Predictors of cesarean section following elective post-dates induction of labor in nullipara with uncomplicated singleton vertex pregnancies

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ABSTRACT

Objectives: Although "post-dates" is among the most common indications for induction of labor, no studies have identified the predictors of cesarean section (C/S) in that population. The high cesarean rate in our institution for this group of women triggered us to assess different induction practices to elicit potential causes.

Methods: We conducted a hospital-based retrospective cohort analysis using chart reviews of all nullipara women with induced labor at the Children's and Women's Health Centre of British Columbia, Vancouver, Canada, during the 2-year period, April 1998 to March 2000. The C/S rate was compared among 3 groups of women who were divided according to their induction method.

Results: Three hundred and thirty-nine women meeting the inclusion criteria were induced. Of the 25 women who received oxytocin "ideally" and the 111 women who did not, 7 (28%) and 53 (48%) were delivered by C/S, (χ^2=3.228 p=0.07; relative risks 0.59 [95% confidence interval 0.30, 1.13]). A significantly lower C/S rate (χ^2=21.9, p<0.0005) was found among women induced with prostaglandin (PG) alone (19.4%) compared with those induced with PG and oxytocin, whether oxytocin was given "ideally" (38.3%) or "not ideally" (45.4%). Of women who received oxytocin, there was no difference in chorioamnionitis (χ^2=0.485, p=0.49) between those who had an early membrane rupture (with or pre-oxytocin, 22.4%) and those who had membrane rupture following a period of oxytocin infusion (18.5%).

Conclusion: The need for oxytocin or >2 doses of PG is associated with increased risk of C/S. Whether oxytocin was given according to protocol (ideally) or not, made no difference to the C/S risk in this population.

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During an uncomplicated pregnancy, the risk of interrupting the pregnancy outweighs the risks of allowing the pregnancy to continue naturally until the onset of spontaneous labor. However, induction of labor has therapeutic merit when the benefits of an expedited delivery outweigh the risks of continuing the pregnancy. In response to the post-term trial,[1] post-term pregnancy is the most common indication for induction in our institution. In nullipara, overall induction is associated with twice the risk of cesarean

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section (C/S) when compared with spontaneous labor.[2] Reports on labor induction have shown that the state of the cervix is the most important predictor of success.[2] The state of the cervix can be objectively assessed by the Bishop's,[3] or modified Bishop's score.[4] The American College of Obstetricians and Gynecologists (ACOG) have suggested that a score of ≥6 is considered favorable and likely to result in successful labor induction, and that a score of >8 predicts that the probability of vaginal delivery after labor induction is similar to that after spontaneous labor.[5] Cervical ripening pre-labor and during the latent phase of labor improves the chances of vaginal delivery.[6,7] A meta-analysis comparing prostaglandin (PG) with placebo or no treatment indicates that PG significantly improves the cervical score and "ripen the cervix". It also concluded that PG increases the chance of labor onset during ripening, decreases the length of induced labor, improves neonatal outcomes, decreases the chance of instrumental delivery, and decreases the C/S rate for "failed induction".[8] Some of those findings were supported by a recent Cochrane review.[7] Induction of labor with only oxytocin infusion is associated with a significant proportion of women remaining undelivered after 24 hours.[5] Artificial rupture of the membranes (ARM) at the time of oxytocin administration appears to sensitize the myometrium to the action of oxytocin, in part by improving head-to-cervix pressure.[9,10] In randomized controlled trials, ARM with oxytocin was superior to oxytocin alone.[11,12]

The Canadian guidelines for the induction of labor recommend the following: (i) In an uncomplicated pregnancy, there is no evidence to support elective induction or cervical ripening prior to 41 completed weeks. (ii) For an unfavorable cervix, in the absence of contraindications, time should be taken to achieve cervical ripening with prostaglandin E_2 (PGE_2) gel or a suitable alternative. (iii) With a favorable cervix, ARM with concomitant administration of oxytocin is the method of choice, and (iv) Oxytocin should be used according to an established protocol.[2] In response to the high C/S rate in our institution (34.7%) for women induced post-dates following an uncomplicated cephalic pregnancy, we examined a retrospective cohort of these women in an attempt to evaluate the institutional practice around induction, with the aim of identifying any deviations from recommended guidelines to determine whether or not adherence to guidelines influences the likelihood of C/S. Since there is a perceived reluctance to perform early ARM in our institution due to fear regarding chorioamnionitis, as a secondary objective, we examined the relationship between any ARM and chorioamnionitis.

Methods. ***Study design.*** We conducted a hospital-based retrospective cohort analysis using data obtained from chart review. The cohort included all nullipara women with induced labor who delivered at the Children's and Women's Health Centre of British Columbia (CWHCBC) during the 2-year period, April 1998 to March 2000. Included were nullipara women with an uncomplicated cephalic singleton pregnancy, who had their labor induced with PGE_2, oxytocin, or both, between 41 and 42 completed weeks of gestation (287-294 days). Exclusion criteria were: multiparity, non-cephalic presentation, complicated or multiple pregnancies, gestational age <287 or >294 days, women who presented in labor at the time of induction, and those who never received PGE_2 or oxytocin (such as ARM only). The following data were collected: patient's age (years); gestational age (days) at the time of induction confirmed by accurate last menstrual period, early ultrasound, or both; recorded variables of Bishop's and modified Bishop's scores at the first dose of PGE_2 or oxytocin; the number of PGE_2 doses received; timing of membrane rupture in relation to oxytocin (pre, with, or post); duration of oxytocin (minutes); maximum dose of oxytocin (mU/minute), whether oxytocin was stopped for >1 hour after reaching the maximum dose; delivery mode (spontaneous vaginal delivery, vacuum, forceps or C/S); presence of chorioamnionitis; and birth weight (grams). Prostaglandin E_2 was given as either Prostin gel (Pharmacia and Upjohn Inc, Mississauga, ON, Canada) one gram or 2 grams every 6 hours to a maximum of 4 doses (292 women) or Cervidil sustained release pessary (Ferring Inc, Toronto, ON, Canada) every 12 hours to a maximum of 3 doses (11 women). Cervidil induces a similar pattern of PGE_2 and $PGF_2\alpha$ metabolite concentrations in maternal circulation as one mg intra-vaginal gel.[13] When calculating the Bishop's score, and in the absence of documentation on cervical effacement, a modified Bishop's scoring system was used where length in centimeters (cm) instead of percentage of effacement (%) was used as a variable (0-0.5 cm = 80% = 3 scores, 0.51-1 cm = 60-70% = 2 scores, 1.1-1.5 cm = 40-50% = 1 score, >1.5 cm = 0-30% = 0 score). A dilatation of ≥4 cm implied 100% effacement, anterior position, and soft consistency, unless otherwise specified (that assumption was verified in the complete data). The women included in the study were divided into 3 groups. Group A represents the "ideal" oxytocin group. For these women (i) If the cervical length was ≥1 cm, oxytocin was initiated only after cervical ripening with PG, (ii) Oxytocin was started at a cervical length of <1 cm, (iii) ARM was performed at the commencement of oxytocin infusion (unless

already previously ruptured), and (iv) Oxytocin was given according to protocol as follows: increasing infusion by one mU/30 min to a maximum of 20 mU/min and not discontinuing the infusion for >60 min once the maximum rate had been reached (unless awaiting C/S). Group B represents the "non-ideal oxytocin" group, and it consists of all women who were given oxytocin, but where protocol infractions occurred. Group C included all women who never received oxytocin. All women in this group followed the hospital dosing protocol described above. *A priori*, our primary hypothesis was that receiving oxytocin in an "ideal" fashion (group A) is associated with a lower risk for being delivered by C/S.

Statistical analysis. Categorical variables were compared using either the Fisher's exact or χ^2 tests as appropriate (SPSS for windows version 11.0) and relative risks (Review Manager version 4.1, Winter tree Software, Oxford, UK). Thus, our type I error rate is probably larger than the nominal significance level used, $P<0.05$.

Results. Within the 2-year period studied, 339 women met the eligibility criteria. Baseline maternal demographics and the modes of induction and delivery are summarized in **Table 1**. The need for oxytocin was associated with increased risk of C/S (**Table 2**). The length or dilatation of the cervix when starting induction did not influence the risk of C/S (**Table 3**). In the absence of oxytocin, the need for more than 2 doses of PG was associated with increased risk of C/S (**Table 4**). Membrane rupture following the commencement of oxytocin infusion did not alter the risk of being delivered by C/S (**Table 4**). The charts of only 60 (17.7%) women had sufficient details of the Bishop's score (at the time of receiving oxytocin) to permit its derivation. Within that group, women with a Bishop's score ≤10 (9/15) at the commencement of the induction with oxytocin were significantly more likely to be delivered by C/S than those with scores >10 (11/45) ($\chi^2 = 6.4$, $p=0.01$; relative risk (RR) 2.46 [95% confidence interval {CI}1.27, 4.75]). The small numbers did not permit a more refined examination of the relationship between pre-induction Bishop's score and C/S rate, and compelled us to examine the cervical state using 2 markers of "ripeness", cervical length and dilatation. Chorioamnionitis complicated 46 (13.6%) labors with no significant difference in its rate between those who had membrane rupture pre- or with oxytocin (26/116, 22.4%) compared with those who had membrane rupture post-oxytocin (17/92, 18.5%) ($\chi^2 = 0.485$ $p=0.49$; RR 1.21 [95% CI 0.70, 2.10]). Of all women receiving oxytocin, only 22% received it in an ideal fashion. However, there was

Table 1 - Baseline maternal demographics, modes of induction, and modes of delivery (N = 339).

Demographics	**Mean (SD)**
Maternal age (years)	30.4 (4.9)
Gestational age (days)	290.7 (1.3)
Birth weight for all (grams)	3720.2 (445)
Birth weight for SVD (grams)	3681.2 (381.2)
Birth weight for vacuum (grams)	3650.6 (516.9)
Birth weight for forceps (grams)	3632.9 (461)
Birth weight for C/S (grams)	3827.6 (484.8)
Induction/augmentation method	**n (%)**
PGE_2 (± oxytocin)	303 (89.4)
Oxytocin (± PGE_2)	210 (61.9)
PGE_2 + oxytocin	174 (51.3)
PGE_2 alone	129 (38.1)
Oxytocin alone	36 (10.6)
Maximum oxytocin infused (mU/min)	10.6 (7)
Oxytocin used "properly"	95/210 (45.2)
Timing of membrane rupture*	**n (%)**
Pre-oxytocin	241 (71.1)
With oxytocin	6 (1.8)
Post-oxytocin	92 (27.1)
Mode of delivery	**n (%)**
SVD	132 (38.9)
Vacuum	24 (7.1)
Forceps	66 (19.5)
C/S	117 (34.5)

*Either spontaneous or artificial,
SVD - spontaneous vaginal delivery, C/S - cesarean section,
PGE_2 - prostaglandin E_2, +; with, -; without, mU - milli-units,
SD - standard deviation

Table 2 - The influence of the pattern of oxytocin use on the risk of being delivered by C/S (N = 339).

Group*	**PGE_2 used n (%)**	**C/S n (%)**	**RR [95% CI]/ χ^2 P**
A) Ideal oxytocin	44/47 (94)	18/47 (38)	
B) Not ideal oxytocin	130/163 (80)	74/163 (45)	
C) No oxytocin	129/129 (100)	25/129 (19)	
A versus B			0.84 [0.57, 1.26]
A versus C			1.98 [1.19, 3.28]
B versus C			2.34 [1.59, 3.46]
			$p<0.001$

*Group A - ideal oxytocin: oxytocin started at a cervical length of <1 cm, membranes ruptured pre/with oxytocin, and oxytocin given as per protocol (see text for details). Group B - non-ideal oxytocin: women who were given oxytocin, but missing any of the 3 criteria of Group A. Group C - all women who never received oxytocin.
PGE_2 - prostaglandin E_2, C/S - caesarean section,
RR - relative risk, CI - confidence interval

Table 3 - The influence of cervical length and dilatation on the mode of delivery (N = 339).

Cervical state at induction	n (%)	Cesarean section n (%)	RR for cesarean section [95% CI]
Cervical length 273 (66 missing)			<1 cm vs ≥1 cm
<1 cm	43 (15.8)	14 (32.6)	0.98 [0.62, 1.56]
≥1 cm	230 (84.2)	76 (33)	
Cervical dilatation 327 (12 missing)			>2 cm vs <2 cm
>2 cm	54 (16.5)	15 (27.8)	0.78 [0.49, 1.22]
≤2 cm	273 (83.5)	98 (35.9)	
Cervical length and dilatation			<1 cm long, >2 cm dilated vs other*
<1 cm long, >2 cm dilated	18 (6.6)	4 (22.2)	0.66 [0.27, 1.59]
other*	255 (93.4)	86 (33.7)	

*cervical length ≥1 cm and/or cervical dilatation ≤2 cm, CI - confidence interval, RR - relative risk, vs - versus

Table 4 - The influence of the number of PGE_2 doses (overall and subdivided according to oxytocin use) and the timing of membrane rupture on the risk of being delivered by caesarean section (N = 339).

Mode of induction (n)	PGE_2 doses (n)/ timing of rupture	Cesarean section n (%)	RR [95% CI]
			≤2 vs ≥3 doses
All PGE_2 (303)	1	48/160 (30)	
	2	36/96 (38)	
	3	16/34 (47)	0.62 [0.44, 0.88]
	4	4/4 (100)	
	Missing	9	
PGE_2 + oxytocin (174)	1	35/85 (41)	
	2	27/52 (52)	
	3	13/28 (46)	0.85 [0.59, 1.24]
	4	4/4 (100)	
	Missing	5	
PGE_2 – oxytocin (129)	1	13/75 (17)	
	2	9/44 (21)	
	3	3/6 (50)	0.37 [0.15, 0.90]
	Missing	4	
Timing of membrane rupture			Early (pre-/with oxytocin and no oxytocin) vs. late (post-oxytocin)
	Early	82/247 (48)	
	Late	35/92 (38)	0.87 [0.64, 1.20]

PGE_2 - prostaglandin, RR - relative risk, CI - confidence interval

no significant difference in the C/S rate between the ideal (A) and "non-ideal" (B) groups (**Table 2**).

Discussion. In this study, we examined the cervical state, and timing of amniotomy in relation to the need for C/S associated with post-dates induction in nullipara. We confirmed that pre-induction Bishop's score predicts the risk of C/S.[7,8] The reported effects of PGE_2 on C/S rate have been inconsistent. While some studies have shown a reduction, most have not shown a significant decrease.[8,14,15] We have shown (**Table 2**) a significant reduction in the C/S rate in the PGE_2 only group in comparison with oxytocin; however, the use of increasing doses of PGE_2 was associated with an increased risk for cesarean delivery (**Table 4**). That was true for all women who received PGE_2 in general, and also for those who never received oxytocin. These women could have benefited from other means of cervical ripening, such as a Foley catheter,[16-22] or further expectant management. On the other hand, this result could be due to selection bias as greater numbers of PG applications were likely required when the cervix was unresponsive. We found that oxytocin use predicted C/S. This finding is open to interpretation. Perhaps women who never received oxytocin had a more "favorable" cervix, and a better Bishop's score (selection bias). Another possibility is, more fetal distress occurring on those whom received oxytocin; however, we do not believe that this alone can explain the 2-fold difference in C/S between women

who required oxytocin and those who did not. The American College of Obstetricians and Gynecologists has stated that any of the oxytocin regimens available are appropriate for labor induction,[5] one of which is the low dose protocol used at our institution. Yet, some studies do show a significantly lower C/S rate in the high dose regimen (6 mU/min increments),[23] and a trend towards a lower C/S rate with an intermediate regimen (4 mU/min increments)[24] compared with the regimen used at CWHCBC. Using a more aggressive regimen than the one used at our institution might have made a difference. Some argue that early rupture of the membranes might increase the risk of chorioamnionitis.[25,26] Our data did not support this observation. More PGE_2 was used in group A compared with group B (**Table 2**), which may indicate that PGE_2 does produce a more "favorable" cervix, as reflected in the trend towards a lower C/S rate in group A. Allowing for a type I error of 5%, the sample size we observed in the 2 oxytocin groups gave us an 80% chance of detecting a 20% decrease in C/S rates even when using a 2 sided test. We believe that a 10% reduction in the C/S rate would be clinically important, but our study was insufficiently powered to find such a difference. Again, by using a stricter definition of an "ideal" induction, we might have been able to determine a true difference between groups A and B (**Table 1**), but both the retrospective nature and the sample size of our study precluded this. There are many potential sources for protocol infractions during induction. For example; was oxytocin increased at least 1 mU/30 min (low dose protocol)? Was oxytocin stopped for a prolonged time before it was resumed again? Was the cervix favorable before oxytocin was commenced? Did the patient receive sufficient oxytocin to validate the decision to perform a C/S for dystocia? Why oxytocin was stopped, interrupted, or not increased (fetal distress, hyperstimulation, or nursing staff related issues)? The retrospective nature of our study precluded the examination of all of these aspects, but we were surprised by the low use of Bishop's score (18%) and the low compliance with an agreed upon oxytocin protocol (45%). The most common infraction protocol was that oxytocin was discontinued for no reason discernible from the review of the chart.

We conclude that the C/S rate in this group of women was high, that the adherence to guidelines was poor, and that an early response to PG (resulting in no exposure to oxytocin) was associated with a reduction in C/S risk. There is tantalizing (p=0.07) evidence to support the use of oxytocin according to the protocol following amniotomy, but an appropriately powered randomized controlled trial is required to determine the impact of labor management in this group of women. Until such a study is carried out, we recommend that caregivers continue to follow the ACOG and Society of Obstetricians and Gynecologists of Canada guidelines for labor induction.

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