



July 2015 Literature Alert

1.

Ultrasound Obstet Gynecol. 2015 Jun;45(6):639-48. doi: 10.1002/uog.13436.

[Neurodevelopmental delay with critical congenital heart disease is mainly from prenatal injury not infant cardiac surgery: current evidence based on a meta-analysis of functional magnetic resonance imaging.](#)

Li Y, Yin S, Fang J, Hua Y, Wang C, Mu D, Zhou K.

Abstract

OBJECTIVE:

No consensus has been reached regarding whether brain injury related to congenital heart disease (CHD) is caused by infant cardiac surgery and/or prenatal injury resulting from the CHD. We performed this meta-analysis to identify the likely cause of neurodevelopmental delay in CHD patients.

METHODS:

We carried out a literature search without language restriction in December 2013, retrieving records from PubMed, EMBASE, the Cochrane Library and the World Health Organization trials center, to identify studies applying functional magnetic resonance imaging (fMRI) evaluation of brain function before surgery and, in some cases, after surgery (both immediate term and short term postoperatively). The preoperative and postoperative fMRI results were extracted, and meta-analysis was performed using Revman 5.1.1 and STATA 11.0, according to the guidelines from the Cochrane review and MOOSE groups.

RESULTS:

The electronic search yielded 937 citations. Full text was retrieved for 15 articles and eight articles (nine studies) were eligible for inclusion: six studies (n = 312 cases) with fMRI analysis before surgery and three (n = 36 cases) with complete perioperative fMRI analysis. The overall average diffusivity of CHD cases was significantly higher than that of controls, with a summarized standard (std) mean difference of 1.39 (95% CI, 0.70-2.08), and the fractional anisotropy was lower in CHD cases, with a summarized mean difference of -1.43 (95% CI, -1.95 to -0.91). N-acetylaspartate (NAA)/choline (Cho) for the whole brain was significantly lower in CHD cases compared with healthy ones, while lactate/Cho was significantly higher in CHD cases. Immediate term postoperatively, significant changes in

NAA/creatinine and NAA/Cho, relative to preoperative values, were found. However, the difference did not persist at the short-term follow-up.

CONCLUSION:

This meta-analysis suggests that the delay in neurological development in newborns with CHD is due mainly to prenatal injury, and cardiac surgery might lead to mild brain injuries postoperatively, but fMRI shows recovery within a short period. Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.

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PMID: 24913334 [PubMed - in process]

2.

Ultrasound Obstet Gynecol. 2015 Jun;45(6):631-8. doi: 10.1002/uog.14882.

[Prenatal diagnosis of critical congenital heart disease reduces risk of death from cardiovascular compromise prior to planned neonatal cardiac surgery: a meta-analysis.](#)

Holland BJ, Myers JA, Woods CR Jr.

Abstract

OBJECTIVE:

To determine if prenatal diagnosis improves the chance that a newborn with critical congenital heart disease will survive to undergo planned cardiac surgery.

METHODS:

A systematic review of the medical literature identified eight studies which met the following criteria: compared outcomes between newborns with prenatal and those with postnatal diagnosis of critical congenital heart disease; compared groups of patients with the same anatomical diagnosis; provided detailed information on cardiac anatomy; included detailed information on preoperative cause of death. A meta-analysis was performed to assess differences in preoperative mortality rates between newborns with prenatal diagnosis and those with postnatal diagnosis. Patients with established risk factors for increased mortality (high risk) and those whose families chose comfort care rather than cardiac surgery were excluded.

RESULTS:

In patients with comparable anatomy, standard risk, a parental desire to treat and optimal care, newborns with a prenatal diagnosis of critical congenital heart disease were significantly less likely to die prior to planned cardiac surgery than were those with a comparable postnatal diagnosis (pooled odds ratio, 0.26; 95% CI, 0.08-0.84).

CONCLUSIONS:

For newborns most likely to benefit from treatment for their critical congenital heart disease, because they did not have additional risk factors and their families pursued treatment, prenatal diagnosis reduced the risk of death prior to planned cardiac surgery relative to patients with a comparable postnatal diagnosis. Further study and efforts to improve prenatal diagnosis of congenital heart disease should therefore be considered.

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PMID: 25904437 [PubMed - in process]

3.

J Pediatr Surg. 2015 Jun;50(6):893-7. doi: 10.1016/j.jpedsurg.2015.03.005. Epub 2015 Mar 14.

[Outcomes in the physiologically most severe congenital diaphragmatic hernia \(CDH\) patients: Whom should we treat?](#)

Kays DW, Islam S, Perkins JM, Larson SD, Taylor JA, Talbert JL.

Abstract

PURPOSE:

Centers that care for newborns with congenital diaphragmatic hernia (CDH) may impose selection criteria for offering or limiting aggressive support in those patients most severely affected. The purpose of this study was to analyze outcomes in newborns with highly severe CDH uniformly treated for survival.

METHODS:

We reviewed 172 consecutive inborn patients without associated lethal anomalies treated at a single institution with a dedicated CDH program. Survival, respiratory outcome, and time to discharge in the most severe 10% (or fewer) of patients based on the physiologic measures of 5-minute Apgar, CDH Study Group (CDHSG) predicted survival, need for ECMO in the first 6 hours, and need for ECMO in the first 3 hours of life were studied. We also identified patients with best PaCO₂ greater than 100 and best pH less than 7.0. A multivariate model (AUC-0.92) predicting mortality was also used to define the most severe 10%.

RESULTS:

Of 172 consecutive inborn patients, 18 had a 5-minute Apgar of 3 or less, and 11 survived (61%), 10 had a 5-minute Apgar of 2 or less, and 6 survived (60%), and 6 had a 5-minute Apgar of 1 or less, and 4 survived (67%). Seventeen had a CDHSG predicted survival less than 25%, and 9 survived (53%). Thirteen of 172 required ECMO for rescue in the first 6 hours of life, and 9 survived (69%), including 7 in the first 3 hours, and 5 survived (71%). Despite focused resuscitation in the delivery room and high levels of ventilatory support, 22 patients had a best PCO₂ greater than 100 and best pH less than 7.0 for 1 hour or longer. Twelve of these 22 survived to discharge (55%). Of 17 defined by multivariate predictive modeling as the most severe, 8 survived (47%) with zero of the 3 ECMO ineligible prematures surviving. Of the 16 (10%) most severe ECMO-eligible patients, 10 of 16 survived (63%). All survivors were discharged home on no ventilatory support greater than nasal cannula oxygen.

CONCLUSION:

In newborn CDH patients without lethal associated anomalies, accepted measures of physiologic severity failed to predict mortality. Survival met or exceeded 50% even in the most severe 10% as defined by these measures. These data support the practice of treating each patient for survival regardless of the physiologic severity in the first hours of life, and selection criteria for not offering ECMO should be reevaluated where practiced.

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PMID: 25933923 [PubMed - in process]

4.

Am J Obstet Gynecol. 2015 Jun;212(6):788.e1-6. doi: 10.1016/j.ajog.2015.01.031. Epub 2015 Jan 28.

[Efficacy of ultrasound-indicated cerclage in twin pregnancies.](#)

Roman A, Rochelson B, Fox NS, Hoffman M, Berghella V, Patel V, Calluzzo I, Saccone G, Fleischer A.

Abstract

OBJECTIVE:

We sought to compare the perinatal outcomes in twin pregnancies with short cervical length (CL) with ultrasound-indicated cerclage (UIC) vs no cerclage (control).

STUDY DESIGN:

This was a retrospective cohort study of asymptomatic twin pregnancies with transvaginal ultrasound (TVU) CL ≤ 25 mm at 16-24 weeks from 1995 through 2012 at 4 separate institutions. Exclusion criteria were: genetic or major fetal anomaly, multifetal reduction >14 weeks, monochorionic-monoamniotic placentation, or medically indicated preterm birth (PTB). Primary outcome was spontaneous PTB (SPTB) <34 weeks. Secondary outcome was SPTB <28 , <32 , and <37 weeks. We also planned to evaluate primary and secondary outcome for the subgroup of twin pregnancies with CL ≤ 15 mm.

RESULTS:

In all, 140 women with twin pregnancy and TVU-CL ≤ 25 mm were managed with either UIC (n = 57) or no cerclage (n = 83). Demographic characteristics were not significantly different except women who underwent UIC presented at an earlier gestational age (GA) at diagnosis of short CL. After adjusting for GA at presentation, there were no differences in GA at delivery or SPTB <28 weeks: 12 (21.2%) vs 20 (24.1%) (adjusted odds ratio [aOR], 0.3; 95% confidence interval [CI], 0.68-1.37), <32 weeks: 22 (38.6%) vs 36 (43.4%) aOR, 0.34; 95% CI, 0.1-1.13), or <34 weeks: 29 (50.9%) vs 53 (63.9%) (aOR, 0.37; 95% CI, 0.16-1.1). In the subgroup of women with CL ≤ 15 mm (32 with UIC and 39 controls) the interval between diagnosis to delivery was significantly prolonged by 12.5 ± 4.5 vs 8.8 ± 4.6 weeks (P $< .001$); SPTB <34 weeks was significantly decreased: 16 (50%) vs 31 (79.5%) (aOR, 0.51; 95% CI, 0.31-0.83) as was admission to neonatal intensive care unit: 38/58 (65.5%) vs 63/76 (82.9%) (aOR, 0.42; 95% CI, 0.24-0.81) when the UIC group was compared with the control group, respectively.

CONCLUSION:

UIC in asymptomatic twin pregnancies with TVU-CL ≤ 25 mm was not associated with significant effects on perinatal outcomes compared to controls. However, in the planned subgroup analysis of asymptomatic twin pregnancies with TVU-CL ≤ 15 mm before 24 weeks, UIC was associated with a significant prolongation of pregnancy by almost 4 more weeks, significantly decreased SPTB <34 weeks by 49%, and admission to neonatal intensive care unit by 58% compared with controls.

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PMID: 25637840 [PubMed - in process]

5.

Am J Obstet Gynecol. 2015 Jun;212(6):784.e1-7. doi: 10.1016/j.ajog.2015.02.025. Epub 2015 Feb 28.

[Posterior axilla sling traction for shoulder dystocia: case review and a new method of shoulder rotation with the sling.](#)

Cluver CA, Hofmeyr GJ.

Abstract

OBJECTIVE:

The purpose of this study was to report on all cases in which posterior axilla sling traction (PAST) has been used to deliver cases of intractable shoulder dystocia and to describe a new method of shoulder rotation with the sling.

STUDY DESIGN:

A record of all published and known cases was collected that included information on preliminary obstetric techniques that were used and how the PAST technique was performed. Maternal outcomes that included maternal injury and length of hospital stay and fetal outcomes, which included birthweight, Apgar scores, nerve injuries, fractures, hospital stay, and outcome, were documented.

RESULTS:

We have recorded 19 cases where PAST has been used. In 5 cases, the babies had died in utero. Ten were assisted deliveries. PAST was successful in 18 cases. In one case, it was partially successful because it enabled delivery of the posterior shoulder with digital axillary traction. The most commonly used material was suction tubing. Once the posterior shoulder was delivered, the shoulder dystocia was resolved in all cases. Time from insertion to delivery was <3 minutes when recorded. The birthweights of the infants varied from 3200-4800 g. Posterior arm humerus fractures occurred in 3 cases. There was one case of a permanent Erb's palsy and 4 cases of transient Erb's palsies. None were of the posterior arm. During this review, we found that, when direct delivery of the posterior shoulder was difficult because of very severe impaction, the sling could be used to rotate the shoulders easily through 180 degrees assisted by counter pressure on the back of the anterior shoulder. This new method was used in 5 cases and may reduce fetal trauma further during difficult shoulder delivery.

CONCLUSION:

This review confirms that PAST can be a lifesaving technique when all another techniques for shoulder dystocia fail. Advantages are that it is easy to use (even by someone who has not seen it used previously), that the sling material is readily available, and that it is inserted quickly with 2 fingers. This is the first report of its use to rotate the posterior shoulder to the anterior position for delivery.

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PMID: 25731695 [PubMed - in process]

6.

Fetal Diagn Ther. 2015 Jun 26. [Epub ahead of print]

[Stomach in Contact with the Bladder: A Sonographic Sign of Left Congenital Diaphragmatic Hernia.](#)

Aiello H, Meller C, Vázquez L, Otaño L.

Abstract

The evaluation of the characteristics of the fetal stomach should be part of every routine prenatal ultrasound after 11 weeks. A position that has not been previously described in the literature is the stomach in contact with the bladder. We describe 6 cases with the ultrasonographic finding of the stomach in contact with the bladder, all of them in fetuses with left-sided congenital diaphragmatic hernia. Even though the reasons for this striking position of the stomach are not clear, our series highlights the fact that the visualization of the stomach in contact with the bladder may be a specific sonographic marker of congenital diaphragmatic hernia. © 2015 S. Karger AG, Basel.

PMID: 26139528 [PubMed - as supplied by publisher]

7.

JAMA. 2015 Jul 14;314(2):162-169. doi: 10.1001/jama.2015.7120.

[Noninvasive Prenatal Testing and Incidental Detection of Occult Maternal Malignancies.](#)

Bianchi DW, Chudova D, Sehnert AJ, Bhatt S, Murray K, Prosen TL, Garber JE, Wilkins-Haug L, Vora NL, Warsof S, Goldberg J, Ziainia T, Halks-Miller M.

Abstract

IMPORTANCE:

Understanding the relationship between aneuploidy detection on noninvasive prenatal testing (NIPT) and occult maternal malignancies may explain results that are discordant with the fetal karyotype and improve maternal clinical care.

OBJECTIVE:

To evaluate massively parallel sequencing data for patterns of copy-number variations that might prospectively identify occult maternal malignancies.

DESIGN, SETTING, AND PARTICIPANTS:

Case series identified from 125 426 samples submitted between February 15, 2012, and September 30, 2014, from asymptomatic pregnant women who underwent plasma cell-free DNA sequencing for clinical prenatal aneuploidy screening. Analyses were conducted in a clinical laboratory that performs DNA sequencing. Among the clinical samples, abnormal results were detected in 3757 (3%); these were reported to the ordering physician with recommendations for further evaluation.

EXPOSURES:

NIPT for fetal aneuploidy screening (chromosomes 13, 18, 21, X, and Y).

MAIN OUTCOMES AND MEASURES:

Detailed genome-wide bioinformatics analysis was performed on available sequencing data from 8 of 10 women with known cancers. Genome-wide copy-number changes in the

original NIPT samples and in subsequent serial samples from individual patients when available are reported. Copy-number changes detected in NIPT sequencing data in the known cancer cases were compared with the types of aneuploidies detected in the overall cohort.

RESULTS:

From a cohort of 125 426 NIPT results, 3757 (3%) were positive for 1 or more aneuploidies involving chromosomes 13, 18, 21, X, or Y. From this set of 3757 samples, 10 cases of maternal cancer were identified. Detailed clinical and sequencing data were obtained in 8. Maternal cancers most frequently occurred with the rare NIPT finding of more than 1 aneuploidy detected (7 known cancers among 39 cases of multiple aneuploidies by NIPT, 18% [95% CI, 7.5%-33.5%]). All 8 cases that underwent further bioinformatics analysis showed unique patterns of nonspecific copy-number gains and losses across multiple chromosomes. In 1 case, blood was sampled after completion of treatment for colorectal cancer and the abnormal pattern was no longer evident.

CONCLUSIONS AND RELEVANCE:

In this preliminary study, a small number of cases of occult malignancy were subsequently diagnosed among pregnant women whose noninvasive prenatal testing results showed discordance with the fetal karyotype. The clinical importance of these findings will require further research.

PMID: 26168314 [PubMed - as supplied by publisher]

8.

Lancet. 2015 Jun 20;385(9986):2492-501. doi: 10.1016/S0140-6736(14)61998-X. Epub 2015 Mar 25.

[Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation \(HYPITAT-II\): an open-label, randomised controlled trial.](#)

Broekhuijsen K, van Baaren GJ, van Pampus MG, Ganzevoort W, Sikkema JM, Woiski MD, Oudijk MA, Bloemenkamp KW, Scheepers HC, Bremer HA, Rijnders RJ, van Loon AJ, Perquin DA, Sporken JM, Papatsonis DN, van Huizen ME, Vredevoogd CB, Brons JT, Kaplan M, van Kaam AH, Groen H, Porath MM, van den Berg PP, Mol BW, Franssen MT, Langenveld J; HYPITAT-II study group. Collaborators (56)

Abstract

BACKGROUND:

There is little evidence to guide the management of women with hypertensive disorders in late preterm pregnancy. We investigated the effect of immediate delivery versus expectant monitoring on maternal and neonatal outcomes in such women.

METHODS:

We did an open-label, randomised controlled trial, in seven academic hospitals and 44 non-academic hospitals in the Netherlands. Women with non-severe hypertensive disorders of pregnancy between 34 and 37 weeks of gestation were randomly allocated to either induction of labour or caesarean section within 24 h (immediate delivery) or a strategy

aimed at prolonging pregnancy until 37 weeks of gestation (expectant monitoring). The primary outcomes were a composite of adverse maternal outcomes (thromboembolic disease, pulmonary oedema, eclampsia, HELLP syndrome, placental abruption, or maternal death), and neonatal respiratory distress syndrome, both analysed by intention-to-treat. This study is registered with the Netherlands Trial Register (NTR1792).

FINDINGS:

Between March 1, 2009, and Feb 21, 2013, 897 women were invited to participate, of whom 703 were enrolled and randomly assigned to immediate delivery (n=352) or expectant monitoring (n=351). The composite adverse maternal outcome occurred in four (1.1%) of 352 women allocated to immediate delivery versus 11 (3.1%) of 351 women allocated to expectant monitoring (relative risk [RR] 0.36, 95% CI 0.12-1.11; p=0.069). Respiratory distress syndrome was diagnosed in 20 (5.7%) of 352 neonates in the immediate delivery group versus six (1.7%) of 351 neonates in the expectant monitoring group (RR 3.3, 95% CI 1.4-8.2; p=0.005). No maternal or perinatal deaths occurred.

INTERPRETATION:

For women with non-severe hypertensive disorders at 34-37 weeks of gestation, immediate delivery might reduce the already small risk of adverse maternal outcomes. However, it significantly increases the risk of neonatal respiratory distress syndrome, therefore, routine immediate delivery does not seem justified and a strategy of expectant monitoring until the clinical situation deteriorates can be considered.

FUNDING:

ZonMw.

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9.

Lancet. 2015 Jun 27;385(9987):2600-5. doi: 10.1016/S0140-6736(14)61904-8. Epub 2015 Apr 8.

[Induction of labour versus expectant management for large-for-date fetuses: a randomised controlled trial.](#)

Boulvain M, Senat MV, Perrotin F, Winer N, Beucher G, Subtil D, Bretelle F, Azria E, Hejaiej D9, Vendittelli F, Capelle M, Langer B, Matis R, Connan L, Gillard P, Kirkpatrick C, Ceysens G, Faron G, Irion O, Rozenberg P; Groupe de Recherche en Obstétrique et Gynécologie (GROG).

Abstract

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.

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10.

Prenat Diagn. 2015 Jun;35(6):517-28. doi: 10.1002/pd.4586. Epub 2015 May 19.

[Why increased nuchal translucency is associated with congenital heart disease: a systematic review on genetic mechanisms.](#)

Burger NB, Bekker MN, de Groot CJ, Christoffels VM, Haak MC.

Abstract

This overview provides insight into the underlying genetic mechanism of the high incidence of cardiac defects in fetuses with increased nuchal translucency (NT). Nuchal edema, the morphological equivalent of increased NT, is likely to result from abnormal lymphatic development and is strongly related to cardiac defects. The underlying genetic pathways are, however, unknown. This study aims to present a systematic overview of genes involved in both cardiac and lymphatic development in mouse embryos. A search of PubMed and the Mammalian Phenotype Browser was performed. Fifteen candidate genes involved in both

cardiac and lymphatic development were identified: Adrenomedullin; Chicken ovalbumin upstream promoter-transcription factor 2 (COUP-TFII); Cyp51; Ephrin-B2; Forkhead box protein C2 (Foxc2); Nuclear factor of activated T cells, cytoplasmic 1 (Nfatc1); Neurofibromatosis type 1 (Nf1); Phosphoinositide 3-kinase encoding isoform p110 α (Pik3ca); Podoplanin; Prospero-related homeobox 1 (Prox1); T-box 1 (Tbx1); Tyrosine kinase with immunoglobulin-like and endothelial growth factor-like domains 1 (Tie1); vascular endothelial growth factor (Vegf)-A; Vegf receptor-3 (Vegfr-3); and Vascular endothelial zinc finger 1 (Vezf1). Mutations in all but one gene (Pik3ca) resulted in both a cardiac defect and nuchal edema. Candidate genes - mainly encoding for endothelium - are involved in both cardiac and lymphatic development. Alterations in candidate genes are associated with the strong relation between increased NT and cardiac defects. © 2015 John Wiley & Sons, Ltd. © 2015 John Wiley & Sons, Ltd. PMID: 25728762 [PubMed - in process]

11.

BJOG. 2015 Jun;122(7):994-1000. doi: 10.1111/1471-0528.12964. Epub 2014 Jul 16.

[A follow-up of a randomised study of metformin and insulin in gestational diabetes mellitus: growth and development of the children at the age of 18 months.](#)

Ijäs H, Väärasmäki M, Saarela T, Keravuo R, Raudaskoski T.

Abstract

OBJECTIVE:

To compare the growth and development of children born to mothers with gestational diabetes mellitus (GDM) requiring pharmacological treatment, and randomised to treatment with metformin or insulin.

DESIGN:

Follow-up of a randomised controlled trial (RCT) comparing metformin and insulin treatment of GDM.

SETTING:

Data were gathered during routine visits to child welfare clinics at the ages of 6, 12, and 18 months, including weight and height measurements, and assessment of motor, social, and linguistic development.

SAMPLE:

The children of mothers with GDM randomised to metformin (n = 47) or insulin (n = 50) treatment during pregnancy.

METHODS:

Data were collected from the structured questionnaire filled in at the child welfare clinics.

MAIN OUTCOME MEASURES:

The growth and development of the children until the age of 18 months.

RESULTS:

Children exposed to metformin were significantly heavier (10.47 versus 9.85 kg, 95% CI 0.04-1.20) at the age of 12 months and taller and heavier (83.9 vs 82.2 cm, 95% CI 0.23-3.03, 12.05 vs 11.32 kg, 95% CI 0.04-1.43) at the age of 18 months. The mean ponderal

index (PI) did not differ significantly. The motor, social, or linguistic development evaluated at the age of 18 months did not differ between the groups.

CONCLUSIONS:

Children prenatally exposed to metformin were heavier at the 12 months measurements and taller and heavier at the 18 months measurements than those exposed to insulin, but their body composition defined by PI did not differ. Over the short term, metformin does not seem to be harmful with regards to early motor, linguistic, or social development.

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PMID: 25039582 [PubMed - in process]

12.

Pediatrics. 2015 Jun;135(6):972-80. doi: 10.1542/peds.2014-4094. Epub 2015 May 18.

[Long-Chain Polyunsaturated Fatty Acids and Cognition in VLBW Infants at 8 years: an RCT.](#)

Almaas AN, Tamnes CK, Nakstad B, Henriksen C, Walhovd KB, Fjell AM, Due-Tønnessen P, Drevon CA, Iversen PO.

Abstract

OBJECTIVE:

To test the hypothesis that supplementation with the long chain polyunsaturated fatty acids docosahexaenoic acid (DHA) and arachidonic acid (AA) to very low birth weight (VLBW) infants would improve long-term cognitive functions and influence neuroanatomical volumes and cerebral cortex measured by MRI.

METHODS:

The current study is a follow-up of a randomized, double-blinded, placebo-controlled study of supplementation with high-dose DHA (0.86%) and AA (0.91%) to 129 VLBW infants fed human milk. Ninety-eight children participated at 8 years follow-up and completed a broad battery of cognitive tests. Eighty-one children had cerebral MRI scans of acceptable quality.

RESULTS:

There were no significant differences between the intervention group and the control group on any of the cognitive measures. Equally, MRI data on segmental brain volumes and cerebral cortex volume, area, and thickness suggested no overall group effect.

CONCLUSIONS:

This study is the first long-term follow-up of a randomized controlled trial with supplementation of DHA and AA to human milk fed VLBW infants investigating both cognitive functions and brain macrostructure measured by MRI. No cognitive or neuroanatomical effects of the supplementation were detected at 8 years of age.

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PMID: 25986018 [PubMed - in process]

13.

Obstet Gynecol. 2015 Jun;125(6):1321-9. doi: 10.1097/AOG.0000000000000863.

[Use of cell-free DNA in the investigation of intrauterine fetal demise and miscarriage.](#)

Clark-Ganheart CA, Fries MH, Leifheit KM, Jensen TJ, Moreno-Ruiz NL, Ye PP, Jennings JM, Driggers RW.

Abstract

OBJECTIVE:

To estimate whether cell-free DNA is present in nonviable pregnancies and thus can be used in diagnostic evaluation in this setting.

METHODS:

We conducted a prospective cohort study of 50 participants at MedStar Washington Hospital Center, Washington, DC, between June 2013 and January 2014. Included were women with pregnancies complicated by missed abortion or fetal demise. All gestational ages were considered for study participation. Participants with fetal demise were offered the standard workup for fetal death per the American College of Obstetricians and Gynecologists. Maternal blood samples were processed to determine the presence of cell-free DNA, the corresponding fetal fractions, and genetic abnormalities.

RESULTS:

Fifty samples from nonviable pregnancies were analyzed. The average clinical gestational age was 16.9 weeks (standard deviation 9.2). The mean maternal body mass index was 30.3 (standard deviation 9.1). Seventy-six percent (38/50) of samples yielded cell-free DNA results, that is, had fetal fractions within the detectable range of 3.7-65%. Among the 38, 76% (29) were classified as euploid, 21% (8) as trisomies, and 3% (1) as microdeletion. A cell-free DNA result was obtained more frequently at ultrasonographic gestational ages of 8 weeks or greater compared with less than 8 weeks (87.9% [n=29/33, 95% confidence interval (CI) 72.7-95.2; and 52.9%, n=9/17, 95% CI 31.0-73.8] of the time, respectively, P=.012). Time from demise was not associated with obtaining a result.

CONCLUSION:

Among nonviable pregnancies, cell-free DNA is present in the maternal plasma with fetal fractions greater than 3.7% in more than three fourths of cases after an ultrasonographic gestational age of 8 weeks.

CLINICAL TRIAL REGISTRATION:

ClinicalTrials.gov, www.clinicaltrials.gov, NCT01916928.

LEVEL OF EVIDENCE:

III.

PMID: 26000503 [PubMed - in process]