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Prolonged second stage of labor is associated with low Apgar score

Authors

Maria Altman[1], Anna Sandström[1,2], Gunnar Petersson[1], Thomas Frisell[1], Sven Cnattingius[1], Olof Stephansson[1,2]

[1] Department of Medicine Solna, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden

[2]Division of Obstetrics and Gynecology, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

Corresponding author

Maria Altman,

Department of Medicine Solna, Clinical Epidemiology Unit, T2, Karolinska Institutet

171 77 Stockholm

Telephone: +46 733 758658, Fax: +46 851779304

Short title

Prolonged Labor and Apgar score

Abbreviations

BMI = body mass index; body weight/length^2, kg/m^2

CI = 95% Confidence Interval

OR = Odds Ratio

SD = Standard Deviation

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Abstract

There is no consensus on the effects of a prolonged second stage of labor on neonatal outcomes. In this large Swedish population-based cohort study, our objective was to investigate prolonged second stage and risk of low Apgar score at 5 minutes. All nulliparous women (n= 32 796) delivering a live born singleton infant in cephalic presentation at ≥37 completed weeks after spontaneous onset of labor between 2008 and 2012 in the counties of Stockholm and Gotland were included. Data were obtained from computerized records. Exposure was time from fully retracted cervix until delivery. Logistic regression analyses were used to estimate crude and adjusted odds ratios (OR) with 95% confidence intervals (CI). Adjustments were made for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference. Epidural analgesia was included in a second model. The primary outcome measure was Apgar score at 5 minutes <7 and <4. We found that the overall rates of 5 minute Apgar score <7 and <4 were 7.0 and 1.3 per 1000 births, respectively. Compared to women with <1 hour from retracted cervix to birth, adjusted ORs of Apgar score <7 at 5 minutes generally increased with length of second stage of labor: 1-<2 hours: OR 1.78 (95% CI 1.19-2.66); 2-<3 hours: OR 1.66 (1.05-2.62); 3-<4 hours: OR 2.08 (1.29-3.35); and ≥4 hours: OR 2.71 (1.67-4.40). We conclude that prolonged second stage of labor is associated with an increased risk of low 5 minute Apgar score.

Introduction

The second stage of labor starts when the cervix is fully retracted, and ends with birth. The decrease in fetal scalp pH and increase in lactate in some fetuses indicates that this last part of labor involves periods of relative lack of oxygen, as the infants' head and the umbilical cord are compressed by contractions in the birth canal. The infant may respond with asphyxia and metabolic acidosis, and lactate levels in the fetus increase by approximately 1 mmol/L per 30 minutes of bearing down.[1]There is a positive association between increasing metabolic acidosis and risks of a depressed infant at birth, clinically measured with Apgar scores, and long-time sequelae.[2, 3]

In nulliparous women, a prolonged second stage of labor is usually considered if the duration exceeds 3 hours with regional anesthesia or 2 hours without regional anesthesia.[4] Although the effects of the duration of the second stage of labor on neonatal outcomes have been investigated in a number of studies, there is no consensus on the effects.[5] Therefore, there is still uncertainty whether there is a time point in the prolonged second stage of labor, when neonatal risks increase, and where obstetrical intervention may prevent adverse events.[6, 7]

Using population-based data from the counties of Stockholm and Gotland, Sweden, our aim was to study the association between duration of second stage of labor and Apgar score at 5 minutes with detailed information on maternal, pregnancy, delivery and infant characteristics. Our hypothesis was that a prolonged second stage of labor would be associated with a negative impact on Apgar scores. We restricted the study population to nulliparous women with term and post term pregnancies, spontaneous onset of labor, who delivered a liveborn singleton infant in cephalic presentation.

Methods

Data sources

Data on mother, delivery and infant characteristics were obtained from computerized antenatal, obstetrical and neonatal records within the counties of Stockholm and Gotland, Sweden (the "Stockholm-Gotland Obstetric Database"). All antenatal, delivery and postnatal care units in the region use the same medical record system (Obstetrix, Siemens Inc.). All data from the medical record system is daily forwarded to the database, which includes detailed information on maternal, pregnancy, delivery and infant health parameters from 2008 and forwards. The study was approved by the regional ethical vetting board in Stockholm, Sweden, nr 2009/275-31 and 2012/365-32. Patient data was retrieved from a medical record system, and there was no informed consent prior to inclusion in the study.

Study Population

There were 49 604 women who delivered their first live singleton infant in cephalic presentation at ≥37 completed gestational weeks from January 1st, 2008 through December 31st, 2012. After excluding elective Caesarean deliveries (n=2 011) and induced deliveries (n=9 372), the study population included 38 221 births. We also excluded 2 683 emergency Caesarean deliveries without data on retracted cervix, 521 deliveries with incomplete data from the labor partograph, 2 185 deliveries with no vaginal examination from retracted cervix to birth and 36 deliveries without data on Apgar score. The final study sample included 32 796 births.

Exposures and outcomes

Labor partograph data were used to measure the duration of second stage of labor, defined as time in minutes from the first notation of a fully retracted cervix until delivery. Duration of second stage of labor was categorised into 5 groups: less than 1 hour (0-59 minutes, reference); 1 to <2 hours (60-119); 2 to <3 hours (120-179); 3 to <4 hours (180-239); and 4 hours or more (≥240 minutes). Outcome was defined as an Apgar score of <7 or <4 at 5 minutes, respectively. Information on maternal height, BMI and smoking was collected at the first attendance to antenatal care, generally at 8-12 gestational weeks. BMI was calculated as weight in kilograms (measured by a midwife) divided by height in square meters (self-reported). Delivery characteristics, such as vaginal examinations, epidural analgesia, oxytocin for labor augmentation, and mode of delivery, were obtained from the partograph and standardized delivery records. Infant characteristics such as time of birth, Apgar score, birth weight and head circumference were registered in the neonatal record. In 94.3% of pregnancies, gestational age was dated based on ultrasound examination, which is offered to all women in early second trimester. If data on ultrasound was not available, last menstrual period was used for pregnancy dating. Birth weight by gestational

age was calculated using the sex-specific Swedish reference curve for normal foetal growth.[8] Variables were categorized according to Table 1.

Statistical analyses

Crude and adjusted odds ratios with 95% confidence intervals (CI) were calculated by logistic regression, and models included adjustments for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference. In a secondary model, we also included epidural analgesia. Epidural analgesia and mode of delivery were a priori considered as possible effect modifiers of the association between duration of second stage of labor and low Apgar scores. Effect modification was tested by stratification and insertion of an interaction variable in the regression models. A p-value <0.05 was considered statistically significant. Oxytocin is commonly used for augmentation of contractions in prolonged labor. As oxytocin often leads to hyperstimulation, with resulting fetal distress and subsequent low Apgar scores,[9] oxytocin was considered an intermediate variable in the causal pathway between prolonged labor and low Apgar scores. Data on oxytocin augmentation was therefore not included in the adjusted models.

Results

The distribution of maternal, delivery and infant characteristics and rates of low Apgar scores at 5 minutes are presented in Table 1. There were 227 infants (0.7%) who had a 5 minute Apgar score <7. Rates of Apgar scores <7 at 5 minutes were increased among infants of older (≥35 years) mothers, mothers with short stature (≤154 cm), epidural analgesia, oxytocin augmentation, longer durations of second stage of labor and post term delivery (≥42 weeks). Male sex, birth weight for gestational age less than the 3rd or more than the 97th percentile, and a large head circumference (≥38 cm) were also associated with increased rates of Apgar scores <7. A total of 40 infants (0.1%) had an Apgar score <4 at 5 minutes. Rates of Apgar scores <4 at 5 minutes were increased among infants of mothers aged 30 or more, mothers with short stature, oxytocin augmentation or longer durations of second stage of labor. Birth weight for gestational age less than the 3rd or more than the 97th percentile were also associated with increased rates of Apgar scores <4.

Duration of second stage of labor and Apgar score <7 at 5 minutes

Of 32 796 nulliparous women with spontaneous onset of labor, the duration of second stage of labor was less than 1 hour in 32.7% of all deliveries, 1 to 2 hours in 28.9%, 2 to 3 hours in 17.9%, 3 to 4 hours in 11.9%, and 4 hours or more in 8.6%. Compared to a second stage of labor of less than 1 hour, a duration of labor from 1 to <2 hours was associated with an 80% increased risk of Apgar score <7 at 5 minutes in analyses adjusted for maternal and infant characteristics. Rates and risks increased gradually with longer durations and a second stage of 4 hours or more was associated with a more than two-fold increased risk of an Apgar score <7 in adjusted analyses (Table 2).

Duration of second stage of labor and Apgar score < 4 at 5 minutes

Compared to a second stage of labor of less than 1 hour, duration of 3 to <4 hours was associated with a more than 4-fold increased risk of an Apgar score <4 at 5 minutes in adjusted analyses. Duration of 4 hours or more was associated with an almost 3-fold increased risk of Apgar score <4 in the crude analysis, but after adjusting for maternal and infant characteristics, the risk was no longer significantly increased (Table 3).

Epidural treatment

There was no significant interaction on the OR scale between epidural analgesia and duration of the second stage of labor with respect to Apgar scores at 5 minutes <7 and <4 (p=0.33 and 0.52, respectively). Sensitivity analyses by restriction to deliveries with epidural analgesia produced similar, although underpowered, results (supplemental table 1). Epidural analgesia was associated with increased rates of low Apgar scores at 5 minutes (Table 1). Rates of epidural analgesia consistently increased with time from retracted cervix to birth: from 44% if time of second stage was less than 1 hour, to 81% if time was ≥4 hours (data not provided in table). Therefore,

epidural treatment was regarded as a confounder, and was adjusted for in multivariable analyses. When analyses were additionally adjusted for epidural analgesia, risk of an Apgar score <7 at 5 minutes generally increased with time of second stage of labor. Compared with a second stage of labor of less than 1 hour, a second stage duration of 3 to <4 hours was associated with a 4-fold increased risk of Apgar score <4 at 5 minutes when also adjusting for epidural analgesia (Table 3).

Mode of delivery

Finally, we detected an effect modification of mode of vaginal delivery (non-instrumental and instrumental vaginal delivery) on the association between duration of second stage of labor and low Apgar scores at 5 minutes ($p<0.05$). Duration of second stage of delivery was positively associated with low Apgar scores in non-instrumental vaginal deliveries, but not in instrumental vaginal deliveries (Table 4).

Discussion

In this large population-based cohort study we found that risks of low Apgar score at 5 minutes increased with duration of second stage of labor, also after taking maternal, delivery and foetal characteristics into account. The positive association between prolonged second stage of labor and low Apgar score was confined to non-instrumental vaginal deliveries.

Virtually all infants born in western countries are assigned an Apgar score at 1, 5 and 10 minutes after birth. The Apgar score was originally created by Virginia Apgar,[10] to predict short-term outcomes of the infant, and to identify infants in need of resuscitation.[10] Recent reviews show that an Apgar score of <7 at 5 minutes also predicts subsequent neurologic disability [11-13] and cognitive impairments in adults.[14, 15] Apgar score at 1 minute is also associated to later morbidity, such as epilepsy[16] and poor functioning in cognitive tests at the age of 18[15], but the association is weaker. Infants that increase their Apgar scores between 1 and 5 minutes have decreased risks of adverse outcomes in later life, compared to those who are still depressed at 5 minutes.[11, 16 , 13]

Most previous studies report no association between the duration of second stage of labor and adverse infant outcomes, such as low Apgar scores at 5 minutes[6, 17, 18Janni, 2002 #1238, 19-21] or umbilical cord acid-base status.[17, 22] However, a low Apgar score at 5 minutes is a rare outcome and all the above mentioned studies were underpowered to detect any associations of realistic magnitude. In contrast, longer durations of second stage of labor have been associated with more common outcomes, such as a low Apgar score at 1 minute[23, 21] and admission to neonatal care units.[17, 18] One large study that investigates the success rates of vaginal delivery in prolonged second stages, reports small absolute increased risks of composite neonatal morbidity, admission to NICU, neonatal sepsis and Apgar < 4 at 5 minutes in nulliparous women with a prolonged second stage, especially if they were not treated with epidural.[24] The above mentioned, and our findings, indicate that a prolonged second stage may influence the infant's condition immediately after birth.

A review of 8 articles published in 1990-2004 found no associations between a prolonged second stage of labor and neonatal outcomes, such as Apgar score at 5 or 10 minutes; umbilical artery acid-base status; or admission to neonatal care units.[5] This review reports that, although most studies included prospectively collected data, there were several limitations to the studies, such as unclear or over-simplified categorizations of second stage of labor that did not consider parity or analgesia, different definitions of the onset of second stage of labor, lack of data on confounding factors and absence of analyses of effect modification. To our knowledge, only two studies

included individual data on epidural analgesia as a confounder in the analyses[25, 26] but there is no report on whether epidural analgesia was tested for effect modification.

Strengths and limitations

Major strengths of the current study include the use of a large population-based database with prospectively collected information during pregnancy and labor. We were able to clearly define the start of the second stage of labor and we had access to all vaginal examinations, interventions during delivery as recorded in the partograph, and many important co-variates. We tested for interaction between time of second stage of labor and epidural analgesia as well as mode of delivery, which is another strength of the study. A limitation is that we did not have access to time or method of pushing during labor. Although we used a large database, the number of infants with Apgar scores <4 was low and led to reduced statistical power. Furthermore, because the study was restricted to first time mothers with spontaneous onset of labor, and the results may not be generalizable to parous women or induced deliveries.

Epidural analgesia is a common intervention during labor, especially in nulliparous women, and was present in almost 60% of the study population. In second stages of labor of more than 4 hours, 81.3% had epidural analgesia. We did not detect any statistically significant interactions between epidural analgesia on the association between prolonged second stage of labor and low Apgar scores. Epidural analgesia was therefore added to the adjusted models, resulting in slightly decreased risk estimates.

Oxytocin augmentation is used to stimulate labor and to treat hypocontractility of the uterus[4] and it becomes more common as the second stage of labor extends in time. Oxytocin may also act as a mediator on the relationship between prolonged second stage and low Apgar scores, and adjusting for oxytocin would therefore underestimate the risk. Because of the complex relationship of oxytocin to labor progression and the association to Apgar scores, and its intertwined relationship to duration of second stage, we decided not to use this variable in the analyses.

Prevention of major disability is a main priority in modern obstetrics. In contrast to previous studies, our results suggest that a shorter duration of second stage of labor is associated with better Apgar scores in new born infants. The effects on more common and later adverse outcomes are, as yet, unknown. As of today, we cannot recommend any treatments that would safely shorten the duration of second stage, but we believe that these results are important in every-day decisions for clinical obstetricians.

Conclusion

A second stage of labor of three hours or more is associated with low 5-min Apgar scores in non-instrumental deliveries of first-born infants also after taking maternal and foetal characteristics into account. In clinical decisions, it is important to consider time from retracted cervix to delivery in relation to risks of adverse neonatal outcomes.

Author contributions

All authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis and the study hypothesis arose before inspection of the data. M.A. has contributed to the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation of the manuscript. A.S., T.F., G.P. S.C. and O.S have contributed to the design and conduct of the study; interpretation of the data; and review of the manuscript. The final version of the manuscript has been approved by all authors.

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Ethical standards

This study was approved by the regional ethical vetting board in Stockholm, Sweden, nr 2009/275-31 and 2012/365-32. Patient data was retrieved from a medical record system, and there was no informed consent prior to inclusion in the study.

Conflict of interest

The authors declare that they have no conflict of interest.

Data sharing

Original study data can be shared, after approvement from the regional ethical vetting board in Stockholm, Sweden.

Tables

Table 1. Maternal, delivery and infant characteristics, and Apgar score at 5 minutes. Nulliparous women with term and post term singleton live births, Stockholm-Gotland Birth Cohort, Sweden, 2008-2012.

		Apgar score at 5 minutes			
	Total	< 7		< 4	
Maternal characteristics	**N**	**n**	**rate/ 1000**	**n**	**rate/ 1000**
	32 796				
Age (years)					
<25	5763	39	6.8	5	0.9
25-29	10866	64	5.9	10	0.9
30-34	11702	82	7.0	17	1.5
≥35	4436	42	9.5	8	1.8
Missing	29	0	-	0	-
Height (cm)					
≤154	1148	24	20.9	4	3.5
155-164	10807	87	8.1	15	1.4
165-174	16936	105	6.2	20	1.2
≥175	3905	11	2.8	1	0.3
BMI (kg/m^2)					
<18.5	1228	8	6.5	0	0.0
18.5-24.9	23087	161	7.0	24	1.0
25-29.9	5456	42	7.7	11	2.0
≥30	1695	7	4.1	4	2.4
Missing	1330	9	-	1	-
Daily smoking					
Non-smoker	31329	223	7.1	39	1.2
Smoker	1451	4	2.8	1	0.7
Missing	16	0	-	0	-
Delivery					
Epidural analgesia					
No	13379	64	4.8	12	0.9
Yes	19417	163	8.4	28	1.4
Time from retracted cervix to delivery (hours)					
<1	10731	44	4.1	7	0.7
1 to <2	9491	66	7.0	10	1.1
2 to <3	5856	43	7.3	5	0.9
3 to <4	3898	35	9.0	10	2.6
≥4	2820	39	13.8	8	2.8
Instrumental delivery					
No	26068	104	4.0	14	0.5
Yes	6728	123	18.3	26	3.8
Infant characteristics					
Sex					
Male	16635	141	8.5	20	1.2
Female	16161	86	5.3	20	1.2
Gestational week					
37	1344	6	4.5	1	0.7
38	3403	20	5.9	6	1.8
39	8005	37	4.6	6	0.7

40	11480	83	7.2	14	1.2
41	7394	61	8.2	11	1.5
>=42	1170	20	17.1	2	1.7
Birth weight for gestational age (percentiles)					
<3rd	357	5	14.0	1	2.8
3rd to <10th	2059	22	10.7	3	1.5
10th to 90th	28491	176	6.2	29	1.0
>90th to 97th	1519	14	9.2	4	2.6
>97th	343	6	17.5	2	5.8
Missing	27	4	-	1	-
Head circumference (cm)					
<36	23967	140	5.8	25	1.0
36	5789	43	7.4	9	1.6
37	2220	19	8.6	2	0.9
≥38	662	9	13.6	1	1.5
Missing	158	16	-	4	-

Table 2. Time from retracted cervix to birth and risk of Apgar score < 7 at 5 minutes. Nulliparous women with term and post term singleton live births.

		Apgar 5 min < 7							
				Odds ratio (95% CI)					
Time from retracted cervix to birth (hours)	**Total 32 796**	**n**	**rate/ 1000**	**Crude**		**Adjusted[a]**		**Adjusted[b]**	
<1	10731	44	4.1	1.00	Reference	1.00	Reference	1.00	Reference
1 to <2	9491	66	7.0	1.70	1.16-2.49	1.78	1.19-2.66	1.71	1.14-2.56
2 to <3	5856	43	7.3	1.80	1.17-2.74	1.66	1.05-2.62	1.55	0.98-2.46
3 to <4	3898	35	9.0	2.20	1.41-3.44	2.08	1.29-3.35	1.91	1.18-3.09
≥4	2820	39	13.8	3.41	2.21-5.25	2.71	1.67-4.40	2.45	1.49-4.02

[a]Adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference.

[b]Adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age, head circumference and epidural analgesia.

Table 3. Time from retracted cervix to birth and risk of Apgar score < 4 at 5 minutes Nulliparous women with term and postterm singleton live births.

		Apgar 5 min < 4							
				Odds Ratio (95% CI)					
Time from retracted cervix to birth (hours)	**Total 32 796**	**n**	**rate/ 1000**	**Crude**		**Adjusted[a]**		**Adjusted[b]**	
<1	10731	7	0.7	1.00	Reference	1.00	Reference	1.00	Reference
1 to <2	9491	10	1.1	1.62	0.62-4.25	1.89	0.68-5.24	1.85	0.67-5.16
2 to <3	5856	5	0.9	1.31	0.42-4.13	1.47	0.44-4.87	1.42	0.42-4.75
3 to <4	3898	10	2.6	3.94	1.50-10.36	4.28	1.52-12.05	4.08	1.42-11.74
≥4	2820	8	2.8	4.36	1.58-12.03	2.77	0.82-9.38	2.62	0.75-9.10

[a]Adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference**.**

[b]Adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age, head circumference and epidural analgesia.

Table 4. Time from retracted cervix to birth and risk of Apgar score < 4 at 5 minutes stratified by mode of delivery (n=32 021). Nulliparous women with term and postterm singleton live births.

	Apgar 5 min < 7							
	Non-instrumental				Instrumental			
Time from retracted cervix to birth (hours)	**n**	**Rate/1000**	**aOR[a]**	**95% CI**	**n**	**Rate/1000**	**aOR[a]**	**95% CI**
<1	20	2.0	1.00	Reference	22	24.1	1.00	Reference
1 to <2	39	4.8	2.66	1.49-4.75	24	19.4	0.89	0.48-1.65
2 to <3	25	5.6	2.65	1.37-5.11	18	14.4	0.60	0.31-1.17
3 to <4	10	4.1	2.41	1.09-5.33	20	15.1	0.61	0.32-1.18
≥4	10	8.3	3.77	1.60-8.88	24	19.4	0.70	0.37-1.36

aOR[a] adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference.

Supplemental table 1. Time from retracted cervix to birth and risk of Apgar score <7 at 5 minutes.

Restricted analyses: Only women with epidural treatment

	Epidural			
	Crude		Adjusted[a]	
Time from retracted cervix to birth	OR	95% CI	OR	95% CI
0-59 min	1.00	Reference	1.00	Reference
60-119 min	1.57	0.97-2.54	1.63	0.98-2.72
120-179 min	1.40	0.83-2.36	1.26	0.72-2.23
180-239 min	1.84	1.09-3.12	1.73	0.98-3.03
240+ min	2.31	1.36-3.93	1.75	0.96-3.17

[a]adjusted for maternal age, height, BMI, smoking, sex, gestational age, sex-specific birth weight for gestational age and head circumference.

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