Obstetrics; *Maternal-Fetal Medicine and Perinatology*

Influence of Morning Versus Midnight Initiation of Induction of Labor in Late-Term Pregnancy on Perinatal Outcome and Time of Birth

Danijel BURSAĆ[1], Katja VINCE[1], Ratko MATIJEVIĆ[1,2]

Zagreb, Croatia

ABSTRACT

OBJECTIVE: The aim of this study was to assess and compare morning vs. midnight initiation of induction of labor on time of birth and perinatal outcome.

STUDY DESIGN: A retrospective cohort study performed at University Hospital Merkur, Zagreb, Croatia; in the period between 2006 to 2017. The participants were low-risk nulliparous women with a gestational age over 41 weeks who had labor induced by an intracervical prostaglandin E2 analogue dinoprostone applied. Two groups were compared; the first one had induction of labor initiated in the morning and the second one at midnight.

RESULTS: A total of 206 pregnant women were included in the study. Women with induction of labor starting at midnight (n=103) gave birth more often during the daytime (7 am-6.59 pm) compared to women with induction of labor starting in the morning (n=103) (p <0.01). The midnight group also gave birth more often during regular hospital working hours (7.30 am - 3.30 pm), but this result was not statistically significant (p=0.091). The rate of epidural analgesia was higher among women in the midnight group, while no other differences were observed in predefined perinatal outcome between the two groups.

CONCLUSIONS: Initiation of induction of labor at midnight compared to morning results in giving birth more often during daytime. This presents a favorable option for reducing out of hours and night work.

Keywords: Initiation of labor induction, Perinatal outcome, Prostaglandins

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Introduction

Induction of labor (IOL) is defined as an artificial initiation of labor before its spontaneous onset (1). The incidence of IOL is rising in recent years; estimates report that up to one in four deliveries in developed countries involve labor induction (2). It can be expected that in upcoming years the incidence will be even higher particularly due to recent published studies, presenting lower frequency of caesarean sections and similar perinatal morbidity and mortality with induced labor at term (3,4). The most common indication for IOL is post-date pregnancy, performed in order to avoid the risks associated with post-maturity (5,6). A pregnancy is considered post-date when it extends beyond 294 days (42+0/7 weeks), while pregnancies beyond 41+0/7 weeks through 41+6/7 weeks of gestation are referred to as late-term pregnancies (7). There is a strong body of evidence suggesting that IOL prior to 42 weeks of gestation is associated with a reduction in perinatal complications (8,9).

Synthetic prostaglandins have been used for initiation of labor induction for decades with proven efficacy and safety (10-14). However, up until now, there is no clear answer how the timing of initiation of labor influences the time of birth and out of hours work as well as perinatal outcome (15,16).

The aim of this study was to assess and compare time of birth and perinatal outcomes between two protocols of IOL differing only in the timing of initiation with intracervical application of dinoprostone (PGE2) gel.

[1] *Department of Gynecology and Obstetrics, University Hospital Merkur, Zagreb, Croatia*
[2] *Department of Gynecology and Obstetrics, School of Medicine, University of Zagreb, Croatia*

Address of Correspondence: *Katja Vince, University Hospital Merkur, Zajčeva 19, 10000 Zagreb, Croatia katjavince@gmail.com*

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ORCID IDs of the authors:
D.B.: 0000-0002-9058-5860, K.V.: 0000-0001-5992-5030
R.M.: 0000-0003-1693-7474

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Material and Method

This is a retrospective cohort study performed by analyzing data from hospital records at University Hospital Merkur, Zagreb, Croatia between June 2006 and June 2017. All study participants had labor induced per Hospital labor-ward protocol by dinoprostone, an intracervical prostaglandin E2 analogue gel (Prepidil®, Pfizer, USA), applied with repeated doses 6, 30, and 36 hours after the initial dose or until Bishop score >8 or in active labor. Two groups were compared. The first one involved women induced between the year 2006 and 2013, when dinoprostone was applied per old Hospital protocol in the morning on the induction day (morning group); while the second one consisted of women induced from 2013 until 2017 when dinoprostone was applied per new Hospital protocol at midnight on the induction day (midnight group).

Inclusion criteria were nulliparous, gestational age 41+3 weeks with intact fetal membranes and without any condition that may influence study outcome (i.e. gestational diabetes, gestational hypertension, hypothyreosis or hyperthyreosis etc.), 40 and less years of age with body mass index (BMI) below 35kg/m^2. Only women with prolonged pregnancies were chosen in order to minimize as much as possible other confounding factors that may influence study outcomes. The only apparent difference between the two study groups was the timing of the initiation of IOL. Maternal data analyzed included maternal age and BMI.

The primary outcome of the study was the time of birth used to evaluate whether initiation of labor induction at midnight results in more women giving birth during daytime or hospital working hours.

Regarding that outcome, two separate analyses were performed. In the first one, time of birth was divided into working hours (from 7.30 am to 3.30 pm) and out of work hours (3.30 pm to 7.30 am). In second one the time of birth was divided as during daytime (from 7.00 am to 6.59 pm) and night time (from 7.00 pm to 6.59 am), which follows midwifery shifts.

Perinatal outcome data assessed as secondary outcome were: time of birth, mode of delivery, use of epidural analgesia, necessity for augmentation of labor using oxytocin infusion, the presence of merconium stained amniotic fluid, episiotomy rate, perineal tear grade III or IV rate and incidence of postpartum hemorrhage. Neonatal data analyzed were birth weight and 5 minute Apgar score.

All statistical analyses were performed using SPSS ver. 21.0. Normality of distribution was tested using the Shapiro-Wilks test, while homogeneity of variance was tested using Levene's test. Differences between groups of independent continuous variables were analyzed using student t-test for two independent samples (groups) while differences in the occurrence of individual conditions (categorical variables) were compared using the chi2 test. Statistical significance was defined as $p < 0.05$. For a difference in the proportion of daytime deliveries of 20% (first proportion 50% and second 70%), using a confidence interval of 95%, power of 80%, taking into account a dropout rate of 10% (due to incomplete data), sample size calculations estimated that a minimum of 101 women should be included in each group (17).

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval for the study was obtained from the University Hospital Merkur Ethical Committee, the number of IRB approval 03/1-6566/1.

Results

A total of 206 pregnant women were included. They gave birth at University Hospital Merkur between June 2006 and June 2017 after IOL due to late-term pregnancy. There were 103 of them who fulfilled inclusion criteria between 2006 and 2013 forming the midnight group, compared with the first 103 women identified in labor ward protocol who fulfilled the same criteria starting from February 2013 retrospectively (morning group). Maternal and new-born characteristics of pregnant women in each group are presented in table I.

Perinatal outcomes of all women who had labor induced are presented in table II, while differences between morning and midnight group are presented in table III.

Table I: *Maternal and new-born characteristics of pregnant women in morning and midnight group*

Pregnant women	Morning group (n=103)	Midnight group (n=103)	*p*
Age (years)	28.12±4.89	28.91±4.72	0.811
BMI (kg/m^2)	28.33±3.11	28.19±3.03	0.364
Newborns			
Birth weight (g)	3644±423	3662±399	0.658
Birth length (cm)	52±1.8	52±1.5	0.085

** Data are presented as: mean ± standard deviation, BMI: Body mass index*

Table II: *Outcomes of labor induction among all pregnant women (n= 206)*

Outcome			Outcome		
Mode of delivery	n	%	**Number of gels**	n	%
- vaginal	150	72.8	- 1	66	34
- C.S.	56	27.2	- 2	93	48
Time of delivery	n	%	- 3 or more	33	17
Regular HWH[1]	55	26.8	**5min Apgar < 7**	1	0.5
Non-regular HSH[2]	150	73.2	**Fetal macrosomia**	37	18
Daytime[3]	117	56.8	**Nuchal cord**	28	14
Night-time[4]	89	43.2	**Oxytocin use**	167	81
Epidural analgesia	83	40.3	**Episiotomy rate**	126	61.2
Meconium	42	20.4	**PPH rate**	14	6.8

**n: Number, C.S. : Caesarean section, HWH: Hospital working hours, PPH: Postpartum hemorrhage.*
1: 7.30 am-3.30 pm, 2: 3.30 pm-7.30 pm, 3: 7 am-6.59 pm, 4:7 pm-6.59 am

Table III: *Differences between morning and midnight group regarding predefined perinatal outcome*

Perinatal Outcome	Morning group n (%)	Midnight group n (%)	*p*
Meconium	22 (21)	20 (19)	0.729
Epidural analgesia	30 (29)	53 (51)	<0.001
Oxytocin use	85 (83)	83 (81)	0.719
Episiotomy rate	68 (66)	58 (56)	0.153
PPH rate	6 (6)	8 (8)	0.580
Time of delivery	n (%)	n (%)	
Regular HWH[1]	25 (24)	34 (33)	0.091
Non-regular HWH[2]	78 (76)	69 (67)	
Day time[3]	49 (48)	68 (66)	<0.05
Night time[4]	54 (52)	35 (34)	
Mode of delivery	n (%)	n (%)	0.188
Vaginal	78 (76)	72 (70)	0.347
C.S.	25 (24)	31 (30)	
Number of gels required	n (%)	n (%)	0.516
1	36 (37)	30 (32)	
2	43 (44)	50 (52)	
3 or more	18 (19)	15 (16)	

** n: Number, PPH: Postpartum hemorrhage, HWH: Hospital working hours, C.S.: Caesarean section. 1: 7.30 am-3.30 pm, 2: 3.30 pm-7.30 pm, 3: 7 am-6.59 pm, 4: 7 pm-6.59 am*

Discussion

The results of this study indicate that pregnant women with IOL starting at midnight gave birth more often during daytime and less often during night time compared to women with IOL starting in the morning and this difference was statistically significant. The midnight group also gave birth more often during regular hospital working hours, but this result despite 30% difference was not statistically significant (p=0.091). These are important findings. According to a recent study that included over 2 million births, delivery complications are higher during night shifts when hospitals are understaffed (18). Also, in developed countries, i.e. UK and Germany; delivery during the night or outside the normal working week is associated with an increased risk of neonatal death (19,20). Despite the fact that expert medical care is readily available for anyone who needs it 24/7, a lower level of medical cover (i.e. senior staff cover, laboratory and imaging service) is available during the night, weekends and holidays (16,19). Also, staff during the night is likely to be less experienced and with increased physical and mental fatigue after usually working through a complete day shift. Giving birth during daytime or regular hospital working hours reduces the risk of intrapartum and postpartum complication, offering a safer and complete service.

Spontaneous onset of labor is proven to have a circadian rhythm, with a shorter duration of labor and fewer obstetric interventions when labor starts in the evening (21). Until now only few reports were performed regarding clinically significant differences concerning maternal or neonatal outcomes when labor was induced either in the morning or in the evening. The only difference found was in women's preference of administration of prostaglandins in the morning (21, 22) and possible reduction of the out of hours work if IOL was initiated in the evening day before IOL (15).

Women in midnight group had a lower rate of meconium stained amniotic fluid, the use of oxytocin and episiotomy, but none of these were statistically significant (p >0.05). The only statistically significant difference between the morning and midnight group was in the rate of epidural analgesia. Higher epidural rate in midnight group can be explained with the active phase of labor during regular hospital working hours and daytime when anesthetic team was more available to provide the service. Also, women in the midnight group were assessed in the period from 2013 to 2017, when there was a general increase of epidural analgesia use compared to the period from 2006 and 2013.

Comparison of two different periods (2006-2013 and

2013-2017) presents the most important limiting factor for this study. The results might be influenced by changes in of labor-ward practice during assessment periods; however, we believe the potential difference is related only to lower episiotomy and higher epidural analgesia rates.

The results of this study demonstrate that women give birth more often during the daytime when IOL was initiated at midnight compared to initiation of IOL in the morning.

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