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Article type : Original Research Article

The Labor Progression Study (LaPS): The use of oxytocin augmentation during labor following Zhang's guideline and the WHO partograph in a cluster randomized trial

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Disclosure of interests
None

Funding
This study was funded by the Research Department, Østfold Hospital Trust, Norway and the Faculty of Health Sciences, Department of Nursing and Health Promotion, OsloMet – Oslo Metropolitan University, Oslo, Norway.

ABSTRACT

Introduction*:* This study aims to investigate the use of oxytocin augmentation during labor in nulliparous women following Zhang's guideline or the WHO partograph. **Material and methods*:*** This is a secondary analysis of a cluster randomized controlled trial in 14 birth care units in Norway, randomly assigned to either the intervention group, which followed Zhang's guideline, or to the control group, which followed the WHO partograph, for labor progression. The participants were nulliparous women who had a singleton full-term fetus in a cephalic presentation and spontaneous onset of labor, denoted as group 1 in the Ten Group Classification System. **Results:** Between December 2014 and January 2017, 7277 participants were included. A total of 3219 women (44%) were augmented with oxytocin during labor. Oxytocin was used in 1658 (42%) women in the Zhang group compared with 1561 (47%) women in the WHO group. The adjusted relative risk for augmentation with oxytocin was 0.98, 95% CI; 0.84 to 1.15; *P*=0.8 in the Zhang versus WHO group, with an adjusted risk difference of −0.8 %, 95% CI; −7.8 to 6.1. The participants in the Zhang group were less likely to be augmented with oxytocin prior to 6 centimeters of cervical dilatation (24%) compared with participants in the WHO group (28%), with an adjusted relative risk of

0.84, 95% CI; 0.75 to 0.94; *P*=0.003. Oxytocin was administrated almost 20 minutes longer in the Zhang group than in the WHO group, with an adjusted mean difference of 17.9, 95% CI; 2.7 to 33.1; *P*=0.021 minutes. In addition, 19% of the women in the Zhang group and 23% in the WHO group were augmented with oxytocin without being diagnosed with labor dystocia. **Conclusions:** Although no significant difference in the proportion of oxytocin augmentation was observed between the two study groups, there were differences in how oxytocin was used. Women in the Zhang group were less likely to be augmented with oxytocin prior to 6 centimeters of cervical dilatation. The duration of augmentation with oxytocin was longer in the Zhang group than in the WHO group.

Keywords

Oxytocin augmentation, labor progression guidelines, labor dystocia, nulliparous, TGCS 1

Abbreviations

WHO: World Health Organization

TGCS: Ten-Group Classification System

CI: Confidence interval

LaPS: The Labor Progression Study

ARR: Adjusted relative risk

ARD: Adjusted risk difference

AMD: Adjusted mean difference

Key message

We did not observe any significant differences in the proportion of oxytocin for augmentation between the two study groups, but women in the Zhang group were less likely to be augmented with oxytocin prior to six centimeters of cervical dilatation.

INTRODUCTION

Augmentation with oxytocin is a widely used method to treat labor dystocia during the active phase of labor[1-4] aiming to produce sufficient uterine contractions for cervical dilatation and fetal descent. At the same time, it is also important to avoid uterine hyperstimulation and fetal compromise. The use of augmentation with oxytocin is recommended by the World Health Organization (WHO)[2] and the National Institute for Health and Care Excellence[5], even if the recommendations are based on low-quality evidence.[2]

A systematic review including randomized studies only, reported an association between oxytocin administration and a reduction in the mean duration of labor of approximately two hours. However, there was no decrease in the rates of cesarean sections or improved birth outcomes for mothers and babies.[6] In addition, observational studies reported that oxytocin augmentation was associated with an increased risk of instrumental vaginal delivery, episiotomy, emergency cesarean section, sphincter ruptures, a low Apgar score, a low cord pH in neonates, and newborn transfer to the neonatal intensive care unit.[7, 8, 9] Synthetic oxytocin has been classified as a potentially harmful medication and is included in the list of high-alert medications by the Institute for Safe Medication Practices in the US.[10] Despite this fact, the rate of oxytocin administration in Western countries has been reported to be from 44% to 75% over the last decade.[11-13]

Labor dystocia has no universal definition. Consensus concerning its management is lacking, and diagnostic criteria and guidelines for labor progression depend on local definitions.[4, 14, 15] For more than six decades, labor progression has been assessed on the basis of Friedman's research.[16] In the early 1970s, Philpott et al. developed guidelines for assessing labor progression according to Friedman's findings.[17] These guidelines consist of an action line to detect abnormal labor progress. In 1994, the WHO partograph[18] was presented based on Philpott's work and is currently used worldwide.[5] Because of a substantial change in labor management over the past half century, questions have been raised on the appropriateness of the recommendations of expected cervical dilatation in labor.[19-22]

In 2010, Zhang et al. presented a hyperbolic labor curve based on a large contemporary cohort that includes 27 170 nulliparous women[21] His findings present a substantially slower labor progression than previously thought, and research suggests that some interventions, such as oxytocin augmentation, might be performed too soon according to the prevailing definitions of labor dystocia.[4] The WHO has identified knowledge gap regarding which design, if any is preferable for a partograph[23] The overall aim of this study is to provide

detailed knowledge on the use of oxytocin augmentation during labor and will be an important contribution when evaluating different labor progression guidelines. The specific aim is to investigate if there were differences in oxytocin for augmentation during labor in nulliparous women randomized to adhere to Zhang's guideline compared with the WHO partograph.

MATERIAL AND METHODS

We used data from the Labor Progression Study (LaPS), a cluster randomized controlled trial undertaken in Norway, with the aim of evaluating the effect of the two different guidelines for labor progression. The study protocol was published in 2017,[24] and detailed methodological considerations, information regarding the intervention and procedures, and the results for the primary outcome are recently published.[25]

Approximately 60 000 babies are born annually in 46 birthing institutions in Norway. Birth care units were eligible to participate if their annual delivery rate exceeded 500 infants. The inclusion criteria for participating individuals were nulliparous women with a singleton fetus in a cephalic presentation and spontaneous onset of active labor, defined as at least 4 cm of cervical dilatation with regular contractions, in gestational week 37 or greater. This group is denoted as group 1 in the Ten Group Classification System (TGCS) by Robson.[26] Women who understood the Norwegian language were included.

The randomization procedure was computer generated, and it was stratified for annual birth number and prior rates of cesarean sections for TGCS group I. Neither the staff at the birth care units nor the participants were masked to group affiliation because of the nature of the design. In this trial, hospitals were the units of randomization, and women were the units of analysis. The estimated day of delivery was determined in a second trimester ultrasound scan. At this examination or upon admission to the labor ward, eligible women received written information about the trial. Data for eligible women who provided informed consent were included in the analyses.

Prior to randomization and trial onset, staff at all sites received information about the LaPS protocol and were trained on how to use the allocated guidelines. Seven birth care units were randomized to the intervention group adhering to Zhang's guideline, and seven birth care units were randomized to the control group adhering to the WHO partograph. Active phase of first stage is defined from at least 4 centimeters of cervical dilatation to 10 centimeters of

cervical dilatation. For women adhering to Zhang's guideline, labor dystocia was diagnosed if the cervical dilatation did not meet the expected progression from one integer centimeter to the next according to the 95th percentile. Labor dystocia in the second stage was diagnosed if the descending phase lasted longer than one hour and 45 minutes, two hours and 30 minutes for women with epidural analgesia, or if the expulsion phase lasted longer than 60 minutes (Supporting information Figure S1). For women adhering to the WHO partograph for labor progression, labor dystocia was diagnosed if the cervical dilatation was slower than one integer centimeter per hour, assessed after four hours i.e. if the four-hour action line was crossed. Labor dystocia in the second stage was diagnosed if the descending phase lasted longer than one hour, two hours for women with epidural analgesia, or if the expulsion phase lasted longer than 60 minutes (Supporting information Figure S2). If labor dystocia was diagnosed, the guideline on treatment because of insufficient contractions was followed as a common routine at all birth care units in Norway.[27]

The primary outcome in the present paper was the proportion of oxytocin augmentation in active labor. The secondary outcome measurements included duration of oxytocin augmentation in minutes, maximum dose of oxytocin in ml/h, dose when initiating augmentation, cervical dilatation when initiating augmentation with oxytocin, proportion of discontinuation of oxytocin, proportion of labor dystocia according to the allocated guideline, and cervical dilatation when labor dystocia was diagnosed. In addition, a comparison between oxytocin augmentation during active labor and labor dystocia was presented. The clinical outcomes were registered in a web-based case report form, designed by the Unit of Applied Clinical Research at the Norwegian University of Science and Technology, to ensure consistent data recording.

Statistical analyses

The LaPS sample size was calculated to show a 25% decrease in the proportion of intrapartum cesarean sections when adhering to Zhang's guideline[25]. The present paper describes secondary and exploratory analyses related to the use of oxytocin augmentation in active labor in the LaPS study (see Supporting information Appendix S1 regarding organization of the LaPS study). A separate statistical analysis plan was prepared for the analyses described in the Supporting Information Appendix S2. The analyses were conducted according to the principle of intention-to-treat to estimate the effect of the two guidelines. Datawith dichotomous outcomes were analyzed with a mixed logistic regression model. For continuous outcomes, a generalized linear mixed gamma model with a logarithmic link

function was used. For both models, birth care units were included as random intercepts and the treatment strategy as a fixed effect. Furthermore, we adjusted for stratification variables (annual intrapartum cesarean section rates and number of deliveries) and for predefined covariates considered to be potential risk factors for oxytocin administration on an individual level (maternal age, body mass index, civil status, and educational level, as well as birthweight and neonatal head circumference). A two-tailed P value ≤ 0.05 was considered significant. Estimates of the adjusted risk ratio, risk difference, and mean difference with confidence intervals (CI) were computed with the delta method.[28] The analyses of the primary and secondary endpoints in this paper were based on all included women, except for the analyses of the duration of oxytocin administration, the maximum dose of oxytocin administration, and cervical dilatation when initiating oxytocin, which was restricted to women with oxytocin administration only. The calculation of cervical dilatation when labor dystocia was diagnosed was restricted to those diagnosed with labor dystocia.

No data were missing for the covariates included in the analyses, except for the body mass index (BMI) (0.3%) and civil status (0.8%). Missing covariate data were imputed using stochastic linear regression single imputation. Some of the eligible women were not included in the study (Figure 1), and the characteristics of these women are presented in the Supporting information, Table S1. All statistical analyses were done in STATA v15 (Stata Corp. 2015. Stata statistical software: release 15.1.1 College Station, TX, USA).

Ethical approval

This study, including patient information, informed consent, and the baseline characteristics of the non-included women, was approved by the Regional Committee for Medical and Health Research Ethics (2013/1862/REK) South East and the Norwegian Social Science Data Services. It was registered at www.clinicaltrials.gov before the enrolment of the participants (NCT02221427), and the study protocol was published in BMC Pregnancy and Childbirth.[24] The protocol was approved and signed by the management at each birth care unit before trial commencement.

RESULTS

During the 26 months of inclusion, between December 1, 2014 and January 31, 2017, 14 birth care units throughout Norway took part in the study. In all, 11 615 mothers in TGCS group 1 were assessed for eligibility to participate. Of these, 7277 were included in the analyses, 3972 and 3305 in the Zhang and WHO groups, respectively (Figure 1). The baseline characteristics of the two study groups are presented in Table I. No data were missing for the primary outcome of oxytocin use for augmentation, and a total of 3219 women (44%) were augmented with oxytocin during active labor. Oxytocin augmentation was used in 1658 (42%) nulliparous women adhering to Zhang's guideline compared with 1561 (47%) nulliparous women adhering to the WHO partograph. No significant difference in the risk of oxytocin augmentation was found; the adjusted relative risk in the intervention group versus the control group was 0.98 (95% CI; 0.84 to 1.15; *P*=0.8), and the corresponding adjusted risk difference was −0.8 % (95% CI; −7.8 to 6.1).

The median duration of oxytocin augmentation was 134 minutes in the Zhang group compared with 115 minutes in the WHO group, with an adjusted mean difference of 17.9 minutes (95% CI; 2.7 to 33.1, *P*=0.021), whereas the median of the maximum dose of oxytocin augmentation was 75 ml/h in the Zhang group compared with 90 ml/h in the WHO group, with an adjusted difference of −0.11 ml/h (95% CI; −13.5 to 13.3, *P*=0.99) (Table 2). Table 2 also shows a detailed description of cervical dilatation in centimeters when initiating oxytocin, presented with a 95% CI among TGCS group 1 women in the two study groups. Women allocated to Zhang's guideline were less likely to receive augmentation with oxytocin prior to 6 cm of cervical dilatation compared with those allocated to the WHO partograph (adjusted relative risk of 0.84 (95% CI; 0.75 to 0.94), with an adjusted risk difference of −4.6 % (95% CI; −7.6 to −1.6). In addition, discontinuation of oxytocin was used for 74 (4.5%) women in the intervention group and 54 (3.5%) women in the control group.

There was no significant difference in the adjusted relative risk for labor dystocia, which was 1.1 (95% CI; 0.96 to 1.28; *P*=0.2) in the intervention group versus the control group, with an adjusted risk difference of 4.8 % (95% CI; −1.8 to 11.3). In Table 3, detailed descriptions of the differences between the two study groups in cervical dilatation when labor dystocia was diagnosed are presented. A comparison between the two study groups for oxytocin augmentation and labor dystocia is presented in Table 4. For the women in the Zhang group, approximately 42% received oxytocin, of whom 81% were diagnosed with labor dystocia. In

the WHO group, 47% women received oxytocin, of whom 77% were diagnosed with labor dystocia. No other differences in maternal and neonatal outcome have been presented elsewhere.[25]

DISCUSSION

Although no significant difference in the proportion of augmentation with oxytocin was observed between the two study groups, there were differences in the use of oxytocin during labor between the two study groups. The women allocated to follow Zhang's guideline were less likely to be augmented with oxytocin prior to 6 centimeters of cervical dilatation compared with the women in the control group, but the median duration of oxytocin augmentation was longer in the Zhang group.

The strength of our study is its rigorous design that helps achieve the research purpose [15, 29] and its appropriate sample size calculation strengthens the internal validity. The external validity is strengthened by the data covering all areas in Norway, which allows the results to be generalized to a larger population. Furthermore, these data have been triple-checked, with few errors and missing values found. To assess the risk and effect of selection bias, we recorded the age, civil status, level of education, smoking habits, BMI, and gestational age of the women not included in the trial; these baseline characteristics are presented in the Supporting information, Table S1.

A limitation of this study is that the included women were not admitted to the maternity ward with the same cervical dilatation and, therefore, did not contribute equally to the measurements of the active phase of labor. The women who were admitted early in labor might be different from those who were admitted later in labor. The intervention during labor could have therefore been influenced by the different cervical dilatations on admission. Furthermore, the definitions of labor dystocia according to current guidelines were based merely on the time of cervical dilatation; not on descent of the fetal head or contractions. This limitation is a known research challenge in the definition of normal labor progression.[30]

Furthermore, the WHO has identified a knowledge gap regarding which design, if any, is preferable for a partograph.[23] Our cluster randomized trial is an important contribution to clinicians and decision makers when deciding which guidelines are preferable to guide clinical practice with regard to oxytocin augmentation and to reduce unnecessary interventions. The results are also an important step towards possibly forming a new guideline. Evidence from trials comparing different guidelines and partographs for labor

progression show a small difference in cesarean section rates,[15, 25] but different labor progression guidelines have been suggested to also have an impact on other interventions during labor.[15] Compared with numbers from the participating hospitals from the year prior to the LaPS study, we observed an overall reduction in oxytocin augmentation in both the Zhang and WHO groups by 14% and 8%, respectively (Supporting information, Table S2). However, we did not observe a significant difference in the overall proportion of oxytocin augmentation between the two study groups. The reduction can therefore not be explained by one of the guidelines alone.

However, total duration of oxytocin augmentation was longer for the women adhering to Zhang's guideline than for those adhering to the WHO partograph. Oxytocin augmentation lasted almost 20 minutes longer in the Zhang group, still without the need for higher doses if adhering to Zhang's guideline. The WHO group reported higher maximum doses of oxytocin during augmentation compared with the Zhang group, but no statistical significant difference. The clinical impact is unknown, but our findings are in accordance with previous research that has identified a high rate of oxytocin augmentation without an improvement in birth outcome for the mother or the baby.[6-8] In few cases, the oxytocin augmentations were discontinued due to the establishment of the woman's own uterine contractions. This is not in accordance with a meta-analysis that suggests discontinuation of oxytocin augmentation when the woman is in the active phase of labor.[31] No difference in the proportion of labor dystocia according to the guidelines was observed in the two study groups. It should be mentioned that the definitions of labor dystocia were different, and that direct comparisons are therefore inappropriate. At the same time, it is remarkable that 21% of the women in TGSC group 1 received augmentation with oxytocin without having labor dystocia diagnosed, and there were more women in the WHO group (23%) who were augmented than those in the Zhang group (19%) without being diagnosed with labor dystocia. The trial has a pragmatic approach and our results represent real world practice. It is well known that oxytocin for augmentation is not only given on indication when labor dystocia is diagnosed, but unfortunately also in cases without labor dystocia. The duration of the active phase was longer for women adhering to Zhang's guideline, and this might be explained by the fact that Zhang's guideline allows a longer time before dystocia is diagnosed, especially before 6 cm dilatation. This result is in accordance with a previous study.[32] The investigators assumed that that women allocated to Zhang's guideline may labor longer because the introduction of an intervention would be delayed compared with the case for the women adhering to the WHO partograph.

CONCLUSION

We observed no significant difference in the proportion of oxytocin augmentation between the two study groups. However, there were differences in the use of oxytocin during labor between the two study groups. Women in the Zhang group were less likely to be augmented with oxytocin prior to 6 centimeters of cervical dilatation compared with the WHO group. The length of oxytocin augmentation was longer for women in the Zhang group. In addition, more women in the WHO group were augmented with oxytocin without an indication of labor dystocia. The results of this multicenter cluster randomized controlled trial make an important contribution to guiding clinical practice.

Acknowledgment

We acknowledge the contribution of all midwives, doctors, and all maternity unit staff in the maternity units of all hospitals that participated in the project.

References

1. American College of O, Gynecology Committee on Practice B-O. ACOG Practice Bulletin Number 49, December 2003: Dystocia and augmentation of labor. Obstetr Gynecol. 2003;102(6):1445-54.
2. World Health Organization. WHO recommendations for augmentation of labour. World Health Organization; 2014.
3. Caughey AB, Cahill AG, Guise JM, Rouse DJ. Safe prevention of the primary cesarean delivery. Am J Obstet Gynecol. 2014;210(3):179-93.
4. Rhoades JS, Cahill AG. Defining and Managing Normal and Abnormal First Stage of Labor. Obstet Gynecol Clin North Am. 2017;44(4):535-45.
5. NICE guidelines. Intrapartum care: NICE National Institute for Health and Clinical Excellence 2014 [Available from: www.nice.org.uk/guidance/cg190.
6. Bugg GJ, Siddiqui F, Thornton JG. Oxytocin versus no treatment or delayed treatment for slow progress in the first stage of spontaneous labour. Cochrane Database Syst Rev. 2013;6:Cd007123.
7. Bernitz S, Oian P, Rolland R, Sandvik L, Blix E. Oxytocin and dystocia as risk factors for adverse birth outcomes: a cohort of low-risk nulliparous women. Midwifery. 2014;30(3):364-70.
8. Oscarsson ME, Amer-Wahlin I, Rydhstroem H, Kallen K. Outcome in obstetric care related to oxytocin use. A population-based study. Acta Obstet Gynecol Scand. 2006;85(9):1094-8.
9. Simpson KR, James DC. Effects of oxytocin-induced uterine hyperstimulation during labor on fetal oxygen status and fetal heart rate patterns. Am J Obstet Gynecol. 2008;199(1):34 e1-5.
10. Clark SL, Simpson KR, Knox GE, Garite TJ. Oxytocin: new perspectives on an old drug. Am J Obstet Gynecol. 2009;200(1):35 e1-6.
11. Osterman M MJ. Changes in cesarean delivery rates by gestational age: United States, 1996–2011. Hyattsville, MD: National Center for Health Statistics. 2013.
12. NHS. Hospital Episode Statistics NHS Maternity Statistics England, 2013-14. NHS.
13. Norwegian Birth Registry of Norway: Norwegian Institute of Public Health; 2018 [Available from: https://www.fhi.no/en/hn/health-registries/medical-birth-registry-of-norway/.
14. Rossen J, Ostborg TB, Lindtjorn E, Schulz J, Eggebo TM. Judicious use of oxytocin augmentation for the management of prolonged labor. Acta Obstet Gynecol Scand. 2016;95(3):355-61.

15. Lavender T, Cuthbert A, Smyth RM. Effect of partograph use on outcomes for women in spontaneous labour at term and their babies. Cochrane Database Syst Rev. 2018;8:CD005461.
16. Friedman E. The graphic analysis of labor. Am J Obstet Gynecol. 1954;68(6):1568-75.
17. Philpott RH, Castle WM. Cervicographs in the management of labour in primigravidae. II. The action line and treatment of abnormal labour. J Obstet Gynaecol Br Commonw. 1972;79(7):599-602
18. World Health Organization. World Health Organization partograph in management of labour. World Health Organization Maternal Health and Safe Motherhood Programme. Lancet. 1994;343(8910):1399-404.
19. Neal JL, Lowe NK, Patrick TE, Cabbage LA, Corwin EJ. What is the slowest-yet-normal cervical dilation rate among nulliparous women with spontaneous labor onset? J Obstet Gynecol Neonatal Nurs. 2010;39(4):361-9.
20. Zhang J, Troendle JF, Yancey MK. Reassessing the labor curve in nulliparous women. Am J Obstet Gynecol. 2002;187(4):824-8.
21. Zhang J, Landy HJ, Branch DW, et al. Contemporary patterns of spontaneous labor with normal neonatal outcomes. Obstet Gynecol. 2010;116(6):1281-7.
22. Laughon SK, Branch DW, Beaver J, Zhang J. Changes in labor patterns over 50 years. Am J Obstet Gynecol. 2012;206(5):419 e1-9.
23. World Health Organization. WHO recommendations: Intrapartum care for a positive childbirth experience 2018 [Available from: http://apps.who.int/iris/bitstream/handle/10665/260178/9789241550215-eng.pdf;jsessionid=F1F5397399F448885328491174AC61C6?sequence=1.
24. Bernitz S, Dalbye R, Oian P, Zhang J, Eggebo TM, Blix E. Study protocol: the Labor Progression Study, LAPS - does the use of a dynamic progression guideline in labor reduce the rate of intrapartum cesarean sections in nulliparous women? A multicenter, cluster randomized trial in Norway. BMC Pregnancy Childbirth. 2017;17(1):370.
25. Bernitz S, Dalbye R, Zhang J, et al. The frequency of intrapartum caesarean section use with the WHO partograph versus Zhang's guideline in the Labour Progression Study (LaPS): a multicentre, cluster-randomised controlled trial. Lancet. 2019;393(10169):340-8.
26. Robson M, Murphy M, Byrne F. Quality assurance: The 10-Group Classification System (Robson classification), induction of labor, and cesarean delivery. Int J Gynaecol Obstet. 2015;131 Suppl 1:S23-7.
27. Norwegian Medical Association. Augmentation of labor: Norwegian Society in Obstetrics and Gynecology; 2014 [Chapter 34]. Available from: http://www.nfog.org/files/guidelines/34%20NGF%20Obst%20Augmentation%20of%20labour%20Eggeb%C3%B8.pdf.
28. Reeve R. Confidence interval of difference of proportions in logistic regression in presence of covariates. Stat Methods Med Res. 2018;27(2):451-65.
29. Cohen WR, Friedman EA. Perils of the new labor management guidelines. Am J Obstet Gynecol. 2015;212(4):420-7.
30. Vahratian A, Troendle JF, Siega-Riz AM, Zhang J. Methodological challenges in studying labour progression in contemporary practice. Paediatr Perinat Epidemiol. 2006;20(1):72-8.
31. Vlachos DE, Pergialiotis V, Papantoniou N, Trompoukis S, Vlachos GD. Oxytocin discontinuation after the active phase of labor is established. J Matern Fetal Neonatal Med. 2015;28(12):1421-7.
32. Lee NJ, Neal J, Lowe NK, Kildea SV. Comparing Different Partograph Designs for Use in Standard Labor Care: A Pilot Randomized Trial. Matern Child Health J. 2018;22(3):355-63.

Supporting information legends

Appendix S1. Organization of the LaPS study

Figure S1. Zhang's guideline1 for calculating the expected progression during the active phase of the first stage of labor according to time intervals from cm to cm.

Figure S2. The WHO partograph2 for labour progression during the active phase of labour with cervical dilatation of at least 1 cm (alert line)3 per hour assessed after 4 hours (action line)4.

Appendix S2. Statistical Analysis Plan

Table S1. Baseline characteristics of the included and non-included women

Table S2. Birth care unit specific oxytocin augmentation rate in 2012 vs LaPS

Figure legend

Figure 1. Flowchart of the inclusion of hospitals and participant

Table. 1 Characteristics of included hospitals (n=14) and participants (n=7277)

	Zhang group		**WHO group**	
	Hospitals (n=7)	**Participants** (n=3972)	**Hospitals** (n=7)	**Participants** (n=3305)
Hospital characteristics				
Deliveries per year				
<3000	6	2688 (36.9)	6	2233 (30.7)
≥3000	1	1284 (17.6)	1	1072 (14.7)
Characteristics related to the mother				
Maternal age at delivery (years)		28.4 (4.6)		28.5 (4.5)
Civil status (Cohabitant or married) *		3741/3946 (94.8)		3137/3271 (95.9)
Higher education ≥12 years		2412 (60.7)		2017 (61.0)
Smoking during first trimester *		230/3963 (5.8)		210/3247 (6.5)
Pre-pregnant body mass index†*		23.6/3966 (4.3)		23.8/3287 (4.3)
Gestational age at onset of active labor (days)		281 (7.0)		281 (8.0)
Characteristics related to labor				
Amniotomy		1396 (35.1)		1223 (37.0)
Epidural analgesia		1913 (48.2)		1653 (50.0)
Labor dyctocia		1882 (47.4)		1512 (45.7)
Operative vaginal delivery		839 (21.1)		581 (17.6)
Cesarean section		271 (6.8)		196 (5.9)
Duration of active phase of labor (hours), median (IQR)		6.6 (3.6-10.5)		6.1 (3.4-9.5)
Duration of 2nd stage (minutes), median(IQR)		76 (40-142) **n=3746		75 (40-126) **n=3134
Characteristics related to the newborn				
Birth weight (gram)		3528 (427)		3518 (414)
Head circumference (cm)		35.0 (1.4)		35.0 (1.4)

No. (%) or mean (SD) unless otherwise stated. *Total numbers are presented due to missing values.
†The body-mass index is the weight in kilograms divided by the square of the height in meters.
**Numbers are restricted to women who reached 10 cm of cervical dilatation.

Table 2 The use of oxytocin augmentation

	Intervention group n=3972	**Control group n= 3305**	**Estimated difference (95%CI)**	**P-value**
Oxytocin augmentation during labor n (%)	1658 (41.7)	1561 (47.2)	ARR: 0.98 (0.84 to 1.15) ARD: -0.8% (-7.8 to 6.1)	0.8
Duration of oxytocin augmentation (in minutes)* median(IQR)	134 (57-270)	115 (50-250)	AMD: 17.9 (2.7 to 33.1)	0.021
Maximum dose of oxytocin augmentation (in ml/h) * median(IQR)	75 (45-120)	90 (60-120)	AMD: -0.1 (-13.5 to 13.3)	0.99
Dose of oxytocin when initiating augmentation (in ml/h)* median(IQR)	30 (30-30)	30 (15-30)	AMD: -0.4 (-3.6 to 2.9)	0.82
Discontinuation of oxytocin * n (%)≠	74 (4.5%)	54 /1554(3.5%)		
Cervical dilatation when initiating oxytocin (in cm) * n (%)**				
4 cm	101 (6.1)	128 (8.2)	ARR: 0.73 (0.55 to 0.98) ARD: -2.2 (-4.2 to -0.1)	0.04
5 cm	244 (14.7)	289 (18.5)	ARR: 0.79 (0.66 to 0.95) ARD: -3.9 (-6.9 to -0.9)	0.01
6 cm	399 (24.1)	443 (28.4)	ARR: 0.84 (0.75 to 0.94) ARD: -4.6 (-7.6 to -1.6)	0.003
7 cm	552 (33.3)	565 (36.2)	ARR: 0.92 (0.83 to 1.01) ARD: -3.0 (-6.3 to 0.2)	0.07
8 cm	712 (42.9)	692 (44.3)	ARR: 0.96 (0.88 to 1.05) ARD: -1.7 (-5.7 to 2.3)	0.40
9 cm	914 (55.1)	835 (53.5)	ARR: 1.01 (0.93 to 1.11) ARD: 0.8 (-4.1 to 5.7)	0.8
10 cm	1658 (100)	1561 (100)	ARR: 0.98 (0.88 to 1.09) ARD: -0.8 (-5.7 to 4.1)	0.8

*Include women with oxytocin augmentation during labor. ≠ Total numbers are presented due to missing values. **numbers in % are cumulative
ARR: Adjusted relative risk
ARD: Adjusted risk difference
AMD: Adjusted mean difference

Table 3 Labor dystocia and cervical dilatation when labor dystocia is diagnosed.

	Intervention group n=3972	**Control group n= 3305**	**Adjusted relative risk (95%CI)**	**Adjusted risk difference (95% CI)**	**P-value**
Labor dystocia n (%)	1882 (47.4%)	1512 (45.7%)	1.1 (0.96 to 1.28)	4.8 (-1.8 to 11.3)	0.16
Cervical dilatation when labor dystocia was diagnosed (cm) * n(%)					
4 cm	49 (2.6)	74 (4.9)	0.54 (0.36-0.80)	-2.2 (-3.7- to 0.8)	0.002
5 cm	173 (9.2)	140 (9.3)	0.97 (0.79-1.20)	-2.7 (-2.2 to 1.7)	0.79
6 cm	217 (11.5)	162 (10.7)	1.06 (0.86 to 1.30)	0.6 (-1.7 to 3.0)	0.59
7 cm	232 (12.3)	106 (7.0)	1.76 (1.37 to 2.25)	5.3 (3.1 to 7.5)	<0.001
8 cm	236 (12.5)	99 (6.5)	1.90 (1.52 to2.38)	5.9 (4.0 to 7.9)	<0.001
9 cm	247 (13.1)	120 (7.9)	1.68 (1.36 to 2.07)	5.3 (3.3 to 7.4)	<0.001
10 cm	728 (38.7)	811 (53.6)	0.72 (0.65 to 0.79)	-15.2 (-19.4 to -11.1)	<0.001

*Include women with labor dystocia only

Table 4 A comparison between oxytocin augmentation and labor dystocia

	Zhang's group n=3972		WHO group n=3305	
	Oxytocin n=1658	No Oxytocin n=2314	Oxytocin n=1561	No Oxytocin n=1744
Labor dystocia n(%)	1351 (81.5)	531 (22.9)	1199 (76.8)	313 (17.9)
No labor dystocia n (%)	307 (18.5)	1783 (77.1)	362 (23.2)	1431 (82.1)

Figure 1. Flowchart of the inclusion of hospitals and participants