

Neonatal Morbidity and Outcome of Live Born Premature Babies After Attempted Illegal Abortion with Misoprostol

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Misoprostol is a synthetic prostaglandin currently employed to induce labor. Association with illegal abortion has been reported; however, neonatal outcome and morbidity after a failed attempt of abortion has not been described.

Objectives: To report the association between misoprostol self-medication and preterm labor and to assess perinatal risk factors, morbidity and early outcomes.

Methods: We conducted a prospective study of all very low birth weight (VLBW) infants delivered in Hospital Fernando Fonseca, during a 5-year period. VLBW infants were assigned to misoprostol group (MG) when preterm delivery was attributed to misoprostol and matched with newborns with similar gestational age, birth-weight, and gender.

Results: During the study period 311 VLBW infants were born. Nineteen belonged to misoprostol group (MG) and 58 were selected for controls. Mothers from MG were significantly younger (21.5 vs 27.5, $p=0.001$) and from African origin (74 vs 31%, $p=0.006$), had significantly less prenatal care (21 vs 67%, $p=0.000$), less antenatal steroids (5 vs 50%, $p=0.001$), and were delivered less often by C-section (11 vs 60%, $p=0.000$). MG infants had significantly higher rates of patent ductus arteriosus (58 vs 29%, $p=0.031$) and chronic lung disease (47 vs 14%, $p=0.026$). Mortality rate at 3 months was similar in both groups, but the incidence of abnormal neurodevelopment at 1 year of age was significantly higher in the MG (50 vs 16%, $p=0.02$).

Comments: The worse outcome of MG infants seems to be determined by prenatal, natal, and postnatal factors and we believe that misoprostol is probably a significant adjuvant cofactor.

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Misoprostol is a synthetic E1 prostaglandin approved to treat peptic ulcer disease (Goldberg, Greenberg, & Darney, 2001). It has also an effect on myometrical contractility and cervical ripening (Sheepers, Van Erp, & Van den Berg, 1998). Although its use has not been approved during pregnancy, unlicensed use to induce labor is increasingly common.

The first report of misoprostol use as an abortifacient came from Brazil in 1986 (Costa, 1998). By 1990, about 70% of women hospitalized in Brazil with abortion-related diagnoses referred to the use of this drug. Abortion remains illegal in Portugal as in many other predominately Catholic nations. Over the past decade, we have seen a rise in the phenomenon of live born infants in our intensive care nursery after attempted abortion very late in pregnancy. These women appear unaware that inducing labor in the third trimester will result in a premature but live born infant. To date the consequences of the illegal use of misoprostol early in the third trimester of pregnancy have not been reported.

Our purpose is to report that self-medication with Misoprostol can be a cause of viable very low birth weight (VLBW) newborns. Because we have seen so many of these infants, we are able to also assess and report perinatal risk factors, neonatal morbidity, and early outcomes.

Methods

We conducted a prospective analysis, with a matched case-control design, of all VLBW infants admitted to the

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American Alternative for Unwanted Infants

by Carole Heath and Anita Catlin

Since 1999, American women have been provided an alternative option for treatment of unwanted babies. The infant safe haven laws allow women or their legal guardians to safely relinquish their infants to a place where medical care will be provided and a safe placement found. To date 46 states have enacted such laws. These laws were initiated as part of the federal Promoting Safe and Stable Families Amendments of 2001 (Public Law 107-133), which amended the Family Preservation Services to allow States to support infant safe haven programs. These babies often come from women in the same crisis as those described in the accompanying article from Portugal; women who are in a state of denial about being pregnant or are afraid to tell anyone. Their desperation contributes to irrational acts that prior to this law led to infants being disposed of in dumpsters or public toilets and left to die.

Carole Heath, EdD, RN, is staff at Sonoma State University, and is active in the California state program for safe infant abandonment. Since the law was enacted in California, 71 infants have been provided safe haven.

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According to the National Conference of State Legislatures (NCSL), in 1998 there were 105 public abandonments and 31,000 babies left in hospitals (Affholter, 2000). And formerly, if caught, women were prosecuted for child neglect, abuse, or murder. Now the mother or mother's representative may drop off the baby at any designated safe haven, such as a fire station or hospital emergency room. She is allowed to remain anonymous and no arrest or prosecution takes place. Personnel at the safe haven bring the child for an immediate medical exam, and then the local child protective agency is contacted and the child is placed in a temporary foster home. The laws allow procedures for a woman to change her mind or for a nonrelinquishing father to attempt custody. If the child is not reclaimed, termination of parental rights and adoption usually follow. This program has proven very successful. The emphasis now is to disseminate information to high school students and young adults about the program's existence.

Reference

Affholter, P. (2000, May/June). Safe havens for abandoned babies. *State Notes: Topics of Legislative Interest*. Located on February 15, 2005 at <http://www.senate.michigan.gov/sfa/Publications/Notes/2000Notes/NotesMayJun00Affholter.PDF>

neonatal intensive care unit (NICU) of the Hospital Fernando Fonseca, Amadora, Portugal, from June 1996 to July 2001. Data were collected from interviewing the mothers and from infant charts.

VLBW infants born from pregnant women who had taken misoprostol, either orally or vaginally, immediately in the 24-48 hours preceding labor, were assigned to the Misoprostol Group (MG). In these cases, without any other risk of prematurity, preterm labor was attributed to misoprostol. These infants were matched with VLBW with similar gestational age, birth-weight, and gender who served as controls (Controls). Infants with major congenital malformations were excluded.

Gestational age was based on the date of the last menstrual period, early prenatal ultrasound, obstetric examination, and/or on the New Ballard scoring system (Donovan et al., 1995). The neurodevelopmental impairment was assessed by physical examination and Griffith's mental developmental scale. Cerebral palsy (CP), blindness or strabismus and sensorineural deafness rates were determined. Cerebral palsy was defined as a group of nonprogressive motor impairment syndromes secondary to lesions of brain arising in the early stages of development (Munth, Alberman, Hagberg, Kodama, & Perat, 1992).

SPSS for Windows 10.0 was used for statistical analysis. Differences between groups were compared using the Mann-Whitney test for continuous variables and a Fisher's exact test for categorical variables. P values <0.05 were considered statistically significant.

Results

During the 5-year study period, 311 VLBW infants were admitted to our unit. Nineteen (6%) belonged to the misoprostol group (MG) and 58 were matched for controls. Throughout this period, the proportion of newborns in the

MG progressively increased, from 4 in 1997, to 8 in the first half of 2001.

Mothers from the MG were more likely to be younger (21.5±4.5 vs 27.5±7.1, p=0.001) and born outside of Portugal (74% vs 31%, p=0.006). Table 1 shows maternal characteristics. Comparing perinatal data (see Table 2), infants from the MG had significant less prenatal care during pregnancy (21% vs 67%, p=0.000), less antenatal steroids (5% vs 50%, p=0.001), and were delivered less often by cesarean section (11% vs 60%, p=0.000).

Comparing neonatal morbidity (see Table 3), the MG had significantly higher rates of patent ductus arteriosus (58% vs 29%, p=0.031) and chronic lung disease (47% vs 14% p=0.026). There were no differences between groups concerning respiratory disease syndrome (RDS), sepsis, intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), or necrotizing enterocolitis (NEC).

The mortality rate at 3 months or NICU discharge was similar in both groups (21% vs 26%, p=ns). In the MG, the incidence of abnormal neurodevelopmental at 1 year of age was significantly higher. The most frequent disability was cerebral palsy (29% vs 3%, p=0.015).

Discussion

Misoprostol used in conjunction with either mifepristone or methotrexate is highly effective for medical abortion (Norman, Thong, & Baird, 1991). However, when used alone to induce complete abortion, its effectiveness has been reported as lower (Ngai, Tang, Chang, & Ho, 2000). The uterus becomes more sensitive to misoprostol with increasing gestational age. Therefore, in the third trimester, small doses of misoprostol can be effective for inducing vaginal delivery within 24 hours (Creinin & Vittinghoff, 1994).

The self-administration of misoprostol in the late second or early third trimester of pregnancy can result in the deliv-

Table 1. Maternal Characteristics

Sociodemographic Data	Misoprostol (n = 19)	Controls (n = 58)	P
Maternal age (yr ± SD)	21.5 ± 4.5	27.5 ± 7.1	0.001
Of African descent (%)	74 (14/19)	31 (18/51)	0.006
Maternal years of schooling (yr ± SD)	8.2 ± 2.2	9.3 ± 3.7	0.528

Table 3. Neonatal Morbidity

Neonatal Morbidity	Misoprostol (n = 19)	Controls (n = 58)	p
Respiratory distress syndrome %	100 (19/19)	85 (49/58)	0.102
Patent ductus arteriosus %	58 (11/19)	29 (17/58)	0.031
Sepsis %	63 (12/19)	52 (30/58)	0.436
Necrotizing enterocolitis (grade >1) %	0 (0/19)	3 (2/58)	1.000
Intraventricular hemorrhage (grade >1)	26 (5/19)	24 (14/58)	1.000
Periventricular leucomalacia %	27 (4/15)	9 (4/43)	0.185
Retinopathy of prematurity (grade >1)	33 (5/15)	12 (5/43)	0.106
Chronic lung disease %	47 (7/15)	14 (6/43)	0.026

ery of a viable VLBW infant and this, to our knowledge, has not yet been reported. We are particularly concerned by the fact that the use of this drug to induce abortion is steadily increasing through a 5-year time span and in some social groups.

Preterm labor is the single most important cause of perinatal mortality and it is also a major determinant of long-term morbidity (Stevenson & Wright, 1998). In our neonatal intensive care unit in Lisbon, Portugal, we found a surprisingly high proportion of VLBW infants born as a consequence of misoprostol, and this is a huge problem that must be considered. In fact, we observed major differences in the obstetrical care of these infants. Mothers from the MG frequently had received no prenatal care and, as expected, procedures such as caesarean section and antenatal steroids were also different.

Antenatal corticosteroid therapy for women at risk for preterm delivery improves survival in their infants and reduces the risk for RDS, chronic lung disease (CLD), IVH and mortality (NIH, 1995). Antenatal steroid use ranges from 72% in the Vermont-Oxford study (Horbar, Badger, Carpenter, Fanaroff, 2002) to 77.6% in the National Portuguese Database (Grupo do Registo Nacional, 2002). We found only 5% of the MG infants had received steroids, probably related to the non-existence of obstetric care in these infants. Although we did not observe a corresponding increase in the frequency of RDS, all infants from the MG required surfactant and intermittent positive pressure ventilation (IPPV), which could also reflect the increased severity of the RDS.

The incidence of patent ductus arteriosus (PDA) was also remarkably higher than expected. It was 20% in the National Portuguese Database (Grupo do Registo Nacional, 2002). We speculate that the prostaglandin nature of Misoprostol might explain this difference. PDA has been implicated as the cause of chronic lung disease (Farrell & Fiascone, 1997). In our study, chronic lung disease reached 47% of surviving MG babies, a surprisingly higher frequency compared to the

Table 2. Perinatal Data

Perinatal Data	Misoprostol (n = 19)	Controls (n = 58)	P
Prenatal care %	21 (4/19)	67 (39/58)	0.000
Antenatal steroids %	5 (1/19)	50 (29/58)	0.001
Cesarean section %	11 (2/19)	60 (35/58)	0.000
Gestational age, mean (SD)	27.3 ± 1,8	27.8 2,1	0.227
Birthweight, mean (SD) g	966 ± 216	1018 ± 238	0.269
Male %	63 (12/19)	57 (33/58)	0.790

Note: Data expressed as a mean ± SD or percentage.

Table 4. Outcome

Outcome Data	Misoprostol (n = 19)	Controls (n = 60)	P
Deaths 3 months	21%(4/19)	26% (15/58)	0.768
Abnormal neurodevelopment	50%(7/14)	16% (6/38)	0.026
Cerebral palsy	29% (4/14)	3% (1/38)	0.015

results referred in the Vermont-Oxford Trial and in the Portuguese National Database. Some authors have suggested that the prophylactic use of indomethacin (antagonist of prostaglandins) reduces the incidence of CLD and IVH (Murphy, Hope, & Johnson, 1997). We ponder whether prophylactic indomethacin should be used in all babies exposed to illegal misoprostol?

Cerebral palsy (CP) is the most frequent neurological sequelae of VLBW infants, ranging from 8% to 11% (Murphy et al., 1997). In our study, 7 of the surviving infants from the MG (50%) presented neurodevelopmental disabilities, 29% of which were CP. We cannot identify an individual factor that explains this high frequency, but among the very preterm babies, the coexistence of several risk factors for cerebral palsy may be more important than an individual factor. PDA and absence of antenatal corticosteroid exposure have been associated with an increased risk of CP (Murphy et al., 1997; Gray, Jones & O'Callaghan, 2001), factors that were significantly different between our groups. Also, CLD has been directly related to most other morbidities, such as neurodevelopment delay (Kaempf, Campbell & Sklar, 2002). However, a reduction in the rate of CP in very preterm babies probably requires an integrated approach to management throughout the antenatal, intrapartum and neonatal periods.

Conclusions

There were major differences between groups. The worse outcome of MG infants seems to be determined by less prenatal care, less antenatal steroids prescribed, and significantly more frequent PDA and CLD. We believe that although differences in obstetric care may play a role in this worse outcome, misoprostol was, probably, a significant adjuvant cofactor. Here in Portugal, and perhaps elsewhere, we feel educational programs must be promoted in order to prevent the use of misoprostol in pregnancy, especially beyond the gestational ages of viability.

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