atrial septal defect - Heart murmur - Undescended testicles - Hernia - Death	 0% (0) 80% (8) 10% (1) 50% (5) 50% (5) 10% (1) 100% (10) 40% (4) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 10% (1)	 16% (7) 49% (22) 0% (0) 2% (1) 0% (0) 0% (0) 31% (14) 0% (0) 4% (2) 7% (3) 2% (1) 0% (0) 2% (1) 2% (1) 2% (1) 0% (0) 0% (0) 0% (0) 0% (0) 2% (1)	 62% (31) 4% (2) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 0% (0) 2% (1) 2% (1) 0% (0) 2% (1) 0% (0) 0% (0) 4% (2) 2% (1) 4% (2) 2% (1) 2% (1) 0% (0)	 <0.001

Note: * Some infants had more than one abnormality/complication.
NICU= neonatal intensive care unit; ICU= intensive care unit; FHR= foetal heart rate; RDS= respiratory distress syndrome, BPD= biparietal diameter.
Data are presented as mean±SD and comparison between the groups was by ANOVA except for Apgar score, which is presented as median and range, and compared with Kruskal-Wallis test, and categorical data, which is presented as percentages and number including NICU and ICU admission and birth abnormalities/complications, and compared Chi square test.

groups for venous pH. Overall, this suggests that 19% of cases might be of concern with umbilical cord artery pH and 7% of cases with venous pH.

The length of maternal hospital stay was longer in the very preterm group at a median of 57 days compared to 10 days in the moderate/late preterm group and 4 days in the term group ($P < 0.001$). There were no cases of uterine hyperstimulation, abnormal FHR patterns, neonatal hypoglycaemia, or polysytole in any of the groups.

There were two cases of neonatal death after live birth, one in the early preterm group and one in the moderate/ late preterm group, who also had polysomy 18. Other birth abnormalities and infant complications were different between the three groups ($P < 0.001$). In the very preterm group, 80% of cases had evidence of respiratory distress syndrome (RDS), and 100% were premature. In the moderate/late preterm group, 49% of cases had evidence of RDS, and 31% were premature. In the term group 62% had no abnormalities or complications, but 4% had evidence of RDS.

Overall, there was no indication of any safety concerns with the administration of mifepristone in the whole cohort. Further analysis of the rates of NICU and ICU admission with inpatient or outpatient administration of mifepristone found that more than expected NICU admissions were found in the inpatients ($P = 0.027$). However, this is likely to be due to the early preterm pregnancies all receiving mifepristone as inpatients. There was no significance in ICU admission with inpatient or outpatient administration of mifepristone.

Discussion

This study aimed to undertake a retrospective analysis of the safety for both mother and newborn infant of high-dose mifepristone as an agent for preparation of the cervix. The use of mifepristone also has the positive effect of reducing the number of emergency caesarean sections that must be performed when the birth process comes to a standstill.

As the term at delivery is directly related to pregnancy outcomes, we divided the cases according to gestational age at delivery. The results indicated that outcomes were as expected for the three groups. There were no cases of uterine hyperstimulation, abnormal FHR patterns, neonatal hypoglycaemia, or polysystole after mifepristone administration. Therefore, this study supports the view that mifepristone is safe for both mother and newborn infant when used for preparation for labour induction.

Despite the long-established safety of mifepristone, there is some concern that in healthy deliveries, its safety profile is not well established. Mifepristone is a progesterone and glucocorticoid antagonist that also has weak anti-androgen effects. Therefore, mifepristone could have direct adverse effects on the mother or the foetus and indirect effects on the foetus through the mother. In terms of maternal safety in this cohort, two women were admitted to the ICU. One of the women had uterine atony, and the other had uterine rupture. Uterine atony is the most common cause of postpartum haemorrhage [45]. Postpartum haemorrhage is thought to complicate around 3% of deliveries [46]. Therefore, there is no suggestion that this was the result of mifepristone administration. Uterine rupture is a rare complication, occurring in around 0.07% of pregnancies, that is most often found in women who have uterine scarring, such as from a previous delivery through Caesarean section [47,48]. The woman in this cohort who was admitted to the ICU with uterine rupture also received balloon induction and Propess (prostaglandin E2). Prostaglandin E2 use may slightly increase the risk of uterine rupture, especially

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in women with previous Caesarean section [49]. On the other hand, previous research suggests mifepristone can be safe in women with a previous Caesarean section [29,35]. So, in this case, it is unlikely that mifepristone was the cause of ICU admission [50].

NICU admission is one indicator of infant safety; however, admission to the NICU can be for many reasons. This study found that 100% of cases in the very preterm group, 43% of cases in the moderate/late preterm group, and 16% of cases in the term group were admitted to the NICU. This follows the general pattern of NICU admission being related to gestational age at birth [48]. Overall, in this study, there were 50 newborn infants admitted to the NICU, a rate of 47%. It is difficult to compare these rates to other studies because NICU admission varies quite widely across different populations and geographical areas; however, a rate of 16 % in the term group is within the expected range [51]. Meta-analysis of labour-induced deliveries after 37 weeks found perinatal death in 0.4 per 1000 (0.1 to 1.9), still birth in 1 per 1000 (0.15 to 1.5), Apgar score less than 7 at 5 minutes 10 per 1000 (7 to 12) [52]. In this study, there were two perinatal deaths, one in the very preterm group and another in the moderate/late preterm group, who had trisomy 18. There were no deaths in the term group. All cases had a live delivery. Apgar score less than 7 at 5 minutes was found in 4% of the cohort, which is within the range of the meta-analysis. Therefore, none of these factors identifies any concerns with the safety of mifepristone for newborn infants.

As mifepristone can cross the placenta, there is a possibility that it could cause hypotension and hypoglycaemia in the neonate [42]. In this study, there were 4 cases of hypoglycaemia but no recorded cases of hypotension. The hypoglycaemia rate of 4% is at the lower end of the expected range of 4 to 12% in healthy newborns [53]. Therefore, it is unlikely that mifepristone administration is causing hypoglycaemia in this study. This is supported by previous studies that have shown no difference in hypoglycaemia rates in infants delivered after mifepristone compared to controls [27,31,36,37,54].

Some studies have raised the possibility of increased risk of uterine hyperstimulation and FHR abnormalities with mifepristone administration [37,38]. If hyperstimulation caused significant foetal distress, then the rates of abnormal FHR patterns would be greater in mifepristone-treated pregnancies. A meta-analysis suggested abnormal FHRs were more common with mifepristone [55]. In this study, we found no evidence of uterine hyperstimulation in any of the cases included in the cohort. This is similar to other studies that examined uterine activity in the first 48 hours after mifepristone administration [28,30,31,33,54,56]. Additionally, abnormal FHR patterns were identified in no cases, supporting the lack of hyperstimulation. It is particularly important that hyperstimulation should be considered in terms of mifepristone being used in the outpatient setting. However, there is no evidence that mifepristone alone causes uterine hyperstimulation, and for this to occur may require the administration of a second uterotonic agent.

Although this study intended to investigate the safety of mifepristone, not its effectiveness in inducing labour, it is interesting that 50% of the cases in this cohort did not require a secondary agent for labour induction. This compares well with previous studies that mifepristone successfully induces labour in about 30% of cases [28,34]. This could be because of the high dose of mifepristone administered at 600mg, while other studies have used various different doses, from 50 to 600mg [30,31,33-38,54]. The Cochrane review meta-analysis of 2009 suggests that the minimal effective dose is 200mg [55].

In conclusion, this study was a retrospective safety analysis of women and newborn infants after preparation for the induction of labour with 600mg mifepristone. The results identified no safety concerns and, in particular, no cases of uterine hyperstimulation or abnormal FHR patterns.

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