High vs. Low Dose Oxytocin for Induction or Augmentation of Labour

Clinical question

Does high dose oxytocin for induction or augmentation of labour safely shorten time to delivery?	
Population:	Women at term requiring either augmentation or induction of labour.
Intervention:	Intravenous high dose oxytocin administration.
Comparison:	Low dose oxytocin administration
Primary Outcome: Secondary Outcomes:	Cesarean section Spontaneous vaginal delivery Time to delivery Uterine hypertonus 5 min Apgar

Search strategy

- Time period: 1990 – 2012.
- Search terms: oxytocin, induction, augmentation, dose, labour.
- Inclusions: meta-analysis, systematic reviews, randomized controlled trials, cohort studies.
- Databases searched: CINAHL; MEDLINE (Ovid SP and PubMed); EMBASE; Cochrane CDSR, CENTRAL, & DARE, Google Scholar.
- Titles reviewed – 374; abstracts reviewed – 37; papers reviewed – 17; papers meeting eligibility for inclusion -15.

Synthesis of the evidence

Systematic reviews report decreased rates of cesarean delivery and increased rates of spontaneous vaginal delivery, shortened duration of labour, and no difference in rates of Apgar scores less than 7 at five minutes among studies with high versus low initial doses and incremental doses of oxytocin for labour augmentation. Findings of individual studies with respect to cesarean section and spontaneous vaginal delivery were inconclusive. Studies consistently reported shorter intervals from administration of oxytocin to delivery and higher rates of hyperstimulation in high dose regimes. Apgar rates less than 7 at five minutes were not different.

Limitations

Regimes for high and low dose oxytocin differ among studies. Systematic reviews also include comparisons of active vs. conservative approaches to labour. Most individual studies lacked sufficient power to determine clinically relevant differences between groups.

Conclusions

Administration of oxytocin in regimes starting at 4 mU/min and increasing incrementally at 4 mU/min is associated with fewer cesarean sections and higher rates of spontaneous delivery without fetal compromise compared to lower dose regimes.

Systematic Review	Inclusion	Intervention	Findings	Comments
Mori R, Tokumasu H, Pledge D, Kenyon S. Cochrane Database of Systematic Reviews. 2011:(10):CD007201. **High dose versus low dose oxytocin for augmentation of delayed labour.**	Randomized and quasi-randomized controlled trials for women delayed in labour requiring augmentation by oxytocin. Included 4 studies. n=660 RCTs 1. Bidgood (1987) 2. Jamal (2004) 3. Supajitkulchi (2003) Quasi-randomized (on day of week) 4. Xenakis (1995) Bidgood restricted to nulliparous women. The other three trials excluded women with previous CS.	High dose: Starting dose and incremental dose (>4mU/min) Low dose: Starting dose and incremental dose (<4mU/min). Increase interval 15-40 minutes.	1. All trials – decrease in CS rate (RR 0.53; 95%CI 0.38 – 0.75) and increased rate of spontaneous vaginal birth (RR 1.37; 95% CI 1.15-1.64) (2 trials, n=350). 2. One trial (n=40) - reduction in length of labour (mean difference -3.5 hr; 95% CI 6.38 - -0.62). No significant difference in hyperstimulation, ruptured uterus, dystocia, chorioamnionitis, epidural analgesia, neonatal mortality, admission to neonatal units, Apgar < 7 at 5 minutes, or umbilical cord pH.	
Wei SQ, Luo ZC, Qi HP, Xu H, Fraser WD. Am J Obstet Gynecol. 2010; Oct;203(4):296-304 Saint-Justine Hospital, University of Montreal, Montreal, Quebec, Canada **High-dose vs low-dose oxytocin for labor augmentation: a systematic review.**	Randomized controlled trials Included 10 studies n=5423 1. Bidgood (1987) 2. Frigoletto (1995) 3. Jamal (2004) 4. Lopez-Zeno (1992) 5. Majoko (2001) 6. Merrill (1999) 7. Rogers (1997) 8. Sadler (2000) 9. Tabowei (2003) **10.** Xenakis (1995) Two studies (n=691) included multiparas	High dose: ≥4 mU/min and increments of ≥4 mU/min. Low dose: 1-4 mU/min and increments of 1-2 mU/min.	Relative Risk, (95% Confidence Intervals) Hi vs. Lo CS 0.85 (0.75-0.97) Spont vag del 1.07 (1.02-1.12) Hyperstimulation 1.91 (1.49-2.45) Labor >12 hrs 0.46 (0.30-0.70) Apgar < 7 at 5 min 1.18 (0.61-2.28)	5 studies compared active management of labour to a more conservative approach and 5 compared high dose to low dose oxytocin for labour augmentation.

Systematic Review	Inclusion	Intervention	Findings	Comments
Crane JM, Young DC. J SOGC, 1998; 20:1215 Memorial University of Newfoundland, Dalhousie University **Meta-analysis of low-dose versus high-dose oxytocin for labour induction**	Randomized controlled trials n=1689 Nulliparous and multiparous 1. Satin (1991) 2. Chua (1991) 3. Mercer (1991) 4. Muller (1992) 5. Lazor (1993) 6. Orhue (1993) 7. Orhue (1993) 8. Orhue (1994) 9. Goni (1995) 10. Crane (unpublished) 11. Singh (unpublished)	Low dose: 0.5 to 2.5 mU/min increasing by 1.0 mU/min to doubling of the dose, in 30 or 60 minute interval with maximum dose16-40 mU/min with maximum dose 24-80 mU/min. High dose: 0.5 to 7.0 mU/min increasing by 1.0 mU/min to doubling of the dose, every 15 to 40 min.	Odds ratio 95% Confidence Intervals Lo vs. hi dose CS 0.78 (0.60-1.02) Spont vag del 1.67 (1.27-2.20) Hyperstimulation 0.41 (0.33-052) 5 min Apgar <7 0.46 (0.09-2.32) High dose oxytocin significantly reduced induction to delivery time by 42-180 minutes	Excessive uterine stimulation defined as hypertonus or tachysystole (>5 contractions in 10 min), with or without hyperstimulation
Randomized controlled trial	**Inclusion**	**Intervention**	**Findings**	**Comments**
Durodola A, Kuti O, Orji EO, Ogunniyi SO, Int J Gynaecol Obstet. 2005:90(2):107-11. Obafemi Awolowo University Teaching Hospitals Complex, Nigeria **Rate of increase in oxytocin dose on the outcome of labor induction.**	n=120 (low risk, healthy, nulliparous, singleton, in vertex position with a Bishop score >7 and fetus without congenital anomalies)	High dose: 4.0 mU/min increasing to 8.0, 16.0, 32mU/min, increased every 30 min. Low dose: 4.0 mU/min increasing to 8.0, 12.0, 16.0, 20.0, 24,0, 28.0, 32.0 Increased every 30 min.	Hi dose Lo dose p value CS 10% 11.7% 0.88 Hyperstimulation 8.3% 6.7% 0.82 1st stage (min) 428.61 365.57 0.001 No difference in neonatal hospital stay, neonatal intensive care admissions or need for respiratory support.	Adequate labour described as 3 contractions in 10 min lasting 40 sec. Hyperstimulation ≥ 6 contractions in 10 min.
Jamal A, Kalantari R. Int J Gynaecol Obstet. 2004; Oct;87(1):6-8. Shariati Hospital, Tehran, Iran **High and low dose oxytocin in augmentation of labor.**	n =200 (singleton, >37 weeks gestation, without malpresentation, placenta previa, previous cesarean section or previous uterine surgery, multiple gestation, high parity, and overdistended uterus)	High-dose: 4.5 mU /min) and increased by 4.5 mU /min every 30 min. Low-dose: 1.5 mU /min (9 mU/h) and increase by 1.5 mU /min every 30 min.	Hi dose Lo dose p value CS 5% 9% 0.2 Hyperstimulation 14% 8% 0.07 No statistically significant differences for length of any phase of labour, induction to delivery time, maternal complications, duration of hospitalization, Apgar <7 , neonatal length of hospital stay	41% in the low dose regime vs. 50% in the high dose regime were nulliparous. Double blind study. Hyperstimulation defined as > 5 contractions in 10 min.

Randomized controlled trial	Inclusion	Intervention	Findings	Comments
Merrill DC, Zlatnik FJ. Obstet Gynecol. 1999; Sep;94(3):455-63. University of Iowa College of Medicine, Iowa City, USA **Randomized, double-masked comparison of oxytocin dosage in induction and augmentation of labor.**	n=1307 (>24 weeks gestational age and booked for induction or augmentation.)	High dose:4.5 mU/min and increased by 4.5 mU/min every 30 min until adequate labour established Low dose:1.5 mU/min and increased by 1.5 mU/min every 30 min	Hi dose Lo dose p value CS 11.3% 15.0% 0.17 CS for fetal dist 4.5% 5.2% 0.79 No times oxy stopped for hyperstimulation 0.8 0.5 0.005 Oxytocin to del 8.5 hrs 10.5 <.001 5 min Apgar <7 5.8% 5.5% 0.98	52.4% of women in the low dose regime and 51.4% in the high dose were nulliparous. Double blind study. Hyperstimulation defined as >7 contractions in 15 min. If induction not successful in 8-10 hours, subjects withdrawn.
Hourvitz A, Alcalay M, Korach J, Lusky A, Barkai G, Seidman DS. Acta Obstet Gynecol Scand. 1996;75(7):636-41. The Chaim Sheba Medical Center, Israel **A prospective study of high- versus low-dose oxytocin for induction of labor.**	n=179 (singleton, 37-42 weeks, cephalic presentation, without previous CS)	High-dose:oxytocin started at 2.5 mU/min, increased to 5, 7.5, 10, 12.5, 15, 20, 25 & 30 mU/min at 30 min intervals. Low-dose: oxytocin started at1.25 mU/min increased to 2.5, 3.75, 5, 6.25, 7.5, 10, 12.5, 15, 20, 25 & 30 at 30 min intervals.	Hi dose Lo dose p value CS 18% 10% ns Spontaneous vag 62% 86% ns Oxytocin to delivery (nullips) <12 hrs 20% 32% .01 Hyperstimulation 16% 2% .01 5 min Apgar <7 10% 5.5% ns No statistically significant differences for length of any phase of labour, maternal complications, duration of hospitalization, neonatal length of hospital stay.	Continuous electronic FHLR and uterine monitoring. Labour defined as 3 contractions in 10 min. Amniotomy performed after active labour diagnosed.

Randomized controlled trial	Inclusion	Intervention	Findings	Comments
Goni S, Sawhney H, Gopalan S. Int J Gynaecol Obstet. 1995; Jan;48(1):31-6. Nehru Hospital, Chandigarh, India. **Oxytocin induction of labor: a comparison of 20- and 60-min dose increment levels.**	n=100 (singleton, term, cephalic presentation, no uterine scar, no cardiac disease, severe anemia or pregnancy-induced hypertension)	High dose: 1 mU/min and doubled q 20 min to maximum of 64 mU/min Low dose: 1 mU/min and doubled q 60 min to maximum of 32 mU/min.	Hi dose Lo dose p value CS 18.0% 10.0% ns Spontaneous vag 62% 86% ns Oxytocin to delivery (nullips) <12 hrs 20% 32% .01 Hyperstimulation 16% 2% .01 5 min Apgar <7 10.0% 5.5% ns	In the high dose group, 70% of women were nulliparous and in the low dose 58%. FHR monitored by intermittent auscultation q 30 min in 1st stage, q 5 min in 2nd stage. Adequate contractions defined as lasting 45 s and occurring q 2-3 min. Hyperstimulation defined as contraction frequency every 2 min or more.
Orhue AA. Obstet Gynecol. 1994;83(2):229-3 University of Benin Teaching Hospital, Nigeria **Incremental increases in oxytocin infusion regimens for induction of labor at term in primigravidas.**	n=124 (nulliparous, singleton, at term, cephalic, maternal age < 35 years, no scar on uterus)	High dose: 2.0 mU/min and doubling every 15 minutes to a maximum of 32 mU/min Low dose: 2.0 mU/min and doubling every 30 minutes to a maximum of 32 mU/min	Induction to delivery was longer in 30 min group, 8 vs 5hrs (p <0.05). Odds ratio, 95% CI Lo vs. Hi CS 0.40 (0.12-1.36) Spont vag del 1.53 (0.26-9.11) Hyperstimulation 0.17 (0.02-1.91) Induction to delivery 8hrs vs. 5hrs ns No difference in postpartum hemorrhage, perineal tears or pyrexia.	Amniotomy performed as soon as feasible. Goal was to achieve 3 contractions in 10 minutes. 1:1 care with midwife. FH monitored by auscultation q 15 min. Hyperstimulation described as 6-7 contractions in 10 minutes or any contraction lasting ≥ 2 min.

Randomized controlled trial	Inclusion	Intervention	Findings	Comments
Lazor LZ, Philipson EH, Ingardia CJ, Kobetitsch ES, Curry SL. Obstet Gynecol. 1993; Dec;82(6):1009-12. University of Connecticut, Hartford Hospital. **A randomized comparison of 15- and 40-minute dosing protocols for labor augmentation and induction.**	n = 865 (term, vertex, singleton, without obstetrical complications)	High dose: 1.0 mU/min and every 15 minute increases of 1-2 mU/min to a maximum of 30 mU/min Low dose: 1.0 mU/min and q 40 min increases of 1.5 – 3.0 mU/min to a maximum of 30 mU/min	Hi dose Lo dose p-value Augmentation: CS 16.7% 11.8% ns Hyperstimulation 8.2% 6.5 <0.001 5 min Apgar <7 0 0 Oxytocin to delivery 5.4hrs 5.8 hrs, ns Induction: CS 18.6% 23.5% ns Hyperstimulation 33.0% 18.6% ns 5 min Apgar <7 0 0 Oxytocin to delivery 9.1hrs 8.8 hrs, ns	Hyperstimulation defined as ≥ 9 contractions in 15 minutes.
Mercer B, Pilgrim P, Saibai B. Oster Gynecol. 1991;77(5):659-63. H.E. Crump Women's Hospital, University of Tennessee, Memphis. **Labor induction with continuous low-dose oxytocin infusion: a randomized trial.**	n=123 (50% of sample nullips) Intact membranes	High dose: oxytocin started at 0.5 mU/min and increased to 1,2,4,8,16,20 & 24 mU/min at 20 or more intervals Low dose; oxytocin started at 0.5 mU/min and increased to 1,2,4,8,12, & 16 mU at 60 min or more intervals	Hi dose Lo dose p value Epidural 77.0% 77.4% ns Meconium 28.8% 25.8% ns 5 min Apgar 0 3.2% ns CS 13.1% 30.7% 0.02 CS for fetal dist 1.6% 9.7% 0.02 Induction to del 11.4hrs 13.2 ns	ARM done as soon as sufficiently dilated. Fetal heart rate and uterine contractions continuously monitored. . Hyperstimulation defined as >5 contractions in 10 min or lasting >90 sec.

Controlled Trial	Inclusion	Intervention	Findings	Comments
Satin AJ, Leveno KJ, Sherman ML, Brewster DS, Cunningham FG. Obstet Gynecol. 1992; Jul;80(1):111-6. Parkland Memorial Hospital **High- versus low-dose oxytocin for labor stimulation.**	n =2788 (singleton cephalic)	High dose: 6.0 mU/min and increases of 6 mU/min every 20 min to a maximum of 42 mU/min Low dose: 1 mU/min and increases of 1 mU/min q20 min to 8 mU/min then 2 mU/min to max 20 mU/min.	Hi dose Lo dose p-value Augmentation: CS 13% 16% 0.07 Hyperstimulation 52% 39% <0.001 5 min Apgar <3 0.3% 0.4% ns Adm to delivery 10.1hrs 13.4hrs<0.001 Induction: CS 19% 18% ns Hyperstimulation 61% 46% 0.001 5 min Apgar <3 1.9% 1.3% ns Adm to delivery 12.4hrs 6.0hrs, <0.001	Augmentation: 61% of high dose group and 60% of lo dose group were nulliparous. Induction: 53% and 55% respectively Groups were formed according to consecutive five month periods. 1:1 nursing care EFM required Goal was 3 contractions in 10 minutes. Hyperstimulation defined as contraction > 2 min or ≥ 6 contraction in 10 min. Managed by turning off the infusion and adjusting subsequent dosage to one half the previous dose
Xenakis EM, Langer O, Piper JM, Conway D, Berkus MD. Am J Obstet Gynecol. 1995; Dec;173(6):1874-8 University of Texas Health Science Center at San Antonio, USA **Low-dose versus high-dose oxytocin augmentation of labor--a randomized trial.**	n=310 (singleton, nulliparous and multiparous women, >37 weeks gestational age, without malpresentation, and VBAC with previous low segment transverse cesarean section)	High dose:4.0 mU/min and increases of 4 mU/min q 15 min Low dose: 1 mU/min and increases of 1 mU/min every 30 min to max 4 mU/min x 2 hrs then continue increments at 1 mU/min every 30 min.	Hi dose Lo dose p-value CS 11.1% 27.7% 0.006 SVD 61.1% 42.6% 0.02 Hyperstimulation 4.6% 5.2% ns 5 min Apgar <3 0 0 ns Time to correct labour abnormality 1.2 hrs 3.1hrs <0.001	Groups were assigned according to the day of the week on admission Continuous EFM, IUPC monitoring. Adequate contractility defined as ≥200 Montevideo units in 10 min.

Prospective Cohort study	Inclusion	Intervention	Findings	Comments
Krening CF, Rehling-Anthony K, Garko C. J Perinat Neonatal Nurs. 2012;26(1):15-24. 9 Centura Health Hospitals Colorado Springs, Colorado, USA **Oxytocin administration: the transition to a safer model of care.**	High dose ≈270 Low dose not stated (nulliparous and multiparous women, vertex presentation)	High dose: 0.5-6.0 mU/min increasing by 1.0-2.0 mU/min every 20-60 min until fetal distress or adequate contractions. Low dose: 0.5-2.0 mU/min increasing by 1.0-2.0 mU/min every 30 to 60 min to a maximum of 20.0 mU/min.	High dose / Low dose / p-value Primary CS 60.5% 55.5% Oxytocin to del Primiparas 9.9 hrs 8.9 <0.005 Multiparas 7.8 hrs 6.2 <0.005 Tachysystole, 54.0% 19.2% 0.0005	Safety checklists used to assure maternal/fetal well-being prior to initiation of oxytocin and increases in dosage.
Retrospective Cohort study	**Inclusion**	**Intervention**	**Findings**	**Comments**
Ghidini A, Wohlleb D, Korker V, Pezzullo JC, & Poggi SH. Open Journal of Obstetrics and Gynecology, 2012; 2(2), 106-111. Inova Alexandria Hospital, Alexandria, USA **Effects of two different protocols of oxytocin infusion for labor induction on obstetric outcomes: A cohort study.**	n =544 (singleton, >39 weeks gestational age, cephalic presentation, absence of non-reassuring fetal heart rate patterns, no uterine scar, no twins, genital herpes or placenta previa)	High dose: 4.0 mU/min increasing to 8.0, 16.0, 32.0 mU/min, increased 30 minutes Low dose: 4.0 mU/min increasing to 8.0, 12.0, 16.0, 20.0, 24.0, 28.0, 32.0 mU/min, increased every 30 minutes	Hi dose / Lo dose / p value CS 30% 27% 0.90 Hyperstimulation 2% 0% 0.37 Adm to delivery 11.7hrs 14.3 0.03 No difference in Apgar Scores < 7 at 5 minutes, NICU admissions, actual values not reported.	Apgar scores not reported Continuous monitoring of fetal heart rate and uterine contractions. Goal was to have 3-5 contractions in 10 min. Hyperstimulation defined as > 5 contractions in 10 min x 20 min and oxytocin was then decreased to the previous dose. Multivariate regression to control for confounders.