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RESEARCH

Induction versus expectant monitoring for intrauterine growth restriction at term: randomised equivalence trial (DIGITAT)

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ABSTRACT

Objective To compare the effect of induction of labour with a policy of expectant monitoring for intrauterine growth restriction near term.

Design Multicentre randomised equivalence trial (the Disproportionate Intrauterine Growth Intervention Trial At Term (DIGITAT)).

Setting Eight academic and 44 non-academic hospitals in the Netherlands between November 2004 and November 2008.

Participants Pregnant women who had a singleton pregnancy beyond 36+0 weeks' gestation with suspected intrauterine growth restriction.

Interventions Induction of labour or expectant monitoring.

Main outcome measures The primary outcome was a composite measure of adverse neonatal outcome, defined as death before hospital discharge, five minute Apgar score of less than 7, umbilical artery pH of less than 7.05, or admission to the intensive care unit. Operative delivery (vaginal instrumental delivery or caesarean section) was a secondary outcome. Analysis was by intention to treat, with confidence intervals calculated for the differences in percentages or means.

Results 321 pregnant women were randomly allocated to induction and 329 to expectant monitoring. Induction group infants were delivered 10 days earlier (mean difference −9.9 days, 95% CI −11.3 to −8.6) and weighed 130 g less (mean difference −130 g, 95% CI −188 g to −71 g) than babies in the expectant monitoring group. A total of 17 (5.3%) infants in the induction group experienced the composite adverse neonatal outcome, compared with 20 (61%) in the expectant monitoring group (difference −0.8%, 95% CI −4.3% to 3.2%). Caesarean sections were performed on 45 (14.0%) mothers in the induction group and 45 (13.7%) in the expectant monitoring group (difference 0.3%, 95% CI −5.0% to 5.6%).

Conclusions In women with suspected intrauterine growth restriction at term, we found no important differences in adverse outcomes between induction of labour and expectant monitoring. Patients who are keen on non-intervention can safely choose expectant management with intensive maternal and fetal monitoring; however, it is rational to choose induction to prevent possible neonatal morbidity and stillbirth.

Trial registration International Standard Randomised Controlled Trial number ISRCTN10363217.

INTRODUCTION

Most infants with intrauterine growth restriction are born at term.[1] Growth restriction so late in gestation is associated with increased perinatal morbidity in the form of fetal distress, hypoglycaemia, seizures, behavioural problems, cerebral palsy, and cardiovascular disease, as well as perinatal mortality.[2-11] Obstetricians often induce labour in cases of intrauterine growth restriction for fear of neonatal morbidity and later stillbirth. However, observational comparisons of such infants with matched fetuses delivered after spontaneous labour have shown no reduction in short term adverse neonatal outcomes. Induction might increase obstetric interventions[12-14] and even cause neonatal morbidity if performed before 39 weeks.[15-18] For these reasons, expectant management with maternal and fetal monitoring is a commonly followed strategy.

The Disproportionate Intrauterine Growth Intervention Trial At Term (DIGITAT) was designed to compare the effect of induction of labour with expectant monitoring on a composite adverse neonatal outcome and on operative delivery rates in infants with suspected growth restriction beyond 36 weeks' gestation. In a pilot trial comparing these two interventions in 33 women, neonatal outcomes and operative

delivery rates were comparable, but the precision of the estimate of the effect size was limited.[19]

METHODS

The trial was run by the Dutch Obstetric Consortium, a collaboration of perinatal centres in the Netherlands, and approved by the University of Leiden institutional review board. The study was staffed by obstetricians, research nurses, and midwives associated with the Dutch Obstetric Consortium. They counselled and recruited participants, monitored compliance with allocated treatment protocols, and collected outcome data.

Recruitment ran from November 2004 to November 2008. The study began in four hospitals, but by the end of the study period recruitment had been rolled out to 52 maternity hospitals in Holland. Making the crude assumptions that the average centre recruited for half the trial duration of three years (that is, 18 months), that each centre delivered 1500 women a year (adjusting for women seen only in labour or who were ineligible because of multiple pregnancy or breech pregnancy), and assuming that half of all growth restricted fetuses are detectable, we anticipated that about 1326 potentially eligible women would be identified over the recruitment period.

Participants

Pregnant women between 36+0 and 41+0 weeks' gestation who had a singleton fetus in cephalic presentation, suspected intrauterine growth restriction, and who were under specialised obstetric care were recruited. Suspected intrauterine growth restriction was defined as fetal abdominal circumference below the 10th percentile, estimated fetal weight below the 10th percentile, flattening of the growth curve in the third trimester (as judged by a clinician), or the presence of all three factors.[20] Both fetuses with abnormal Doppler flow velocity measurements and those with normal Doppler flow velocity measurements were included.

The DIGITAT recruitment period overlapped with recruitment for the Hypertension Intervention Trial At Term (HYPITAT),[21] which compared similar interventions in women with gestational hypertension and mild pre-eclampsia at term. Patients with both suspected intrauterine growth restriction and hypertension were preferentially recruited to DIGITAT, and women could not participate in both studies. Gestational hypertension and pre-eclampsia were defined according to criteria from the International Society for the Study of Hypertension in Pregnancy.[22] Oligohydramnios was defined as an amniotic fluid index of 5 cm or less.

Exclusion criteria were previous caesarean section, diabetes mellitus or gestational diabetes requiring insulin therapy, renal failure, HIV seropositivity, prelabour rupture of membranes, severe pre-eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes, and low platelet count), or a fetus with aneuploidy or congenital abnormalities suspected on ultrasound. Fetuses with decreased or absent movements, and those with abnormal heart rate tracings, were also excluded.

Cervical length was measured using transvaginal sonography and vaginal digital examination was performed to assess the Bishop score before randomisation.[23]

Randomisation

Participant data were entered into a secure web based database. Women were randomly allocated to either induction or expectant monitoring in a 1:1 ratio using varied sized block randomisation with stratification for centre and parity (nulliparous or parous women). Women who declined consent for randomisation but authorised use of their medical data were treated at the discretion of the local obstetrician and included in the database. These data were used to study external validity of the trial. Women who refused both randomisation and collection of identifiable data were registered anonymously. It was not possible to blind participants, obstetricians, or outcome assessors. Written informed consent was obtained from all participants before randomisation.

Participants allocated to the induction of labour group were induced within 48 hours of randomisation. If the Bishop score at randomisation was greater than 6, labour was induced with amniotomy and, if necessary, augmented with oxytocin. Otherwise cervical ripening was performed with intracervical or intravaginal prostaglandin (E1 or E2 analogue, repeated once after six hours) or a Foley balloon catheter filled with 30 mL sodium chloride.[24]

Participants allocated to the expectant monitoring group were monitored until the onset of spontaneous labour with daily fetal movement counts and twice weekly heart rate tracings, ultrasound examination, maternal blood pressure measurement, assessment of proteinuria, laboratory tests of liver and kidney function, and full blood count. Women were monitored as either an outpatient or an inpatient, according to local protocol. In the expectant monitoring group, induction of labour or planned caesarean section was performed for obstetrical indications—such as suboptimal fetal heart rate tracings, prolonged rupture of membranes, or postmaturity between T+7 and T+14 days—at the obstetrician's discretion.

Outcomes

The primary outcome was a composite measure of adverse neonatal outcome. This was defined as death before hospital discharge, five minute Apgar score of less than 7, umbilical artery pH of less than 7.05, or admission to neonatal intensive care. If the umbilical artery pH data were missing and all other components of the composite outcome were normal, the neonatal outcome was classified as normal. Secondary outcomes were delivery by caesarean section, instrumental vaginal delivery, length of stay in the neonatal intensive care or neonatal ward, length of stay in the maternal hospital, and maternal morbidity. The latter was defined as postpartum haemorrhage of more than 1000 mL, development of gestational hypertension or pre-eclampsia (according to International Society for the Study of Hypertension in Pregnancy criteria),[21]

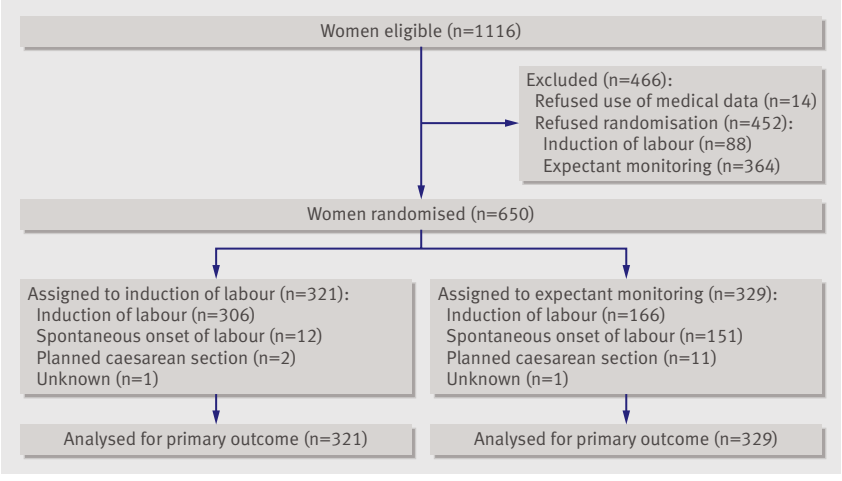
eclampsia, pulmonary oedema, thromboembolism, or any other serious adverse event.

Study design, sample size, and statistical analysis

The trial was designed as an equivalence trial in which the null hypothesis was that the difference in the risk of the composite outcome between the two treatment groups was greater than 5.5% (absolute percentage). Assuming that the rate in the control group was 6% (on the basis of data from the National Dutch Perinatal Registry[25]), this meant that we would exclude the null hypothesis and conclude that the two treatments were equivalent if the boundaries of the confidence interval of the observed risk difference were between −5.5% and 5.5%. With a 0.05 risk of type I error (α) and 80% (1−β) power, we calculated that we would require 650 participants (325 per group). The sample size formula for equivalence testing on page 39 of Jones et al[26] was used to calculate these numbers, assuming that the induction rate and the control rate were both equal to 6% under the alternative of equivalence.

Data were analysed according to the intention to treat principle. Continuous variables were summarised as means with standard deviations, or medians with interquartile ranges (IQR). Treatment effects were presented as differences in means or percentages with 95% confidence intervals (CI). Equivalence of the primary outcome measure was tested by checking if the 95% CI of the risk difference lay within the equivalence margins. Continuous variables were compared using the Student's *t* test or the non-parametric Mann-Whitney U test. The χ^2 test was used for categorical variables. Instances were more than 5% of the observations were missing are indicated in the footnotes of the tables.

In a secondary analysis, the primary and secondary outcomes for the two groups were compared after exclusion of women with hypertension related diseases (pre-existing hypertension, gestational hypertension, and pre-eclampsia) at randomisation. Given that randomisation was stratified for centre and parity, we also performed a stratified analysis for the primary outcome by using logistic regression with parity as fixed covariate and centre as random covariate. Statistical analyses were performed using SPSS software (version 16.0; IBM, Chicago, IL) and Stata software (version 10.1; Stata Corp, College Station, TX).



Flow diagram of the trial process

RESULTS

A total of 1116 potentially eligible women were identified. Of these women, 14 refused any use of identifiable data and 452 declined randomisation. This left 650 participants, who were randomly assigned to induction (n=321) or expectant monitoring (n=329; fig 1). The baseline characteristics of participants in the two randomised arms and in the non-randomised group are shown in table 1. Compared with the induction group, women in the expectant monitoring group were more likely to have a Bishop score of less than or equal to 6 and have gestational hypertension, but otherwise the two randomised arms were comparable. Women who declined randomisation were older, had a higher education level, were less likely to smoke, had a lower body mass index (BMI), and were less likely to have a fetal abdominal circumference below the 10th centile. Most women who were randomised met either the fetal abdominal circumference below 10th centile inclusion criterion or the estimated fetal weight below the 10th centile criterion. Only 13 women in the induction group and 10 women in the expectant monitoring group were included because of flattening of the growth curve in isolation.

Details of the onset of labour are shown in table 2, and pregnancy outcomes are shown in table 3. Trial compliance was good, with induction performed in 306 (95.6%) women in the induction group and in only 166 (50.6%) in the expectant monitoring group, resulting in a median time from randomisation to onset of labour of 0.9 days (IQR 0.7–1.7) in the induction group and 10.4 days (IQR 5.6-16.0) in the expectant monitoring group.

Labour was induced in 166 (50.6%) women in the expectant monitoring group: 92 for suspected fetal distress; 21 for hypertensive disorders; 24 on maternal request; nine for prelabour rupture of membranes; five for post-term pregnancy; and 15 for unspecified maternal reasons. Planned caesarean section was performed in two (0.6%) women in the induction arm: one because of fetal distress, the second because of primary genital herpes infection. A total of 11 (3.3%) women in the expectant monitoring arm had a planned caesarean section: in 10 cases for fetal distress and one for unpredicted breech position. In the expectant monitoring arm, the median time from randomisation to delivery among women who delivered by planned caesarean section was 4.5 days. The numbers of operative and instrumental deliveries were comparable between the groups (27 (8.4%) in the induction group and 27 (8.2%) in the expectant monitoring group).

One (0.3%) woman allocated to induction of labour died at home 10 days after delivery. She had delivered a healthy child vaginally at 38+4 weeks of gestation

Table 1 | Demographic and baseline characteristics of randomised and non-randomised participants

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Non-randomised group (n=452)
Nulliparous	182 (56.7)	201 (61.1)	275 (61.0)
Maternal age	27 (23-31)	27 (23-31)	31 (27-34)
BMI at study entry†	22 (20-25)	22 (20-26)	21 (20-24)
Gestational age (days)	263 (258-269)	263 (258-270)	262 (258-269)
White race‡	254 (83.6)	253 (81.1)	344 (83.3)
Education			
Lower professional school	168 (52.3)	170 (51.7)	149 (33.0)
Medium professional school	26 (8.1)	37 (11.2)	93 (20.6)
Unknown	127 (39.6)	122 (37.1)	209 (46.3)
Maternal smoking§	138 (46.9)	127 (40.8)	114 (26.9)
Blood pressure at booking			
Systolic	115 (105-120)	114 (106-120)	115 (110-120)
Diastolic	70 (60-75)	66 (60-75)	70 (60-75)
Gestational hypertension	9 (2.8)	19 (5.8)	25 (5.5)
Pre-eclampsia	18 (5.6)	27 (8.2)	27 (6.0)
Inclusion criteria			
Fetal abdominal circumference <10th percentile	262 (81.6)	270 (82.1)	354 (78.5)
Estimated fetal weight <10th percentile	296 (92.2)	308 (93.6)	418 (92.5)
Deceleration of fetal abdominal circumference curve	83 (25.9)	84 (25.5)	95 (21.0)
Fetal abdominal circumference (mm)	287 (278-297)	289 (279-297)	289 (278-299)
Oligohydramnios¶	87 (31.0)	101 (34.5)	145 (34.4)
Umbilical artery Doppler††			
Pulsatility index in the umbilical artery	0.98 (0.85-1.13)	0.93 (0.82-1.10)	0.96 (0.84-1.11)
Absent	7 (2.7)	7 (2.5)	4 (1.0)
Reversed	0	0	1 (0.2)
Cervical length with transvaginal sonography (mm) ‡‡	30 (22-37)	30 (24-38)	33 (22-41)
Bishop score ≤6§§	280 (94.0)	293 (97.3)	64 (98.5)

Table shows median (interquartile range 25th to 75th percentile) or number (%).
†n=275 for induction, n=295 for expectant monitoring, n=364 for non-randomised.
‡n=304 for induction, n=312 for expectant monitoring, n=413 for non-randomised.
§n=294 for induction, n=311 for expectant monitoring, n=424 for non-randomised.
¶n=281 for induction, n=293 for expectant monitoring, n=421 for non-randomised.
††n=262 for induction, n=277 for expectant monitoring, n=381 for non-randomised.
‡‡n=299 for induction, n=312 for expectant monitoring, n=31 for non-randomised.
§§n=298 for induction, n=301 for expectant monitoring, n=65 for non-randomised.

after spontaneous onset of labour. No cause for her death was found at post mortem and it was classified as a serious unrelated adverse event. No women in the expectant monitoring group died during the study.

Neonatal outcomes are shown in table 4. There were no stillbirths or perinatal deaths. A total of 17 (5.3%) neonates in the induction arm and 20 (6.1%) neonates in the expectant monitoring arm had the primary composite adverse neonatal outcome (difference −0.8%, 95% CI −4.3% to 2.8%). No differences between groups in any of the components of the composite adverse neonatal outcome were found. Median birth weight was lower in the induction group than in the expectant monitoring group (2420 g *v* 2550 g; difference −130 g, 95% CI −188 to −71; P<0.001). Despite this difference, more fetuses in the expectant monitoring arm had a birth weight below the third percentile (100 (31%) *v* 40 (13%); difference −18.1%, 95% CI −24.3% to −12.0%; P<0.001).

Table 2 | Onset of labour

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Difference in mean or percentage (95% CI)
Time between randomisation and onset of labour (days)	0.9 (0.7-1.7)	10.4 (5.6-16.0)	−9.6 (−10.8 to −8.5)
Gestational age at birth (days)	266 (261-271)	277 (269-283)	−9.9 (−11.3 to −8.6)
Onset of labour			
Spontaneous	12 (3.7)	151 (46.0)	−42.3 (−48.1 to −36.5)
Planned caesarean section	2 (0.6)	11 (3.3)	−2.7 (−4.9 to −0.6)
Induction	306 (95.6)	166 (50.6)	45.0 (39.2 to 50.9)

Table shows median (interquartile range 25th to 75th percentile) or number (%).

The numbers of infants admitted to neonatal intensive care and median duration of stay in unit was comparable between the two groups (9 (2.8%) from the induction group and 13 (4.0%) in the expectant monitoring group; duration 9 days, IQR 6–14 and 13 days, IQR 6–22, respectively). However, more neonates in the induction group were admitted to a ward providing an intermediate level of neonatal care (155 (48.4%) *v* 118 (36.3%); difference 12.1%, 95% CI 4.6% to 19.7%; P<0.05).

Exclusion of pregnancies complicated by hypertensive disease at randomisation did not alter the results for the composite adverse neonatal outcome or caesarean section (data not shown). Stratified analysis for centre and parity using logistic regression showed no treatment differences among the participating centres (data not shown).

DISCUSSION

This study has shown that among women with a singleton pregnancy complicated by suspected intrauterine growth restriction at a gestational age of between 36+0 and 41+0 weeks, a policy of labour induction affects neither the rate of adverse neonatal outcomes nor the rates of instrumental vaginal delivery or caesarean section.

The present study has only ruled out a difference in adverse neonatal outcomes larger than 4.3%. We have not ruled out an effect on the rarer outcome of perinatal death. One theoretical argument in favour of induction is that it might pre-empt intrauterine fetal death, so clinicians who wish to follow expectant management should monitor the ongoing pregnancy closely.

In our study the number of admissions to neonatal intensive care was comparable in both arms, but more neonates in the induction group were admitted to intermediate levels of care. This finding might be an artefact

Table 3 | Pregnancy outcomes

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Difference in mean or percentage (95% CI)
Mode of delivery			
Spontaneous vaginal delivery	249 (77.6)	257 (78.1)	−0.5 (−6.9 to 5.8)
Vaginal instrumental	27 (8.4)	27 (8.2)	0.2 (−4.0 to 4.4)
Caesarean section	45 (14.0)	45 (13.7)	0.3 (−5.0 to 5.6)
Indications for caesarean section			
Suspected fetal distress (with or without arrest of labour)	37 (82.2)	40 (88.9)	−6.7 (−21.1 to 7.8)
Arrest of labour	5 (11.1)	2 (4.4)	6.7 (−4.3 to 17.6)
Other	3 (6.7)	3 (6.7)	0.0 (−10.3 to 10.3)
Indications for instrumental vaginal delivery			
Suspected fetal distress (+/− arrest of labour)	21 (77.8)	25 (92.6)	−14.8 (−33.3 to 3.7)
Arrest of labour	6 (22.2)	2 (7.4)	14.8 (−3.7 to 33.3)
Adverse maternal outcome			
Maternal death	1 (0.3)	0	NA
Progression to gestational hypertension	1 (0.3)	6 (1.8)	−1.5 (−3.1 to 0.1)
Progression to pre-eclampsia	12 (3.7)	26 (7.9)	−4.2 (−7.7 to −0.6)*
Eclampsia, lung oedema, thromboembolic events	0	0	NA
Abruption placentae (partial)	1 (0.3)	0	NA
Postpartum haemorrhage	10 (3.2)	15 (4.7)	−1.5 (−4.5 to 1.5)
Maternal admission (days)†			
Length of stay in hospital	4 (2-6)	4 (2-7)	**

Table shows median (IQR 25th to 75th percentile) or number (%).
*P<0.05; **P=0.2 (Mann-Whitney test).
†n=232 admitted for induction, n=242 admitted for expectant monitoring. NA=not applicable.

Table 4 | Neonatal outcomes

	Induction of labour group (n=321)	Expectant monitoring group (n=329)	Difference in mean or percentage (95% CI)
Birth weight (g)	2420 (2220–2660)	2550 (2255–2850)	−130 (−188 to −71)**
Birthweight percentiles†			
<Third percentile	40 (12.5)	100 (30.6)	−18.1 (−24.3 to −12.0)**
Third to fifth percentile	82 (25.5)	79 (24.2)	1.3 (−5.3 to 8.0)
Fifth to 10th percentile	88 (27.4)	62 (18.9)	8.5 (−2.0 to 14.9)
10th to 25th percentile	88 (27.4)	66 (20.2)	7.2 (0.7 to 13.8)
>25th percentile	23 (7.2)	20 (6.1)	−1.1 (−2.8 to 4.9)
Composite adverse neonatal outcome	17 (5.3)	20 (6.1)	−0.8 (−4.3 to 2.8)
Fetal deaths	0	0	—
Neonatal deaths	0	0	—
Apgar score after five minutes <7	7 (2.2)	2 (0.6)	1.6 (−0.2 to 3.4)
Arterial pH <7.15‡	34 (12.2)	38 (13.2)	−1.0 (−6.5 to 4.5)
Arterial pH <7.10‡	12 (4.3)	19 (6.6)	−2.3 (−6.0 to 1.4)
Arterial pH <7.05‡	4 (1.4)	10 (3.5)	−2.1 (−4.6 to 0.5)
Arterial base excess < −10‡	16 (5.7)	26 (9.0)	−3.3 (−7.6 to 1.0)
Admission to intensive care	9 (2.8)	13 (4.0)	−1.2 (−4.0 to 1.6)
Neonatal admission			
Intermediate care	155 (48.4)	118 (36.3)	12.1 (4.6 to 19.7)*
Maternal ward	89 (27.8)	116 (35.7)	−7.9 (−15.0 to −0.7)*
No admission	67 (20.9)	78 (24.0)	−3.1 (−9.5 to 3.4)
Length of stay (days)			
Infants in the neonatal intensive care unit	9 (6-14)	13 (6-22)	***
All admissions	4 (2-8)	4 (2-8)	0.2 (−1.4 to 1.8)

Table shows median (IQR 25th to 75th percentile) or number (%).
*P<0.05; **P<0.001; ***P=0.2 (Mann-Whitney test).
†Percentiles according to Dutch fetal growth charts (weight related to gestational age).[36]
‡n=279 for induction, n=288 for expectant monitoring.

of the inevitable lower birth weight in this group given that the policy was to admit infants below a certain weight, but complications of late prematurity cannot be ruled out. Limiting induction to infants with a gestational age of greater than 37 weeks would reduce the incidence of this outcome, but we cannot know whether this approach would be associated with better long term outcomes.[27]

The higher median birth weight in the expectant monitoring group indicates that infants in this group gained on average 130 g during the roughly 10 additional days' gestation they experienced compared with the induction group. Presumably, although most neonates in the present trial were born with a weight below the 10th percentile, a number were not really growth restricted but rather constitutionally small. Constitutionally small infants have the potential to grow at term, whereas growth restricted infants might experience intrauterine undernourishment and decelerated growth. We also observed that the number of children with a birth weight below the third percentile differed significantly between the induction of labour group (12.5%) and the expectant monitoring group (31%). This suggests that a substantial number of children in the expectant monitoring group did not continue to grow along their own expected growth curves. Being born severely growth restricted appears to be associated with worse long term outcomes.[27] Although not defined as a primary outcome in our study, this suggestion could be a compelling reason for induction and certainly merits further investigation.

When women with hypertension or pre-eclampsia at the time of randomisation were excluded, the incidence of the composite adverse neonatal outcome did not differ between the study groups, nor did this result in a lower incidence of caesarean section among women in the expectant monitoring group. Results from the HYPITAT trial support a strategy of inducing women who develop a hypertensive disorder after 37 weeks of pregnancy to prevent possible maternal complications.[21] This probably also applies to women who develop hypertensive disorders in addition to growth restriction, but the number of such women in this trial was too small to investigate this possibility in detail.

Comparison with other studies

Previous observational studies suggest that antenatal detection and induction are associated with an increased incidence of obstetric interventions, without a demonstrable neonatal benefit.[12-14] However, our finding of no effect of induction on adverse neonatal outcomes, which is from a randomised trial, should supersede findings from observational studies. The finding that induction did not affect the rate of operative deliveries in our study should also not be surprising because observational studies that suggested an increase in operative intervention with induction have been contradicted by later randomised trials. Observational studies of the effect of induction near term for other fetal indications—such as post-maturity, ruptured membranes, and hypertensive disease—on the rate of operative deliveries have been similarly misleading.[28,29]

A similar trial of timed delivery among much more severely compromised pre-term fetuses, the Growth Restriction Intervention Trial (GRIT), was reported in 2004.[30,31] At two year follow-up, the risk of disability was reduced in the delayed delivery group compared with the immediate delivery group among babies younger than 31 weeks of gestation at randomisation. Because growth restriction is associated with a less favourable neurodevelopmental outcome in the term period as well as poor outcomes at delivery,[32] we plan to investigate the wellbeing of the children randomised during DIGITAT at two year follow-up.

Strengths and limitations of study

The main strength of this study is the comparison of randomised groups and the large size of the study population. There have been no other randomised trials in this area.

Identifying fetuses at risk of true intrauterine growth restriction is a diagnostic challenge. Customised growth centile charts[33] are rarely applied in the Netherlands and were not used in the present study, but might identify fetuses at risk. Although we encountered no perinatal deaths among the randomised women, the association between low birth weight and perinatal death is well accepted.[1-4] However, many thousands of participants would be required to power a study on the effects of induction on perinatal death.

The relatively favourable neonatal outcomes in both study groups could reflect the fact that participants and clinicians were more alert to possible complications and women received cautious attention from their doctors. Monitoring is also intensified in ordinary practice in the Netherlands, but monitoring and therefore neonatal outcomes could have been biased because of the study setting. The study results should be extrapolated with caution to settings where close monitoring cannot be offered.

It was possible to defer delivery in the expectant monitoring group for on average 9.6 days after randomisation, resulting in an average gestational age of 39+3 weeks. Prolongation of gestational age in this group led to more instances of spontaneous vaginal delivery than in the induction group, but did not reduce the number of caesarean sections. Compared with other countries (that is, the United States and the United Kingdom), rates of caesarean section in the Netherlands have always been relatively low,[34] and the rate in this group of high risk pregnancies was even lower than the average rate of 15% in the Netherlands.[25]

The fact that women who declined randomisation were older, more highly educated, and smoked less might suggest that the study recruited a slightly biased group of women. This may have an effect on the generalisability of the results.

Conclusions and policy implications

In conclusion, we found equivalent fetal and maternal outcomes for induction and expectant monitoring in women with suspected intrauterine growth restriction at term, indicating that both approaches are acceptable. In practice, however, obstetricians and patients will let factors other than growth restriction guide decision making at delivery.[35] It is reasonable for patients who are keen on non-intervention to choose expectant management with intensive maternal and fetal monitoring because, as far as we can tell, this approach is safe for the baby. However, it is more rational to choose induction to prevent possible neonatal morbidity and stillbirth on the grounds that we showed no increase in operative and instrumental delivery rates. However, our study was underpowered to show differences in late pregnancy loss.

By inducing labour in cases of intrauterine growth restriction, infants who will not grow any further can be released from their undernourished environment. Future studies should focus on how to distinguish before childbirth fetuses with genuine growth restriction and those that are constitutionally small, and on elucidating which antepartum factors predict adverse outcomes.

WHAT IS ALREADY KNOWN ON THIS TOPIC

Induction of labour is commonly recommended for intrauterine growth restriction near term to prevent possible neonatal morbidity or stillbirth

Induction might also increase neonatal respiratory problems and operative delivery rates; therefore, expectant management with maternal and fetal monitoring remains a commonly followed strategy

WHAT THIS STUDY ADDS

Fetal and maternal outcomes after induction of labour are equivalent to those with expectant monitoring in women with suspected intrauterine growth restriction at term

Induction is not associated with any increase in operative and instrumental delivery rates

Infants with suspected growth restriction are more likely to be admitted to an intermediate level of care after induction of labour than after expectant monitoring, possibly as a result of complications of late prematurity

It is rational to choose induction in patients with intrauterine growth restriction near term to prevent possible neonatal morbidity and stillbirth, and future studies should focus on the optimal timing of induction

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