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PRACTICE

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UNCERTAINTIES

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

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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).[1] 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[2-4] 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[9] with risk of neonatal sepsis and of unplanned caesarean section with associated risks of infection and bleeding.[10-12]

Oxytocin—Treatment for a confirmed delay in labour is with intravenous oxytocin[1 5] 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.[13] 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,[14] despite calls for a standardised regimen.[15]

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.[1 16]

With respect to the effectiveness of high dose regimens of oxytocin, the Cochrane review[17] 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

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This is one of a series of occasional articles that highlight areas of practice where management lacks convincing supporting evidence. The series adviser is David Tovey, editor in chief, the Cochrane Library. This paper is based on a research priority identified and commissioned by the National Institute for Health Research's Health Technology Assessment programme on an important clinical uncertainty. To suggest a topic for this series, please email us at uncertainties@bmj.com.

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

Uterine tachysystole—Increased uterine contractions; >5 uterine contractions in 10 minutes for 20 minutes

Uterine hyperstimulation—Tachysystole with abnormal features of the fetal heart rate suggestive of hypoxia

to 0.86), although there was some doubt about this estimate because of heterogeneity of treatment effect estimates (risk ratio 0.67; 0.38 to 1.18) under alternative model assumptions. The only trial reporting length of labour[17] included only 40 women and reported a reduction with high dose of oxytocin (mean difference −3.50 hours; 95% CI −6.38 to −0.62). Two of the trials included both nulliparous and multiparous women, which limits interpretation of findings. No differences were noted in other maternal and neonatal outcomes or adverse effects.

There is uncertainty as to women's views of the use of oxytocin, with most trials focusing on clinical outcomes.[18] Limited qualitative evidence from interviews with women who experienced prolonged labour suggests that intervention is acceptable to women[19] and that, in case of a delay, women preferred to defer decision making to professionals.[20]

Is ongoing research likely to provide relevant evidence?

No further trials have been reported since publication of the Cochrane review, but several are ongoing. We searched the WHO International Clinical Trials Registry Platform and Clinicaltrials.gov in January 2017 and identified three ongoing trials comparing low dose and high dose oxytocin for delay in the first stage of labour in nulliparous women (see box 2 for details).

These studies are likely to provide evidence on effectiveness and safety of a high dose oxytocin regimen in delayed labour to reduce duration of labour and improve chances of spontaneous vaginal birth. The trials are taking place in America, Sweden, and the UK.

Box 3 lists recommendations for further research.

What should we do in light of the uncertainty?

Nulliparous women and women with a higher body mass index have higher risk for slow progress in labour.[21] At the antenatal visit close to term, discuss with the woman and her partner the expected duration and stages of labour and the possibility of prolonged labour. Emphasise the importance of remaining mobile and hydrated during labour. Explain that, if labour progresses more slowly than expected, there is an increased chance of infection and of requiring a caesarean section. At the start of labour, inform the woman that progress of labour and wellbeing of the fetus will be monitored throughout. Regular vaginal examinations will be done to assess cervical dilatation. As there is variation in the definitions of delay in labour, rely on the relevant guidelines to make a diagnosis (table 1⇓).

Women with prolonged labour can opt to wait and see how labour progresses without augmentation by oxytocin. Intravenous oxytocin may be offered to strengthen uterine contractions and accelerate progress, but there is only limited evidence that this will increase the likelihood of spontaneous delivery.

In case of a delay, offer pain relief and intravenous oxytocin until the woman gives birth. Further evidence is required before offering high dose oxytocin outside of a research setting. Oxytocin should be given only where close monitoring of the mother and fetus is possible and where adequate pain relief can be given. If the woman is in labour outside an obstetric unit, timely referral to a hospital for assessment and appropriate intervention is recommended.

The authors are members of the HOLDS Collaborative Group. The remaining co-applicants on the HOLDS grant are Dr Jane Daniels, Professor Andrew Ewer, Ruth Hewston, and Mr Jason Waugh. All the co-applicants reviewed and agreed the paper.

Contributors: SK drafted the paper which was seen and commented on by all members of the HOLDS Collaborative Group.

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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 ≥6 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 better to 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.

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Table

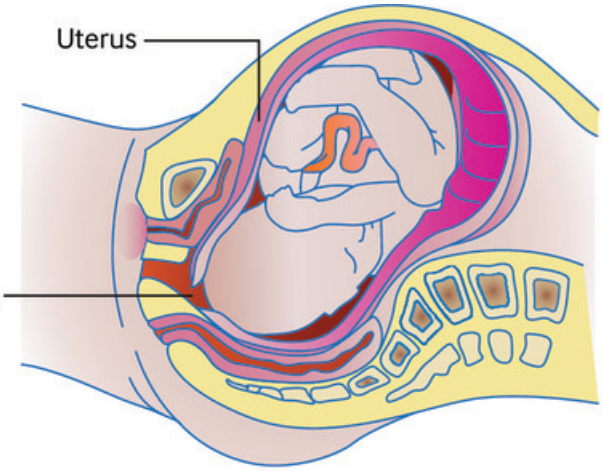
Table 1| Summary of professional guidelines for normal duration of labour, definition of delay in the first stage of labour, and recommended treatment with oxytocin in nulliparous women

Professional organisation, year published	Normal length of labour	Definition of delay or prolonged labour	Recommended regimen of oxytocin
National Institute for Health and Care Excellence (NICE), 2014[1]	8-18 hours	Suspected delay <2 cm dilation in 4 hours, with delay confirmed with progress of <1 cm 2 hours later	2 mU/min increasing every 30 minutes to maximum of 32 mU/min
American College of Obstetricians and Gynecologists, 2014[5]	<20 hours	6 cm dilation with ≥4 hours of adequate contractions or ≥6 hours of inadequate contractions	None detailed or recommended
Royal Australian and New Zealand College of Obstetricians and Gynaecologists, 2014[6]	Not defined	Dilation <1 cm/hour in active phase (period of labour with dilatation of cervix from ~3–4 cm to 10 cm)	None detailed or recommended
World Health Organization, 2014[7]	Not defined	<0.5-1 cm/hour during active phase	None detailed or recommended
Society of Obstetricians and Gynaecologists of Canada, 2016[8]	Not defined	<0.5 cm/hour over 4 hour period	None detailed or recommended

Figure

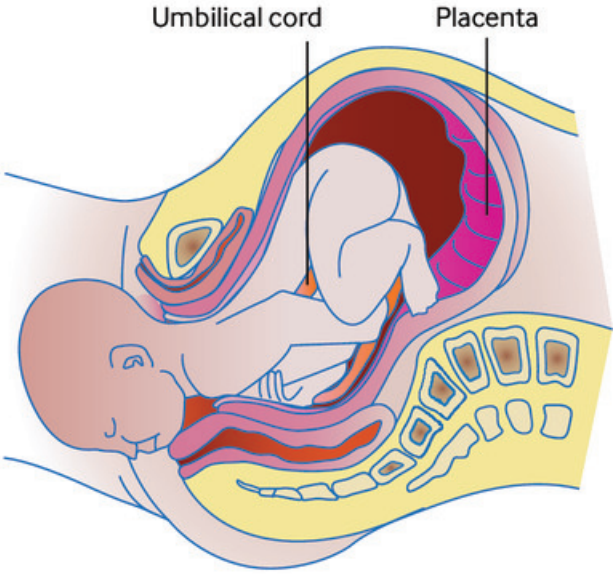
Stage 1
The cervix relaxes, causing it to dilate and thin out

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

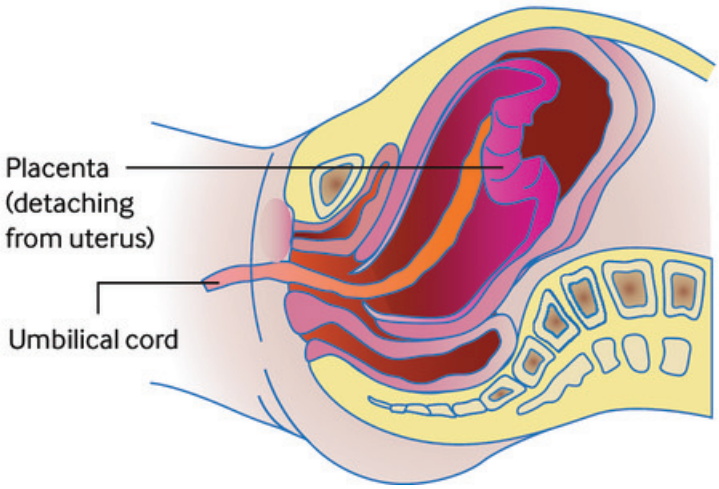


Fig 1 The three stages of labour and their expected duration[1]