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Oxytocin augmentation or induction of labor in term pregnant women: a randomized controlled trial to evaluate a 15 - versus 40 - minute dose increment interval

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ABSTRACT

Objectives 1. To compare efficacy of a 15-vs. a 40-minute interval for increasing the dosage oxytocin infusion in induction or augmentation of labor.
2. To determine whether an increase in the oxytocin dosage interval would decrease the incidence of uterine hyperstimulation and other complications.

Design A randomized controlled trial study.

Setting Srinagarind Hospital, Faculty of Medicine, Khon Kaen University.

Subjects and Methods We included 210 full-term pregnant women requiring induction or augmentation of labor by oxytocin infusion between September 1999 and June 2000. Patients were randomly allocated by cealed envelope technic to incremental increases at 15-minute intervals (105 patients) or 40-minute intervals (105 patients). The main outcomes assessed were efficacy (duration and maximum dosage of oxytocin infusion, operatived delivery, emergency cesarean section, neonatal outcomes), uterine hyperstimulation and other complications (i.e. postpartum hemorrhage, precipitation of labor and suspected fetal distress).

Results The 40-minute interval protocol resulted in significantly lower maximum dosage of oxytocin infusion (p-value = 0.004) and less uterine hyperstimulation (RR 0.40,95% CI 0.21 - 0.75). There was a trend in reduction in the occurrence of suspected fetal distress (RR 0.61, 95% CI 0.36 -1.03), precipitation of labor (RR 0.66,95% CI 0.13 -3.31), postpartum hemorrhage (RR 0.56, 95% CI 0.17-1.83), operative delivery (RR 0.8, 95% CI 0.61-1.22) and emergency cesarean sections (RR 0.93,95% CI 0.57-1.53), but these differences did not reach statistical significance. There were also no differences between groups in the duration of oxytocin infusion or the number of days in hospital. Neonatal outcomes were unaffected by the dosage interval.

Conclusions For the induction and augmentation of labor in full-term pregnancies an increased oxytocin infusion rate at 40-minute intervals was superior to the 15-minute protocol in reducing the maximum dosage of oxytocin infusion and reducing the incidence of uterine hyperstimulation.

Key words: oxytocin infusion regimen, augmentation, induction

Oxytocin is a valuable tool in the induction and augmentation of labor. Postterm pregnancy, intrauterine growth retardation, pregnancy-induced hypertension, premature rupture of membranes represent some common indications for oxytocin administration. Many other medical complications during pregnancy demand oxytocin administration for labor induction. However, inappropriate oxytocin administration may result in many complications, such as uterine hyperstimulation, precipitated labor, fetal distress and uterine rupture.[1] In order to reduce the risk of these potential complications, the current recommendation is to administer oxytocin by intravenous infusion with incremental increase in the rate at regular 15-minute intervals, until adequate uterine contraction is achieved.[2-3]

Orhue *et al.* (1994)[4] compared a 15-minute vs. a 30-minute intervals incremental increase in infusion rate for the induction of labor in primigravida. The 30-minute group, had a lower rate of uterine hyperstimulation (odds ratio 0.17, 95% CI 0.015-1.906) and precipitated labor (odds ratio 0.233, 95% CI 0.042-0.557). No significant differences in progress of labor were found between the two groups.

Thinkhamrop *et al.* (1997)[5] reported that oxytocin infusion for the induction or augmentation of labor at Srinagarind Hospital was one of the significant factors associated with postpartum hysterectomy.

Seitchik *et al.* (1986)[6] reported that approximately 40 minutes was required for any particular dose of oxytocin to reach a "steady-state" and a maximal uterine contractile response.

Seitchik *et al.* (1984)[7] reported that a steady-state of plasma oxytocin concentration was achieved at 40-minute intervals. Was the oxytocin infusion rate made more frequent than every 40 minutes, it would result in hyperuterine contraction. This was our presupposition.

Our study was designed to evaluate the effectiveness of oxytocin infusion during labor among Thai women by varying the interval of increasing doses of oxytocin between 15 vs. 40 minutes.

Materials and methods

Participants in the study included low risk pregnant women who came to Srinagarind Hospital for delivery between October 1, 1999 and June 30, 2000. Inclusion criteria included patients with no antenatal complications and with gestational ages between 37 and 41 weeks. Well trained counselors explained the details of the study and obtained the written informed consent from each patient. Patients were then and randomly allocated into two groups using cealed envelope technic. Cervical dilatation were evaluated periodically until delivery.

The oxytocin infusion was 10 units of oxytocin in 1,000 mL of 5 % detrose / NSS. The infusion started at 1.5 mU/min (*viz.* 3 drops/min) using an automatically controlled infusion pump. Infusion rates were increased by 1.5 mU/min every 15 minutes (Group 1) or 40 minutes (Group 2). Uterine contractions and fetal heart rates were assessed every 15 minutes. Pelvic examinations for cervical dilatation were performed every 4 hours in the latent phase and every 2 hours in the active phase or immediately after membranes ruptured. The maximum rate of oxytocin infusion was not allow to exceed 40 mU/min.

If delayed cervical dilatation was observed, artificial rupture of membranes was performed when cervical dilatation was at least 3 cm. and the station was at least "0". Electronic uterine contraction monitoring was done to confirm that the uterine contraction was adequate (duration 40-60 sec, interval 2-3 min). If the fetal heart rates were less than 120 beats/min or more than 160 beats/min, oxytocin infusion was stopped and intrauterine fetal resuscitation was done immediately. The patient was then managed according to the hospital protocol.

For uterine hyperstimulation (greater than 5 times/10 min), the oxytocin infusion rate was reduced gradually until optimal uterine contractions were achieved.

Baseline data was collected from antenatal care records and confirmed by direct questioning. The experimental data was collected from labor room records by trained personnel. The student t-test was

used to test differences between the two groups for the duration of induction or augmentation of labor, length of hospital stay, and maximum oxytocin dosage by SPSS computer program.

Differences in the following variables were assessed by relative risks and 95% confidence intervals adjusted for potential confounding factors by SPSS computer program: 1) complications due to oxytocin administration 2) rate of operative obstetric deliveries (forceps and vacuum extraction) and cesarean section 3) rate of birth asphyxia (5-min Apgar scores <7).

This study was approved by the Ethics Committee, Khon Kaen University.

Table 1. Parity, cervical dilatation status, and indication for oxytocin use

	Group 1 (n=97)		Group 2 (n=98)	
	Mean	**SD**	**Mean**	**SD**
Age (yr)	25	3.9	26	4.4
Height (cm)	154.8	4.9	155.6	4.5
Weight (kg)	63.7	7.7	64.5	8.8
Gestational age (wk)	38.7	1.1	38.7	1.2
	Number of Patients	**Percent**	**Number of patients**	**Percent**
Parity				
Nulliparous	73	69.5	63	60.0
Multiparous	32	30.5	42	40.0
Cervical dilation				
≤ 3 cm	64	60.9	69	65.7
> 3 cm	41	39.0	36	34.3
Indication for oxytocin use				
PROM	10	9.52	8	7.82
Augmentation	95	90.48	97	92.18

Table 2. Duration of oxytocin infusion by cervical dilatation and parity

	Group 1		Group 2		p-value
	Mean (hr)	**SD**	**Mean (hr)**	**SD**	
Cervical dilation					
≤ 3 cm	4.25	3.02	5.31	3.20	0.06
> 3 cm	3.51	2.19	3.13	2.14	0.23
Parity					
Nulliparous	4.20	2.59	4.13	2.22	0.81
Multiparous	4.04	2.33	5.24	4.21	0.11

Table 3. Complication of oxytocin infusion

	15'	40'	
Complication	**Group 1/97**	**Group 2/98**	**RR 95% CI**
Hyperstimulation	28	8	0.40 (0.21 to 0.75)
Fetal distress	21	10	0.61 (0.36 to 1.03)
Postpartum hemorrhage	5	2	0.56 (0.17 to 1.83)
Precipitated labor	2	1	0.66 (0.13 to 3.31)

Table 4. Number of operative delivery and cesarean section

Type of deliveries	**Group 1**	**Group 2**	**RR 95% CI**
Operative obstetric deliveries	17	13	0.8 (0.61 to 1.22)
Cesarean section indication			
- Fetal distress	2	0	
- Cephalopelvic disproportion	6	7	
Total Number of cesarean section	8	7	0.93 (0.57 to 1.53)

Table 5. Neonatal outcomes and length of hospital stay

	Group 1		**Group 2**		**p-value**
	Mean	**SD**	**Mean**	**SD**	
Neonatal outcomes 5-min. Apgar score <7	0	-	0	-	-
Newborn weight (g)	2975	515	3081	352	0.09
Number of days in hospital	2.68	0.93	2.79	1.05	0.40

Results

Two hundred and ten patients, who came to deliver at Srinagarind Hospital, Khon Kaen University Faculty of Medicine, between October 1, 1999 and June 30, 2000, were randomly assigned into two groups of 105 patients each.

The maximum dosage of oxytocin administration (mU/min) was significantly higher in the 15-minute group (5.37 ± 3.72 versus 4.06 ± 2.59, p-value 0.004).

The duration of oxytocin infusion was defined or the time from the beginning of induction or augmentation until completed cervical dilatation. Patients who were delivered by cesarean section were excluded from this analysis, leaving 97 patients in Group 1 and 98 in Group 2. The durations of oxytocin infusion were 4.13 ± 2.48 hours in Group 1 and 4.35 ± 3.08 hours in Group 2, which was not a significantly different (p = 0.40).

The duration of oxytocin infusion was analyzed by stratifying cervical dilatation into categories of ≤ 3 cm and > 3 cm. Sixty percent of Group 1 and 65.7% of Group 2 patients had cervical dilatation of ≤ 3 cm when oxytocin infusion was started. Comparison of duration of oxytocin administration between the groups revealed

no significant differences. Stratifying patients by parity (into categories of nulliparous and multiparous patients) and comparing the duration of oxytocin administration between the two groups revealed no significant difference (Table 2).

Complications, including suspected fetal distress, postpartum hemorrhage, and precipitated labor, were more common in Group 1 than in Group 2, however the differences did not reach statistical significance. Uterine hyperstimulation was the only complication that was found to be significantly higher in 15-minate interval group (RR 0.40, 95% CI 0.21-0.75) (Table 3). The rates of operative delivery and cesarean section were not significantly different between the two groups, although both were more common in Group 1 (Table 4). No significant differences were found in neonatal outcomes or length of hospital stay between the two groups (Table 5).

Discussion

A significantly higher maximum dosage of oxytocin infusion and uterine hyperstimulation were recorded in the 15-minute group. There was a reduction in the occurrence of suspected fetal distress, precipitated labor, operative delivery, and emergency cesarean section rate in the 40-minute group though these differences did not reach statistical significance. There were no differences in the duration of oxytocin infusion, length of postpartum hospital stay, or neonatal outcomes between the two groups.

Chua *et al.* (1991)[8] compared a 15-minute vs. a 30-minute interval at the National University Hospital in Singapore. They had 112 patients in each group and also did not find any significant differences in the duration of labor, the cesarean section rate, hyperstimulation, abnormal fetal heart rate patterns, neonatal outcomes, or the length of postpartum hospital stay. The conclusion was that a 15-minute interval did not offer any advantage over a 30-minute one.

Satin *et al.* (1991)[9] also compared 15- vs. 30-minute increases in oxytocin infusion rates. They found a significantly higher failure rate among those in the 30-minute group ($p < 0.005$). However, their study was conducted among women who had unripe cervixes while ours was among pregnant women with ripe cervixes.

Foster *et al.* (1988)[10] reported a retrospective study on 174 pregnant women who were placed on oxytocin for augmentation. They also compared rate increases at a 15- vs. a 30-minute interval. They found significantly higher rates of uterine hyperstimulation and maximum dosage in the 15-minute group ($p = 0.0017$).

Orhue *et al.* (1993) [11] compared 45-minute vs. a 15-minute intervals for induction in high parity the 45-minute interval regimen resulted in longer induction-delivery interval (difference in median 2 hours, 95% CI 1-4 hours). In our study when stratifying patient by parity and cervical dilatation, the multiparty and initial cervical dilatation 3 cm subgroups of the 40-minute group were slightly longer in duration of oxytocin infusion. The other parameters had shown the same as our results.

The strength of this study composed of type of study design (randomized controlled trial), method of study and data collection (appropriated electrical machine and well trained personels), appropriated data analysis and conclusion. The limitation of this study was the propulation in this study composed of people lived in Khon Kaen province and nearby provinces that might be different in genetic composition with other parts of the Thai people, the suggestion was multicenter study might reduce this limitation.

In conclusion, after comparing increasing oxytocin infusion rates at 15-minute vs. 40-minute intervals for the induction or augmentation of labour, we concluded that the rate of uterine hyperstimulation and maximum dosage of oxytocin were significantly better at a 40-minute interval. There were also lower rates of fetal distress, precipitated labor, postpartum hemorrhage, operative delivery and emergency cesarean section in the 40-minute interval protocol though we found no significant differences in duration

of oxytocin use, number of days in the hospital and neonatal outcomes.

Our study suggests that increasing the oxytocin infusion rate for induction or augmentation of labour at 40-minute intervals is better than a 15-minute one.

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