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Kenyon, Sara; Sanders, Julia; Middleton, Lee; Johnston, Tracey

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What is the best treatment to reduce the need for caesarean section in nulliparous women at term with delayed first stage of labour?

Sara Kenyon professor of evidence based maternity care, Julia Sanders reader, consultant midwife, Lee Middleton senior statistician, Tracey Johnston consultant in maternal and fetal medicine

1Institute of Applied Health Research, University of Birmingham, Birmingham B15 2TT, UK; 2Healthcare Sciences, Cardiff University, Cardiff CF24 0AB, UK; 3Birmingham Clinical Trials Unit, School of Cancer Sciences, Robert Aitken Institute, University of Birmingham, Birmingham; 4Birmingham Women's and Children's NHS Foundation Trust, Birmingham

Labour is commonly divided into three stages. The duration of the first and second stages of labour vary, dependent on parity. Figure 1 depicts the stages of labour and expected duration as defined by the National Institute for Health and Care Excellence (NICE). Nulliparous women tend to have a longer labour than multiparous women. Delay can result from poor uterine contractions or the relationship between size, presentation, and position of the fetus and the maternal pelvis that obstructs vaginal delivery. Uterine contractile dysfunction affects between 11% and 30% of nulliparous women and is the focus of this paper.

Delayed labour—There is some variation worldwide in the definition of delayed labour (table 1). The World Health Organization considers delay as a rate of cervical dilation of less than 0.5-1 cm in four hours once labour is established, whereas NICE recommends waiting a further two hours with cervical dilation of less than 1 cm before delay is confirmed. Prolonged labour is associated with higher rates of chorioamnionitis with risk of neonatal sepsis and of unplanned caesarean section with associated risks of infection and bleeding.

Oxytocin—Treatment for a confirmed delay in labour is with intravenous oxytocin to re-establish effective uterine contractions. The dose is titrated against the strength and frequency of uterine contractions by means of a variable rate infusion pump and taking into account fetal wellbeing through electronic fetal heart monitoring. Adverse effects include uterine tachysystole and uterine hyperstimulation (see box 1 for definitions), which are associated with hypoxic ischaemic encephalopathy and neonatal death. Mother and baby therefore need to be intensively monitored during treatment with oxytocin. Injudicious use of oxytocin and inappropriate management during labour have resulted in cases of fetal hypoxia and resultant controversy around its use. There is no consensus on the optimal dose regimen of oxytocin for delay in the first stage of labour in nulliparous women at term (37-42 weeks' gestation) to reduce unplanned caesarean section and increase vaginal birth with minimal adverse events. Recommendations are lacking apart from in the UK (table 1), and the regimens used vary widely even within the same country, despite calls for a standardised regimen.

What is the evidence of uncertainty?

Limited evidence from randomised trials suggests that use of oxytocin at a low dose shortens labour but does not affect whether the baby is born normally, by means of instruments (forceps or ventouse), or by caesarean section. With respect to the effectiveness of high dose regimens of oxytocin, the Cochrane review published in 2013 (including 644 women, three randomised controlled trials, and one quasi-randomised trial) compared high dose oxytocin regimens with low dose regimens in women delayed in normal labour. Because of variation in the dose regimens in the trials, the authors defined high dose oxytocin as starting dose and increments >4 mU/minute and low dose oxytocin as starting dose 1-4 mU/minute and increments of 1-2 mU/minute. High dose regimens were associated with a decrease in the rate of caesarean section (risk ratio 0.62; 95% confidence interval 0.44
What you need to know

- Prolonged labour is associated with adverse outcomes for mother and fetus, and intravenous oxytocin is the mainstay of treatment
- There is uncertainty as to the optimal regimen of oxytocin to decrease the chances of caesarean section with minimal adverse effects, and there is some evidence that high dose regimens may be effective
- Administer oxytocin in hospital where the mother and baby can be closely monitored

Box 1: Definitions of terms used

Nulliparous—Woman who has not given birth before
Utterine tachysystole—Increased uterine contractions; >5 uterine contractions in 10 minutes for 20 minutes
Utterine hyperstimulation—Tachysystole with abnormal features of the fetal heart rate suggestive of hypoxia

Box 2: Ongoing randomised controlled trials comparing low dose oxytocin regimens with high dose regimens for delay in the first stage of labour for nulliparous women

NCT01587625 OxyHighLow trial
Double blind randomised controlled trial of high dose versus low dose oxytocin for augmentation of delayed labour. Study start date April 2012, recruitment due to be completed in December 2016
Setting and population—Three hospitals in southwest Sweden; 1376 nulliparous women at term in spontaneous active labour (regular painful contractions, effaced cervix, dilated >3-4 cm) whose progress is delayed defined with a 3 hour partogram action line
High dose regimen—Initial infusion 6.6 mU/minute increasing every 20 minutes by 6.6 mU to maximum of 59.4 mU/minute
Low dose regimen—Initial infusion 3.3 mU/minute increasing every 20 minutes by 3.3 mU to maximum of 29.7 mU/minute (this is the recommended standard dose in Sweden)
Primary outcome—Caesarean section

NCT02487797
Randomized double blind clinical trial comparing oxytocin low dose and high dose regimens for labour augmentation. Study start date September 2015, due to complete recruitment in June 2018
Setting and population—Northwestern Memorial Hospital, Prentice Women’s Hospital, Chicago, USA; 1002 nulliparous women >36 weeks pregnant with a singleton diagnosed with 36/ regular uterine contractions within 60 minutes of observation, plus at least one of the following: cervix ≥3 cm dilated or 80% effaced, or spontaneous rupture of membranes
High dose regimen—Initial infusion 6 mU/minute increasing every 15-30 minutes by 6 mU/minute
Low dose regimen—Initial infusion 2 mU/minute increasing every 15-30 minutes by 2 mU/minute
Primary outcome—Caesarean section

ISRCTN99841044, high or low dose Syntocinon for delay in labour (HOLDS)
Multicentre, randomised, double blind controlled trial. Recruitment due to start in March 2017 and be completed by August 2018. Trial will be closed in May 2019
Setting and population—30 maternity units in UK; 1500 nulliparous women with confirmed delay in the first stage of labour and ruptured membranes. Labour is established by regular, painful contractions and progressive cervical dilation from 4 cm. Delay is suspected when cervical dilation is <2 cm in 4 hours once labour is established. Delay is confirmed by progress of <1 cm in 2 hours on repeat vaginal examination
High dose regimen—Initial infusion 4mU/minute increasing every 30 minutes to maximum of 64 mU/minute
Low dose regimen—Initial infusion 2mU/minute increasing every 30 minutes to maximum of 32 mU/minute
Primary outcome—Caesarean section

Box 3: Recommendations for further research
Population—Nulliparous women with a singleton pregnancy at term with delayed progress in the first stage of spontaneous labour
Intervention—High dose regimens of oxytocin
Comparison—Low dose regimens of oxytocin
Outcome—Mode of birth (vaginal birth or caesarean section), safety, harms, duration of labour, women’s acceptability and satisfaction

Sources and selection criteria
We searched the websites of English speaking Colleges of Obstetricians and Gynaecologists internationally for definitions of normal and delayed labour and treatment. We also searched WHO Guidelines and in the UK NICE guidelines (detailed in table 1). For evidence of effectiveness of oxytocin, we searched the Cochrane Database of Systematic Reviews and Clinical Evidence in January 2017 with search terms “delay in labour,” “augmentation,” “spontaneous vaginal birth,” and “caesarean section.” We found one Cochrane review.

Education into practice

- What ideas does this article offer you on how to better describe normal labour, particularly to nulliparous women?
- Are you aware of how prolonged labour is managed in your local maternity setting? What is usual practice?
- How could you best describe the management options for women with prolonged labour?

How patients were involved in the creation of this article
The patient representative on our research group highlighted the lack of evidence on women’s views on the experience of prolonged labour, which we have included.

13 Staal PJ. Oxytocin should not be used to augment labour: FOR; there is too much risk for too little benefit. BJOG 2015;125:1543. doi:10.1111/1471-0528.13571 pmid:26406259.


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<table>
<thead>
<tr>
<th>Professional organisation, year published</th>
<th>Normal length of labour</th>
<th>Definition of delay or prolonged labour</th>
<th>Recommended regimen of oxytocin</th>
</tr>
</thead>
<tbody>
<tr>
<td>National Institute for Health and Care Excellence (NICE), 2014</td>
<td>8-18 hours</td>
<td>Suspected delay &lt;2 cm dilation in 4 hours, with delay confirmed with progress of &lt;1 cm 2 hours later</td>
<td>2 mIU/min increasing every 30 minutes to maximum of 32 mIU/min</td>
</tr>
<tr>
<td>American College of Obstetricians and Gynecologists, 2014</td>
<td>&lt;20 hours</td>
<td>6 cm dilation with ≥4 hours of adequate contractions or ≥6 hours of inadequate contractions</td>
<td>None detailed or recommended</td>
</tr>
<tr>
<td>Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2014</td>
<td>Not defined</td>
<td>Dilation &lt;1 cm/hour in active phase (period of labour with dilatation of cervix from ~3–4 cm to 10 cm)</td>
<td>None detailed or recommended</td>
</tr>
<tr>
<td>World Health Organization, 2014</td>
<td>Not defined</td>
<td>&lt;0.5-1 cm/hour during active phase</td>
<td>None detailed or recommended</td>
</tr>
<tr>
<td>Society of Obstetricians and Gynaecologists of Canada, 2016</td>
<td>Not defined</td>
<td>&lt;0.5 cm/hour over 4 hour period</td>
<td>None detailed or recommended</td>
</tr>
</tbody>
</table>
Figure

Stage 1
The cervix relaxes, causing it to dilate and thin out

Expected duration:
8-18 hours for nulliparous women
5-12 hours for multiparous women

Stage 2
Uterine contractions increase in strength and the infant is delivered

Expected duration:
3 hours for nulliparous women
2 hours for multiparous women

Stage 3
The placenta is expelled

Expected duration:
1 hour

Fig 1 The three stages of labour and their expected duration¹