THELANCET-D-13-08994R2
S0140-6736(14)61904-8
Embargo: [add date when known]

This version saved: 14:28, 05-Feb-15

Induction of labour versus expectant management for large-for-date fetuses: a randomised controlled trial

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Summary

Background Macrosomic fetuses are at increased risk of shoulder dystocia. We aimed to compare induction of labour with expectant management for large-for-date fetuses for prevention of shoulder dystocia and other neonatal and maternal morbidity associated with macrosomia.

Methods We did this pragmatic, randomised controlled trial between Oct 1, 2002,and Jan 1, 2009 in 19 tertiary-care centres in France, Switzerland, and Belgium. Women with singleton fetuses whose estimated weight exceeded the 95th percentile, were randomly assigned (1:1), via computer-generated permuted-block randomisation (block size of four to eight) to receive induction of labour within 3 days between 37^{+0} weeks and 38^{+6} weeks of gestation, or expectant management. Randomisation was stratified by centre. Participants and caregivers were not masked to group assignment. Our primary outcome was a composite of clinically significant shoulder dystocia, fracture of the clavicle, brachial plexus injury, intracranial haemorrhage, or death. We did analyses by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00190320.

Findings We randomly assigned 409 women to the induction group and 413 women to the expectant management group, of whom 407 women and 411 women, respectively, were included in the final analysis. Mean birthweight was 3831 g (SD 324) in the induction group and 4118 g (392) in the expectant group. Induction of labour significantly reduced the risk of shoulder dystocia or associated morbidity (n=8) compared with expectant management (n=25; relative risk [RR] 0·32, 95% CI 0·15–0·71; p=0·004). We recorded no brachial plexus injuries, intracranial haemorrhages, or perinatal deaths. The likelihood of spontaneous vaginal delivery was higher in women in the induction group than in those in the expectant management group (RR 1·14, 95% CI 1·01–1·29). Caesarean delivery and neonatal morbidity did not differ significantly between the groups.

Interpretation Induction of labour for suspected large-for-date fetuses is associated with a reduced risk of shoulder dystocia and associated morbidity compared with expectant management. Induction of labour does not increase the risk of caesarean delivery and improves the likelihood of spontaneous vaginal delivery. These benefits should be balanced with the effects of early-term induction of labour.

Funding Assistance Publique–Hôpitaux de Paris and the University of Geneva.

Introduction

Macrosomia is a risk factor for unfavourable delivery outcomes, including operative vaginal or caesarean delivery and shoulder dystocia.[1,2] Shoulder dystocia can cause neonatal morbidity, including fracture of the clavicle, brachial plexus injury, or asphyxia. Elective caesarean section can be done to avoid a vaginal delivery complicated by macrosomia. However, findings from a decision analysis[3] suggested that the number of elective caesarean sections needed to avoid one permanent brachial plexus injury is quite high. This strategy is thus recommended only when fetal weight is estimated to exceed 4500 g for women with diabetes and 5000 g for those without diabetes.[4]

Another option would be to induce labour, which reduces the opportunity for continued fetal growth and, theoretically, decreases the risk of caesarean section for cephalopelvic disproportion, and reduces the risk of operative vaginal delivery, perineal trauma, and shoulder dystocia. Nonetheless, induction of labour can fail, which would make caesarean delivery necessary. Early-term (37–38 weeks) delivery, especially by elective caesarean section, might also increase the risk of mortality and morbidity of the neonate, including long-term development issues.[5,6]

Several investigators have raised questions about induction of labour for macrosomic fetuses, especially because most observational studies have associated this strategy with an increased risk of caesarean delivery, with no significant decrease in shoulder dystocia.[7] A systematic review,[8] which included the few randomised trials published,[9,10] showed no difference in the risk of caesarean section between the labour induction and expectant management groups, but also no benefit of labour induction in prevention of neonatal trauma. The conclusions were limited by the relatively small sample size of the trials and by the inclusion of women, usually at 40 weeks of gestation or more, carrying a fetus with an

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estimated weight of more than 4000 g. Inclusion of these women is likely to restrict the benefit of induction of labour, because this intervention at that stage of gestation leads to very small differences between induced labour and expectant management groups, in both mean gestational age at birth and birthweight.

We assessed the risks and benefits of induction of labour compared with expectant management in women with large-for-date fetuses. We postulated that induction of labour would prevent shoulder dystocia and other neonatal and maternal morbidity associated with macrosomia, with no major changes in the risk of caesarean section.

Methods

Study design and participants

We did this multicentre, randomised controlled trial in 19 tertiary-care university hospitals in France, Switzerland, and Belgium. Recruitment started on Oct 1, 2002, in four hospitals and was extended to France in 2005, which added 15 more hospitals. Recruitment ended on Jan 1, 2009.

Eligible women had a singleton macrosomic fetus in cephalic presentation and no contraindications to planned vaginal delivery. We identified the women in two stages, between 36 weeks and 38 weeks of gestation, during routine antenatal care visits. First, we screened for large-for-date fetuses (weighing more than the 90th percentile), on the basis of either fundal height or fetal weight estimated with the Leopold manoeuvres. Then, if the fetus was estimated to weigh more than the 90th percentile, we estimated fetal weight sonographically with Hadlock's formula.[11] We included women if the estimated weight of the fetus was more than the 95th percentile (3500 g at 36 weeks of gestation, 3700 g at 37 weeks, and 3900 g at 38 weeks).

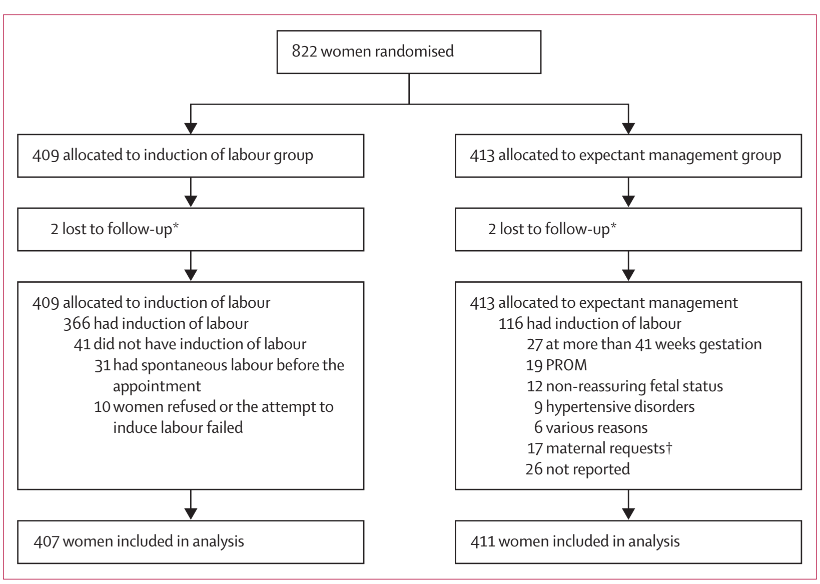

Figure: **Trial profile**
*Participants were lost to follow-up before delivery, so had no data for assessment of the measurement outcomes. †Included fear of delivery of a large neonate.

Exclusion criteria were any contraindication to induction of labour or vaginal delivery, history of caesarean section, neonatal trauma or shoulder dystocia, severe urinary or faecal incontinence, and insulin-treated diabetes.

We based gestational age on last menstrual periods. If the sonography, routinely done in all centres during the first trimester, showed a discrepancy of more than 5 days, we used the sonographic date.

The study protocol was approved for all centres in France by the Ethics Committee of the Poissy Saint-Germain Hospital (Comité de Protection des Personnes), in Saint-Germain en Laye. The protocol was approved by the institutional ethics committees in Switzerland and Belgium. All women provided written informed consent.

Randomisation and masking

Women were randomly assigned (1:1), via centralised computer-generated randomisation with permuted blocks (block size of four to eight), to receive induction of labour or expectant management. Randomisation was stratified by centre. Clinicians and participants had no access to the list, but were not masked to group allocation, which was made known after entry of the women, screening, and confirmation of consent. Investigators were masked only in the assessment of uncertain primary outcome. The decision about the non-significance of shoulder dystocia in these cases was made by investigators masked to the group allocation.

Procedures

We induced labour between 37^{+0} weeks and 38^{+6} and within 3 days after randomisation. The attending physician chose the method for cervical ripening and labour induction, according to local practice. Women with an unfavourable cervix had cervical ripening with prostaglandin E2 or misoprostol. Oxytocin was then used to induce uterine contractions, if labour did not start during ripening. Expectant management continued until either spontaneous labour or diagnosis of a condition necessitating induction according to the hospital's policy (eg, pregnancy continuing beyond 41 weeks of gestation, premature rupture of membranes).

Outcomes

The primary outcome was a composite of significant shoulder dystocia, fracture of the clavicle or a long bone, brachial plexus injury, intracranial haemorrhage, or death. We defined clinically significant shoulder dystocia as difficulty with delivery of the shoulders that was not resolved by the McRoberts' manoeuvre (flexion of the maternal thighs), usually combined with suprapubic pressure. Manoeuveres whose use suggested significant shoulder dystocia were those involving rotation of the fetus to displace the anterior shoulder impacted behind the maternal pubic bone (Woods, Rubin, or Jacquemier manoeuvres).[12] The definition also included births with an interval of 60 s or more between delivery of the head and the body.[13]

Our prespecified secondary outcomes were: maternal morbidity, defined as caesarean section, operative vaginal delivery (vacuum or forceps), postpartum haemorrhage (1000 ml or more), blood transfusion, and anal sphincter tear; and neonatal morbidity, defined as arterial cord blood pH less than 7·10, Apgar score at 5 min less than 7, and admission to the neonatal intensive-care unit. We also obtained information about other outcomes, including concentrations of blood bilirubin. We defined clinically significant hyperbilirubinaemia as a maximum value exceeding 350 mmol/L.

Statistical analysis

Analysis was by intent to treat. We report baseline characteristics and outcomes as means SDs, medians (IQRs), or numbers and percentages. We report the effects of the intervention on outcomes as relative risks (RRs), risk differences, and numbers needed to treat, with 95% CIs. Stratified analysis with the Mantel-Haenszel method enabled adjustment of the RR estimate for parity (primiparity and multiparity), obesity (body-mass index ≤30 kg/m² and >30 kg/m²), and centre. We tested significance with Fisher's exact test. We did analysis with SPSS (versions 18 and 20).

We based the initial sample size calculation on detection of a difference in percentages of the primary outcome, with a power of 80% and a type 1 error of 5%. We assumed the risk in the control group to be 5–10% and the risk in the induction of labour group to be 1·65–5·00% (ie, an RR of 0·33–0·50). The calculation showed that a total sample size of about 1000 women (500 per group) was sufficient to show these differences. Financial constraints made it necessary to end recruitment at a predetermined date (Jan 1, 2009), before we did any analyses.

The study is registered with ClinicalTrials.gov, number NCT00190320.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MB had full access to all the data in the study and MB and PR had final responsibility for the decision to submit for publication.

Results

The figure shows the trial profile. We randomly assigned 822 women to the induction of labour group (n=407) or the expectant management group (n=409). Four (1%%) women were lost to follow-up before delivery, leaving 818 women in the final analysis. Labour was induced in 366 (90%%) women in the induction group and 116 (28%) women in the expectant management group (figure). Baseline characteristics were similar between groups (table 1). Mean birthweight was 3831 g (324) in the induction group and 4118 g (392) in the expectant group. 125 neonates had a birthweight of 4000 g or more and 13 neonates weighed 4500 g or more in the induction

	Induction of labour group (n=407)	Expectant management group (n=411)
Maternal age (years)	29·2 (5·3)	29·8 (5·3)
BMI before pregnancy (kg/m²)	26·1 (5·7)	25·6 (5·4)
Weight gain (kg)	14·7 (6·2)	15·6 (6·6)
Gestational age at randomisation (weeks)		
36+0 to ≤37	42 (10%)	44 (11%)
37 to ≤38	177 (44%)	181 (44%)
38 to ≤39	187 (46%)	184 (45%)
Nulliparity	191 (47%)	208 (51%)
Previous history of macrosomia*†	65/212 (31%)	62/200 (31%)
Gestational diabetes‡	39 (10%)	43 (11%)
Fundal height (cm)	36·3 (2·3)	36·3 (2·4)
Estimated weight (g, clinical)	3850 (297)	3901 (296)
Estimated weight (g, sonography)	3964 (229)	3971 (238)
Male fetus	232 (57%)	236 (57%)

Numbers are mean (SD), n (%), or n/N (%). *In multiparous women. †Some information missing. ‡Treated with diet only.

Table 1: **Baseline characteristics in the induction of labour and the expectant management groups.**

	Induction of labour group (n=407)	Expectant management group (n=411)	RR (95% CI) or p value
Composite primary outcome	8 (2%)	25 (6%)	0·32 (0·15–0·71)
Significant shoulder dystocia	5 (1%)	16 (4%)	0·32 (0·12–0·85)
Delay of ≥60 s	2 (1%)	10 (2%)	0·20 (0·04–0·92)
Fracture	2 (1%)	8 (2%)	0·25 (0·05–1·18)
Brachial plexus injury	0	0	..
Intracranial haemorrhage	0	0	..
Death	0	0	..
Any shoulder dystocia	15 (4%)	32 (8%)	0·47 (0·26–0·86)
Mode of delivery			
Spontaneous vaginal	239 (59%)	212 (52%)	1·14 (1·01–1·29)
Forceps or vacuum	54 (13%)	68 (17%)	0·80 (0·58–1·12)
Caesarean section	114 (28%)	130 (32%)	0·89 (0·72–1·09)
Perineal tear (episiotomy or second degree)	148 (36%)	158 (38%)	0·95 (0·79–1·13)
Anal sphincter tear	6 (2%)	2 (1%)	3·03 (0·62–14·92)
Vaginal laceration or cervical tear	5 (1%)	1 (<1%)	5·05 (0·59–43·02)
Blood transfusion	4 (1%)	3 (1%)	1·35 (0·30–5·98)
Haemorrhage (≥1000 mL)	12 (3%)	21 (5%)	0·58 (0·29–1·16)
Retained placenta	3 (1%)	4 (1%)	0·76 (0·17–3·36)
Sepsis	1 (<1%)	1 (<1%)	1·01 (0·06–16·1)
Fever (>38·5°C)	3 (1%)	6 (2%)	0·58 (0·29–1·16)
Duration of hospital stay			
Before delivery (h)	16·2 (8·1–31·4)	7·6 (4·6–11·6)	p<0·0001
After delivery (days)	4·0 (4·0–5·0)	4·0 (4·0–5·0)	p=0·61

Data are n (%) or median (IQR), unless otherwise stated. RR=relative risk.

Table 2: **Main, secondary, and other maternal outcomes**

	Induction of labour group (n=407)	Expectant management group (n=411)	p value
Apgar score <7 at 5 min	3 (1%)	2 (1%)	0·99
Cord blood pH			
<7·10	12 (3%)	12 (3%)	1·00
<7·00	1 (<1%)	1 (<1%)	1·00
Highest bilirubin concentration (mmol/L)			
>250	36 (9%)	12 (3%)	0·0004
>350	0	0	1·00
Phototherapy	45 (11%)	27 (7%)	0·03
Hypoglycaemia	9 (2%)	13 (3%)	0·40
Admission to neonatal intensive care unit	15 (4%)	23 (6%)	0·19
Transient tachypnea of the newborn (wet lung)	1 (<1%)	1 (<1%)	1·00
Use of CPAP	2 (1%)	1 (<1%)	0·99

Data are n (%), unless otherwise indicated. CPAP=continuous positive airway pressure therapy.

Table 3: **Other neonatal outcomes**

group, compared with 254 neonates who weighed 4000 g or more and 61 who weighed 4500 g or more in the expectant group. The mean difference in time between randomisation and delivery was of 4·9 days (4·1) in the induction group and and 15·4 days (8·4) in the expectant management group.

Table 2 shows the number of occurrences of the elements of the composite primary outcome measure. We recorded the primary outcome in eight (2%) of 407 deliveries in the induction group and 25 (6%) of 411deliveries in the control group (table 2; p=0·004). The risk difference was 4% (95% CI 1·4–6·8) and the number needed to treat was 25 (95% CI 15–70). The estimated benefit did not change when the definition of the primary outcome excluded the interval of 60 s or more between delivery of the head and body (RR 0·34, 95% CI 0·14–0·78). No brachial plexus injuries, intracranial haemorrhage, or perinatal were recorded. The main outcome occurred in three neonates in the induction group and four in the expectant management group in the neonates less than 4000 g. In neonates with birthweights of 4000 g or more, we noted the primary outcome in five neonates in the induction group and 21 in the expectant management group. The RRs adjusted for parity (0·32, 95% CI 0·15–0·71), obesity (RR 0·32, 95% CI 0·15–0·71), and centre (RR 0·31, 95% CI 0·14–0·72) did not differ from the crude RR.

The incidence of caesarean section and operative vaginal delivery did not differ significantly between the groups (table 2). The likelihood of spontaneous vaginal delivery increased significantly in the induction of labour group (table 2). Anal sphincter tears were infrequent and did not differ significantly between groups (table 2). Postpartum haemorrhage of more than 1000 ml happened in 12 (3%) women in the induction group and 21 (5%) women in the expectant management group (table 2).

The prespecified neonatal outcomes did not differ significantly between groups (table 3). The number of neonates admitted to the neonatal intensive-care unit (15 [4%] in the induction group and 23 [6%] the expectant management group) was similar in each group, and each group included one baby with transient tachypnea. No neonate in either group had hyperbilirubinaemia exceeding 350 mmol/L, although when we lowered the cut-off to 250 mmol/L, incidence was higher in the induction group (table 3). Phototherapy was used more often for neonates in the induction group (table 3), especially for those randomised to induction of labour before 38 weeks of gestation (28 [13%] of 219 neonates in the induction group *vs* 16 [7%] of 225 neonates in the expectant group; randomisation at 38 weeks: 17 [9%] of 187 neonates in the induction group *vs* 11 [6%] of 185 in the expectant group).

Discussion

Our findings show that induction of labour for large-for-date fetuses significantly reduces the risks of shoulder dystocia and bone fracture, and increases the likelihood of spontaneous vaginal delivery. We recorded no brachial plexus injuries, intracranial haemorrhages, or perinatal deaths, nor did we detect differences between the groups for markers of asphyxia at birth.

Our results differ from those of a systematic review,[7] which reported an increased risk of caesarean delivery with no decrease in the risk of neonatal trauma. These previous results form the basis of present guidelines that advise against induction of labour to prevent macrosomia.[4,14] In 2012, the results of a very large database study[15] showed that women with babies weighing more than 4000 g induced at 39 weeks had fewer caesarean sections than women whose labour was either induced or spontaneous at 40 weeks or later. An important limitation, however, is that its analysis was according to known birthweight, rather than estimated fetal weight.

The only two published randomised trials[9,10] did not show a significant benefit to the mother or child from induction of labour, although these studies had small sample sizes (273 women and 40 women) and used inclusion criteria that restricted their ability to show a difference. Women were included when the fetus was estimated to weigh more than 4000 g, which is usually at around 40 weeks, when the daily probability of spontaneous labour is high. Labour induction was done only a few days before labour would have begun spontaneously, so the difference in birthweight between the induced labour and expectant management groups was very small (63 g). The benefits for prevention of shoulder dystocia and other macrosomia-associated morbidities were thus smaller than they would have been had the intervention been done earlier. Nonetheless, one of these studies[9] reported a lower incidence of fetal trauma (fracture or brachial plexus injury) in the induction group, with all six cases recorded in the expectant management group.[9] An unpublished pilot randomised trial (ISRCTN98146741), which included 59 women, also showed no benefit for induction of labour. Our trial is larger than previous studies, with earlier inclusion and intervention and therefore greater differences in birthweight between groups and a higher probability of differences being associated with induction.

A limitation of our trial is that the sample size was smaller than initially planned. We originally planned to include 1000 women, with an interim analysis after the first 500 women. Because recruitment was slower than expected and funding was ending, we revised this plan and decided to stop recruitment on a prespecified date, before we did any analysis; the trial results did not affect the decision to stop recruitment. Moreover, although recruitment stopped early, our study has a larger sample size than previous randomised trials.

Another limitation is the absence of masking of both clinicians and women, which would be impossible in view of the nature of the intervention. This absence might have led doctors to do caesarean section in some women based on the knowledge of estimated weight, which was larger in fetuses in the expectant management group than in those in the induced labour group. An observational study[16] has shown that clinicians are more prone to do a caesarean section when macrosomia is suspected than when it is not.

Any strategy to detect macrosomic fetuses is limited by the imprecision of the methods for estimation of fetal weight.[17] Fundal height is imprecise, subject to measurement errors, and dependent on the thickness of the maternal abdominal wall and the amount of amniotic fluid.[18] Ultrasound is also imprecise in estimation of fetal weight, especially for large-for-date fetuses.[19] However, our two-step procedure was sufficiently reliable for screening of large fetuses that might benefit from induction of labour. Restriction of sonographic estimation of the fetal weight to fetuses regarded as clinically large ensured that the number of scans needed was not unduly increased.

The components of the composite primary outcome that we noted in our study—clinically significant shoulder dystocia and bone fractures—are unfavourable for women and babies, and for clinicians are among the most frequent causes of litigation and damage awards.[20] Fortunately, we recorded no instances of permanent brachial plexus injury or death, which are at the severe end of the composite primary outcome components. A trial to assess the advantages of earlier induction of labour for these two events would probably be impossible to do because of their very low occurrence (less than 10% in neonates with shoulder dystocia); we estimate a sample size of 7800 would be needed to show a difference between 0·6% and 0·2%. However, we detected a difference between the groups for all components of our primary outcome, and the magnitude of the benefit increased with the severity of the definition. We therefore postulate that induction of labour might prevent shoulder dystocia that is associated with permanent brachial plexus injury or death.

***Panel*: Research in context**

Systematic review

Fetal macrosomia is a risk factor for a complicated delivery. Neonates with increased birthweight have an increased risk of shoulder dystocia and associated morbidities (fracture, brachial plexus injury, and asphyxia) whereas the mother is at risk for caesarean section, instrumental delivery, and perineal tears. This issue is complicated by the inaccuracy of the various methods to estimate fetal weight. We searched Medline and the Cochrane Library from inception to July 1, 2014 with the search terms “induction of labour”, “macrosomia”, “shoulder dystocia”, and “randomised”, according to the strategy of the Cochrane Collaboration. Our search identified two published randomised trials[9,10] and one unpublished trial (ISRCTN98146741) comparing induction of labour with expectant management for women with a fetus estimated to be large for date or macrosomic. The meta-analysis of these trials[8] showed no benefit associated with induction of labour.

Interpretation

Our results show that a policy of labour induction at 37–38 weeks of gestation for women with large-for-date fetuses reduces the risk of clinically significant shoulder dystocia or bone fracture at birth, without increasing the risk of caesarean section. These benefits should be balanced with the effects of early-term induction of labour.

The primary outcome did not include the less severe forms of shoulder dystocia that can be resolved by the McRoberts manoeuvre, because their assessment is often subjective. Additionally, in some settings, this manoeuvre is done routinely, despite the absence of evidence that it prevents shoulder dystocia in suspected macrosomia.[21] Accordingly, we do not believe that use of the McRoberts manoeuvre in cases of suspected macrosomia represents a real complication of childbirth. Most cases of shoulder dystocia were in neonates with a birthweight of 4000 g or more, which concurs with the fact that birthweight is a risk factor, and suggests that induction of labour reduces the occurrence of this outcome by reducing birthweight.

Our definition of the primary outcome included an interval of 60 s or more between delivery of the head and body, which has been suggested to be an objective definition of shoulder dystocia that should reduce the risk of detection bias.[13] Some obstetricians might question the importance of this delay, because they already wait for spontaneous delivery of the shoulders after the delivery of the head of the fetus. However, exclusion of this component of the composite outcome did not change the estimate of the effect. By excluding the McRoberts manoeuvre and attempting to use objective criteria to define our primary outcome, we aimed to reduce the risk of both detection and performance bias caused by the absence of masking. However, we recorded no cases of brachial plexus injury or death and do not think that we can fairly claim to have shown more than a significant reduction in surrogate outcomes.

Despite the benefits of early induction of labour in prevention of shoulder dystocia and fracture, a policy of this procedure raises questions. The best gestational age for delivery remains controversial, because morbidity is associated with all interventions that pre-empt spontaneous labour.[22] A large before and after study[23] showed that a policy that restricts both induction of labour and elective caesarean section before 39 weeks of gestation is associated with reduced risk of admission to the neonatal intensive care unit, but an increased risk of stillbirth. We did not detect an increased risk of admission to the neonatal intensive-care unit or transient tachypnea of the newborn, although the absence of an increase in risk of transient tachypnea might have been because most women in our study experienced labour, rather than caesarean delivery before the onset of labour.[24] Induction of labour was associated with hyperbilirubinaemia. Most neonates had phototherapy for fairly low concentrations of bilirubin, and the bilirubin concentration for which phototherapy is recommended (350 mmol/L) was never attained.[25]

In summary, our findings show that induction of labour for large-for-date fetuses reduces the risk of shoulder dystocia and bone fracture, and increases the likelihood of spontaneous vaginal delivery (panel). This intervention could be offered to women with a large-for-date fetus between 37 weeks and 39 weeks of gestation.

Contributors

MB and OI did the literature search and drafted the first protocol. All authors discussed the design of the study during Groupe de Recherche en Obstétrique et Gynécologie meetings and wrote the final version of the protocol. All authors contributed to the recruitment of the participants. MB did the data analysis, with input from PR. MB and PR were responsible for writing. All authors commented on the final version of the manuscript.

Declaration of interests

We declare no competing interests.

Acknowledgments

This trial was supported by a research grant from the Département à la Recherche Clinique Ile-de-France, Assistance Publique–Hôpitaux de Paris (number PHRC AOM 04038) and by the Department of Gynecology and Obstetrics of the University of Geneva. We thank Jo Ann Cahn for doing the final editing of the manuscript; Eric Antonelli for participation in the study design; Nicole Jastrow for participation in the report writing; Riccardo Pfister for participation in the design of the neonatal data collection forms and discussions of the results for the neonate; Véronique Othenin-Girard for participation in the recruitment of participants and data collection in Geneva; and Shoreh Azimi for opening the trial's sites, verifying the data collection, and monitoring the study in France. This work was presented orally at the 32nd Congress of the Society for Maternal-Fetal Medicine (SMFM), Dallas, TX, USA, 2012.

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