Amendement DIGITAT study protocol

amendement 1 op studie nr PO4.210 DIGITAT
datum: 22 januari 2005

Geachte commissie,

Via dit amendement wil ik goedkeuring vragen voor een uitbreiding van studie PO4.210 getiteld “DIGITAT: Disproportionate Intrauterine Growth Intervention Trial At Term” met patiënten met pre-eclampsie en zwangerschapshypertensie voorbij een zwangerschapsduur van 36 weken.

De DIGITAT studie betreft een gerandomiseerde vergelijking naar de effecten van het inleiden van de baring versus het afwachten op een spontane baring bij zwangeren met een amenorroeduur van 36 weken of meer met een foetale groeivertraging. Hierbij wordt zowel gekeken naar foetale uitkomst als naar het verloop van de baring.

Foetale groeivertraging is geassocieerd met het optreden van zwangerschapshypertensie en/of pre-eclampsie, waarschijnlijk omdat beide ziektebeelden hun oorsprong vinden in de placenta. In het huidige protocol zijn pre-eclampsie en zwangerschapshypertensie geen exclusie-criteria, en een substantieel deel van de patiënten die nu in DOGOTA geïncludeerd worden, heeft pre-eclampsie of zwangerschapshypertensie, dan wel krijgt het in de loop van de studie, indien er voor afwachtend beloop gekozen wordt.

De vraagstelling bij een zwangere met pre-eclampsie of zwangerschapshypertensie a terme (i.e. een zwangerschapsduur van 36+0 weken) maar zonder groeivertraging de zwangerschap moet worden beëindigd is echter ook relevant. Ongeveer 10% tot 15% van alle zwangerschappen wordt gecompliceerd door pre-eclampsie en/of zwangerschapshypertensie (19.000 vrouwen per jaar in Nederland). De grote meerderheid van deze gevallen is a terme, en er is geen oorzakelijke behandeling.

Op dit moment wordt in ongeveer de helft van de patiënten met een dergelijk ziektebeeld de bevalling ingeleid, terwijl bij de anderen een spontane baring plaatsvindt. Er is geen consensus over de vraag welk beleid het beste is. Inleiden van de baring zou complicaties bij moeder en kind kunnen voorkomen, maar inleiden leidt mogelijk ook tot een hoger percentage vaginale kunstverlossingen en sectio caesarea’s. Er is niets bekend over de impact van beide strategieën op de kwaliteit van leven van de moeder, zowel als de kosten.

Het uitvoeren van de DIGITAT-studie in een multicenter setting is een unieke mogelijkheid om ook bovenstaande vraagstelling ten aanzien van patiënten met zwangerschapshypertensie/ pre-eclampsie a terme te beantwoorden. Dit kan door patiënten met zwangerschapshypertensie en/of pre-eclampsie in bovenstaande studie te includeren. De aanpassing van het protocol betreft alleen de inclusie criteria. De te verrichten interventies (inleiden van de baring of wachten op een spontane partus) en de te meten eindpunten blijven gelijk.

Ten aanzien van de power kan gesteld worden dat het huidige primaire eindpunt in de DIGITAT-studie, te weten neonatale uitkomst, boor de extra te onderzoeken patiënten met zwangerschapshypertensie/pre-eclampsie niet zinvol is, omdat een slechte neonatale uitkomst in deze groep weinig voorkomt (LVR-data). Het voorstel is dan ook om in deze patiënten groep (patiënten met zwangerschapshypertensie/pre-eclampsie zonder groeivertraging) kwaliteit van leven als primaire uitkomst te beschouwen.

Hieronder is in het DIGITAT protocol aangegeven welke wijzigingen in het protocol nodig zijn om bovenstaande wijziging mogelijk te maken.
The Disproportionate Intrauterine Growth Intervention Trial At Term (DIGITAT)

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Introduction

It is since the end of the sixties, that being 'small for gestational age' (SGA) is recognised and defined on the basis of a birth-weight below the 10th percentile. It is well known that reduced foetal growth also in term infants is exponentially associated with a higher perinatal mortality (RR 5.2) and morbidity [1,2]. The incidence of poor direct neonatal outcome as defined by a low Apgar score and/or low umbilical artery pH, but also neonatal admittances to hospital is relative high ranging form 17.1% to 34.0% [3-5]. Also long-term morbidity can be poor ranging from behavioural problems, minor developmental delay to spastic cerebral palsy [6]. Both the direct cost related to neonatal care for the compromised neonate as well as cost in the long term are enormous. However, not all studies, even at pre-school age show this trend of increased problems in SGA infants [7-9]. No differences in direct adverse neonatal outcome were found in term antenatal diagnosed or under-diagnosed SGA infants, although interventions, as more frequent foetal monitoring or induction of labour were much higher in the SGA diagnosed group, thus failing to support the commonly held view that antenatal diagnosis and subsequent interventions might improve outcome [3].

A SGA foetus is defined as a foetus with a foetal weight below the 10th percentile. A SGA foetus can be suspected based on physical examination or using sonography. One variable related to a ‘SGA’ foetus might be due to differences in 'ethnicity' [10, 11]. Special emphasis will be paid to this phenomenon by using so called customized fetal growth charts, correcting fetal growth for ethnic background [12]. In The Netherlands, there exists at present no clarity on the management of women with a SGA child at term. Although there is no doubt that the intra-uterine growth retarded pregnancy should be considered as high risk, and should be monitored by obstetricians, there is no consensus on diagnostic measures and subsequent intervention. It is unclear whether in this situation either induction of labour expectant management is beneficial for the mother and her baby, since evidence on the subject is lacking. For preterm pregnancies complicated by intra-uterine growth retardation, an international randomised clinical trial recently showed that expectant management had little benefit over early delivery with respect to short term neonatal outcome [13]. However, results of this trial cannot be extrapolated to the situation at term.

The lack of consensus on the subject in The Netherlands is demonstrated by the fact that in 2002 in women with a SGA child, labour was induced in 32% of these women, whereas labour started spontaneously in 56% of these women (The other 11% had a primary caesarean section). These data are based on actual birth weight, and the clinical situation is even complicated by the fact that the diagnosis ‘SGA child’ is often missed in clinical practice.

Approximately 10% to 15% of all pregnancies are complicated by hypertensive disorders, i.e. pregnancy induced hypertension or pre-eclampsia (19.000 women per year in The Netherlands). The large majority of these cases occur at term. There is no causal treatment but termination of pregnancy. In case of pre-term pregnancies complicated by hypertension, conservative management is advocated to as long as the risks for the mother are acceptable. However, there is no consensus whatsoever on the question in such cases at term. Induction of labour might prevent maternal and neonatal complications, but it is also thought to increase the instrumental delivery rate. Nothing is known about the impact of both policies on the psychological well-being of the mother, as well as the costs of both. In The Netherlands in 2002, labour was induced in 9000 women with pregnancy induced hypertension or pre-eclampsia, whereas labour started spontaneously in 10.000 women.

In view of this clinical dilemma, we propose a randomised clinical trial in which induction of labour, if necessary preceded by artificial cervical ripening, is compared to expectant monitoring in women with a suspected SGA child at term and/or pre-eclampsia and pregnancy induced hypertension. We will compare maternal outcome, neonatal outcome and maternal quality of life, as well as costs. Moreover, we will assess whether the diagnostic tests foetal heart rate pattern, sonographic measurement of the amniotic fluid index, and Doppler measurement [14, 15] of the umbilical artery and the medial cerebral artery are useful in the distinction between women that benefit from intervention and women that benefit from expectant management.

Clinical study

In this prospective equivalence study we aim to confirm the findings of several retrospective studies that demonstrated that both obstetrical management approaches would result in an equal maternal and neonatal outcome. The study will be performed in 12 hospitals, which have recently joined research efforts to increase population size of studies. We hypothesize that we will not find relevant differences between maternal and neonatal outcome in the two strategies.

General methods
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The proposed research concerns a multi-centre randomised clinical trial in potential participants who are suspected of having a SGA child and/or have pregnancy induced hypertension/preeclampsia at a gestational age between 36+0 and 41+0 weeks. Randomisation will be performed through a web-based database located in the central data collection unit in the AMC in Amsterdam. Women will be randomly allocated to either induction of labour or expectant monitoring.

Patients who are offered randomisation, but who decide not to participate in the study will be treated according to one of the two protocols at the discretion of the attending obstetrician, and analysed separately. We will ask their consent to be included in further follow-up studies. The study will be an open label study, as it is impossible to blind the health care workers involved for the strategy to which the woman is allocated. Cross-over between the two strategies would complicate the interpretation of study result. Although it will not be possible to prevent all cross-overs, both strategies will be performed according to strict criteria (see below). Moreover, a dedicated research nurse will monitor the study protocol in each centre by attending patient meetings and providing feedback on potential protocol violation.

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The study will be staffed by research midwives, who will counsel patients and ask informed consent. In every centre an independent gynaecologist will be available for more detailed information both for patients and colleagues. Data will be collected using a website dedicated to studies in the consortium. The expertise for this technology is already available to the study group, and applied in a study on external version of pregnancies with the foetus in breech position (see addendum). If possible, data collection will be limited to data that are not entered in the databases for obstetric and neonatal registration (LVR-2 and LNR). The local research nurse will check data entered in the LVR-2 and LNR for consistency. At the end of each study year, the study database will be merged with the local LVR-2 and LNR database.

Study population and data

Patients will be eligible if they are suspected of having a SGA foetus and/or have pregnancy induced hypertension/preeclampsia at a gestational age between 36+0 and 41+0 weeks of gestation. A diagnosis SGA is suspected based on physical examination, and has to be confirmed at foetal biometry, and there should be no uncertainty about gestational age (accurate LMP or accurate ultrasound-dating scan before 16 weeks). A diagnosis of pregnancy induced hypertension is made in case the diastolic blood pressure is above 95 mm Hg at two occasions at least six hours apart in a woman who was normotensive at the start of pregnancy. Women with a diastolic blood pressure > 110 mmHg will not be included in the study, as termination of pregnancy is thought to be warranted in these women. A diagnosis of pre-eclampsia is made in case there exists a proteinuria > 300 mg total protein in an 24 hour urine collection in a woman who meets also the criteria for pregnancy induced hypertension. Women in whom the total protein in 24 hours exceeds 5 gram will not be included, as termination of pregnancy is thought to be warranted in these women. Only women with a singleton pregnancy in a vertex position will be included. Exclusion criteria are diabetes mellitus, renal disease, a previous caesarean section, Sicco, wat mij betreft deze eruit), HELLP syndrome, oliguria < 500 mL in 24 hours, pulmonary oedema or cyanosis, and abnormalities at the CTG.

All women will have a Doppler ultrasound of the umbilical artery and, if possible, the medial cerebral artery. Moreover, the amount of amniotic fluid will be assessed at sonography by measuring the largest amniotic fluid pocket. After a patient has given informed consent for participation in the study, vaginal examination will be performed (Bishop score), and cervical length will be measured using transvaginal sonography, both to assess cervical ripeness. Subsequently, the patient will be randomised to either a policy that aims termination of pregnancy (intervention group) or a policy that aims expectant management for spontaneous delivery (expectant group). Randomisation will be done through a web-based database at the Academic Medical Centre (AMC) in Amsterdam. Randomisation will be stratified for centre, parity and presence of a diagnosis SGA and hypertensive disorders according to the criteria above.

Interventions:

In the intervention group, patients will be induced within 24 hours after randomisation. Patients with a cervix that is judged to be 'ripe' at vaginal examination (Bishop score > 6), labour will be induced with amniotomy and, if labour does not start within 1 hour, augmentation with oxytocin. In case the cervix is judged to be 'unripe', cervical ripening will be stimulated with use of intracervical or intravaginal prostaglandins (according to the local protocol). In case the cervix is judged to be unripe the day after 'priming', the cervical ripening will be repeated. If the cervix remains 'unripe', day 3 will be a rest day. Cervical ripening will be repeated at day 4 and 5. We expect the number of women that need such repeat ripening to be very low. All patients in the intervention group will be monitored clinically until after delivery.
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In the expectant group, patients will be monitored until the onset of spontaneous delivery. Monitoring will consist of assessment of fetal movements as reported by the mother, as well as electronic foetal heart rate monitoring at least twice a week. An increase of the frequency of these checks as well as admission to hospital is based on the judgement of the attending clinician. Ultrasound examination for foetal growth and amniotic fluid assessment will be performed each 10 days, and Doppler assessment of the umbilical artery and the a. cerebri media twice a week.

In case of presence of hypertension or pre-eclampsia, maternal evaluation consists primarily of frequent evaluation of blood pressure measurement and screening of urine for protein using a dipstick or protein/creatinin ratio twice a week (24 hour urine collection for protein is case of positive screening). Blood tests (platelet count, liver enzymes and renal function) will be performed in case of abnormal maternal blood pressure and/or proteinuria.

In the expectant monitoring group, intervention is recommended in case the foetal condition does not justify expectant management anymore (no foetal movements reported by the mother, non-optimal CTG). Moreover, induction of labour is recommended in case the diastolic blood pressure is > 110 mmHg, in case the total amount of protein in the urine exceeds 5g/24 hours, or in case of eclampsia. In case in the expectant group an indication rises for induction of labour, for example prelabour rupture of membranes for > 48 hours or meconium stained liquor, induction of labour is indicated (See flowchart, Appendix).

We will collect the following data:
At baseline: a normal non-stress test, an amniotic fluid index (AFI), pregnancy weight and booking weight, maternal height, ethnic origin and parity to calculate the customised birth weight standard, cervical ripeness at digital examination, an abdominal circumference measurement, a recording of the umbilical artery wave-form and a recording of the medial cerebral artery wave-form. If possible, foetal heart rate will be monitored with a computer registration, allowing measurement of the short-term variability.

During admission in the hospital: number of days of antenatal monitoring after study entrance, laboratory findings, ultrasound examinations, complications. Maternal mortality and morbidity will be specified until date of discharge from hospital and six weeks post partum.

At delivery: Time to delivery, number and mode of antenatal monitoring, birth weight, mode of delivery, condition at birth (Apgar scores, Umbilical artery pH), maternal admission (type and days). Neonate: Neonatal admission (type and days). Neonatal mortality and morbidity will be specified until date of discharge from hospital. We will register intravenously treated hypoglycemia, neonatal convulsions, NEC, head circumference, neonatal length, birth weight, skin fold thickness, and Ponderal Index (g/cm3).

For the assessment of mild to moderate differences in neonatal morbidity between the intervention groups the MAIN outcome score will be calculated. This score captures the global nature of neonatal morbidity and its use is appropriate and well validated for obstetric clinical trials with gestational ages as proposed in this study.

Each woman will complete a questionnaire addressing health related quality of life (SF-36, EuroQoL, HUI-III), state anxiety (STAI) as well as a questionnaire containing information on pain and well being. Questionnaires will be completed at baseline, one day after randomization and subsequently twice a week for two weeks. Quality of life will also be measured after 6 weeks and 6 months. A pain scale will be completed at the day of delivery.

Outcome parameters:
The primary outcome measure will be a composite neonatal status. Bad neonatal outcome will be defined as perinatal mortality, a 5-minute Apgar score < 7, an umbilical artery pH < 7.05 or admission to the neonatal intensive care. Secondary outcomes will be severe maternal morbidity, maternal quality of life, anxiety, pain and costs. Maternal and neonatal condition will be assessed at 6 weeks post partum. In case of a non-optimal maternal or neonatal condition at 6 weeks post partum, the mother and/or her child will be followed until 6 months.

Moreover, we will register the mode of delivery, neonatal admission (days), neonatal complications, and maternal an neonatal condition at 6 weeks and 6 months post partum.

Each woman will complete a questionnaire addressing health related quality of life (SF-36, EuroQoL, HUI-III), state anxiety (STAI) as well as a questionnaire containing information on pain and well being. Furthermore, patients preferences will be assessed. Questionnaires will be completed at baseline, one day after randomization and subsequently twice a week for two weeks. Quality of life will also be measured after 6 weeks and 6 months. A pain scale will be completed at the day of delivery.

In the present proposal, no funding is asked for long term follow-up of the child. However, if additional funding can be obtained we will use a parental questionnaire at 2 and at 4 years (the Child Behaviour Checklist (CBCL)). The study appraisal has to provide the possibility for the suspected children to be further investigated.
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Power analysis
Bad neonatal outcome will be tested for equivalence. We anticipate the prevalence of bad neonatal outcome to be smaller than 15%. To exclude a difference in bad neonatal outcome of 15% versus 7.5% in favour of one of the two strategies, 600 women have to be randomised (300 per arm) (Alpha 5%, Beta 80%). Based on data of the Dutch perinatal registration (10,000 deliveries per year), a difference between the two groups is not to be anticipated.

In case of equivalent maternal and neonatal outcome, the study will be cost-minimisation analysis. If we assume the cost of spontaneous labour to be €1,000, the costs of instrumental delivery to be €10,000 (composite of instrumental vaginal delivery and caesarean section) and the costs of expectant management to be €900 per patient, and if we assume that in the group in whom spontaneous labour is awaited the instrumental delivery rate is 15%, than the instrumental delivery rate should be 25% in the induction of labour group to reach a break-even point in the costs of the two approaches. Assuming an average difference in cost of €1000 per patient as a relevant difference, we will need 626 women to be randomised (313 per arm). Thus, the study aims to recruit 626 patients.

The twelve participating centres estimate a recruitment of 245 patients per year. With an inclusion period of thirty months, ad 12 participating centers, we think this aim is reasonable.

An interim analysis is planned for when complete data had been received on the first 300 women randomised, with the aim of stopping the study if a difference in bad neonatal outcome will be found between groups at $p<0.002$ (twosided).

For patients with pregnancy induced hypertension/preeclampsia, but without a SGA fetus, the SF-36 will be considered as the primary endpoint. Assuming a 5-point difference in the Physical Component Summary scale and Mental Component Summary scale as relevant, we will need 2 groups of 250 patients to find a relevant difference (alpha .05; beta .80; SD 20). In view of the unpredictability of other quality of life measures, we feel that such a sample is adequate to detect other relevant differences.

Statistical analysis
The analysis will be done by intention to treat. The experimental and the standard policy will be compared. Relative risks and 95% confidence intervals will be calculated for the relevant outcome measures. The analysis will be stratified for centre and parity. Moreover, we will evaluate whether the relative benefits of induction of labour will be stronger in women with a ripe cervix at baseline, in women with a short cervical length at transvaginal sonography, and in women with a small amount of amniotic fluid. In case of equivalence between outcomes, the analysis will be repeated on a 'parprotocol' basis. Quality of life will be analysed using repeated measures analysis of variance. This technique is used to establish changes in health related quality of life over time (time effect), differences in health related health related quality of life over time and treatment (time by treatment effect).

References
11. Negrers Y, Goldenberg RL, Cliver SP, Hoffman HJ, Cutter GR. The relationship between maternal and
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Appendix A

Inclusion criteria:
Pregnant women gestational age > 36+0 week until 41+0 weeks
Suspected small gestational age child (estimated foetal weight at sonography < 10th percentile)

Exclusion criteria:
Diabetes mellitus, renal disease, previous caesarean section, HELLP syndrome, oliguria < 500 mL in 24 hours, cerebral or visual disturbances, pulmonary oedema or cyanosis, non vertex position

Assess cervical ripeness with cervical ripeness with Bishop score.

Expectant management (n=313)

Intervention (n=313)

* Monitoring until onset spontaneous delivery
* Cervical ripeness Bishop > 6: induction
* Maternal monitoring: blood pressure, proteinuria
  Augmentation with oxytocin
  Start at day 1 after randomisation
* Fetal monitoring: fetal heart rate monitoring, fetal movements (at least 2/week)
  * If Bishop score ≤ 6: cervical ripening with
  * Ultra sound examination foetal growth, amniotic fluid each 10 days
    prostaglandins (day after randomisation)
* Doppler a umbilicalis (and Doppler a. Cerebri media if possible) 2/ week

* Start with Prepidil 0.5 mg intracervical.

* Intervention: maternal reasons
  after 4 hours Prostin 1 mg intravaginal,
  - diastolic blood pressure ≥110 mm Hg
  - eclampsia
  Repeat at day 2 after randomisation if cervix remains unripe
  - rupture of membranes > 48 hours or with meconium stained liquor
    Repeat at day 4 and 5
  - HELLP syndrome
  - proteinuria > 5g/24 hours

foetal reasons
  - less than 8 foetal movements per day
  - non reassuring CTG
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**Women with gestational age (36+0 to 41+0 weeks) AND suspected small gestational age child (estimated fetal weight or FAC at sonography < 10th percentile)**

- Assessment of exclusion criteria
  - diabetes mellitus, renal disease, a previous caesarean section, HELLP syndrome, oliguria < 500 mL in 24 hours, pulmonary edema or...

- Informed consent?
  - Yes: Randomisation
  - No: Vaginal examination

**Vaginal examination Cervical length**

- Randomisation: central office stratification for parity centre

**Induction of labour**

- Cervical ripening
  - BS ≤ 6: Amniotomy and oxytocin
  - BS > 6: Amniotomy and oxytocin

**Expectant monitoring**

- At least 2/week: Electronic fetal heart rate monitoring
- Assessment of fetal movements as reported by the mother

**Registration of outcomes**

Neonatal outcome, maternernal outcome, costs

Questionnaires will be completed at baseline, one day after randomization and subsequently twice a week for two weeks.

Quality of life will also be measured after 6 weeks and 6 months. A pain scale will be completed the day of delivery.

Assessment of patient preferences
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Appendix B

Protocol

Cervical ripeness:

**Bishop score**

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1-2</th>
<th>3-4</th>
<th>5-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilatation of cervix</td>
<td>0</td>
<td>1-2</td>
<td>3-4</td>
<td>5-6</td>
</tr>
<tr>
<td>Effacement cervix</td>
<td>0-30%</td>
<td>40-50%</td>
<td>60-70%</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>Consistency cervix</td>
<td>Firm</td>
<td>medium</td>
<td>soft</td>
<td></td>
</tr>
<tr>
<td>Position cervix</td>
<td>Posterior</td>
<td>central</td>
<td>anterior</td>
<td></td>
</tr>
<tr>
<td>Station of foetal head in relation to spines</td>
<td>3 cm above</td>
<td>2 cm above</td>
<td>1-0 cm above</td>
<td>1-2 cm below</td>
</tr>
</tbody>
</table>

Intervention group:
- Bishop score > 6: amniotomy, augmentation with oxytocin
- Bishop score ≤ 6: cervical ripening by use of prostaglandines
  - Start with Prepidil 0.5 mg intracervical
  - after 4 hours Prostin 1 mg intravaginal
  - in case of minimal reaction another Prostin 2 mg

**Indication instrumental delivery:**

- Caesarean section: foetal distress without possibility for foetal blood sample or failure to progress first stage
- Obstructed labour second stage
- Foetal distress: foetal blood sample ph < 7.25. **Moet hier niet 7.20 staan ??**
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Patiënteninformatie ten behoeve van een wetenschappelijk onderzoek naar de effecten van al dan niet ingrijpen bij vermeende groeivertraging (DIGITAT).

Geachte mevrouw,

In aansluiting op het gesprek met uw arts ontvangt u hierbij de schriftelijke informatie met betrekking tot het wetenschappelijk onderzoek waarvoor uw medewerking is gevraagd.

Inleiding
Bij u is tijdens de controles van de zwangerschap het vermoeden gerezen dat de groei van uw baby achterblijft bij de groei zoals die normaal is voor deze zwangerschapsduur. U baby is echter wel in goede conditie omdat het een normaal hartritmepatroon heeft. Het is bekend dat het achterblijven van de groei effecten kan hebben op het uiteindelijk functioneren van het kind op latere leeftijd. Dat is de reden dat een aantal gynaecologen soms besluit de bevalling vroegtijdig in te leiden. Hiermee zou men de eventuele nadelige effecten van de groeivertraging, veroorzaakt door de slecht functionerende moederkoek, kunnen beperken. Deze veronderstelling is echter nooit bevestigd. Er zijn mogelijk ook nadelen verbonden aan het inleiden zelf. Behalve dat de baby wordt geboren bij een kortere zwangerschapsduur, is er bijvoorbeeld ook een verhoogde kans op een keizersnede.

Doel van het onderzoek
Het doel van het onderzoek is om de effecten te bestuderen van het al dan niet vroegtijdig inleiden van de bevalling bij vermeende groeivertraging.

Opzet en belasting
Mocht u besluiten aan dit onderzoek mee te doen, dan wordt door middel van loting bepaald of bij u de bevalling al dan niet vroegtijdig wordt ingeleid. Indien u in de groep bent ingeloot waarbij de bevalling vroegtijdig wordt ingeleid, dan wordt er op korte termijn daarvoor met u een afspraak gemaakt. Als u in de groep bent ingeloot waarbij dit niet het geval is, dan wordt het spontane beloop van de zwangerschap afgewacht. Hierbij wordt de conditie van uw baby nauwkeurig in de gaten gehouden. Na afloop van het onderzoek worden beide groepen met elkaar vergeleken. Bovendien vragen wij u om een enquête in te vullen als uw kind 2 is. U krijgt deze op dat moment per post toegestuurd. Door middel van deze enquête willen wij beoordelen hoe het met de kinderen gaat. Het invullen ervan duurt ongeveer een half uur.

Vrijwillige deelname
Uw medewerking aan dit onderzoek is vrijwillig Als u toestemming geeft om aan dit onderzoek mee te doen, heeft u te allen tijde de vrijheid om op die beslissing terug te komen. U hoeft hiervoor geen verklaring te geven. Het wel of niet meedoen heeft op geen enkele wijze gevolgen voor uw verdere behandeling of de relatie met uw arts.

Nadere inlichtingen en advies
Mw. Dr. A. Middeldorp, gynaecoloog, heeft zich bereid verklaard zonodig extra informatie en uitleg te verschaffen en uw vragen aangaande dit protocol te beantwoorden.

Vertrouwelijkheid van uw gegevens
U kunt ervan verzekerd zijn dat al uw gegevens, die tijdens dit onderzoek over u verzameld worden, vertrouwelijk worden behandeld en dat alleen daartoe bevoegde buitenstaanders inzage hebben in uw gegevens. Wanneer de resultaten van het onderzoek worden gepubliceerd, bent u niet herkenbaar.

Tot slot
Mocht u naar aanleiding van deze informatie nog vragen hebben over dit onderzoek, dan kunt u dieën rechtstreeks bij uw behandelend arts.

Dr. J.A. van der Post, gynaecoloog
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