April 2016 Literature Alert


An update on the use of massive transfusion protocols in obstetrics.

Pacheco LD, Saad e GR, Costantine MM, Clark SL, Hankins GD.

Abstract

Obstetrical hemorrhage remains a leading cause of maternal mortality worldwide. New concepts involving the pathophysiology of hemorrhage have been described and include early activation of both the protein C and fibrinolytic pathways. New strategies in hemorrhage treatment include the use of hemostatic resuscitation, although the optimal ratio to administer the various blood products is still unknown. Massive transfusion protocols involve the early utilization of blood products and limit the traditional approach of early massive crystalloid-based resuscitation. The evidence behind hemostatic resuscitation has changed in the last few years, and debate is ongoing regarding optimal transfusion strategies. The use of tranexamic acid, fibrinogen concentrates, and prothrombin complex concentrates has emerged as new potential alternative treatment strategies with improved safety profiles.

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KEYWORDS:

hemostatic resuscitation; massive transfusion; obstetrical hemorrhage

PMID: 26348379 [PubMed - in process]


Integrase inhibitors in late pregnancy and rapid HIV viral load reduction.


Abstract

BACKGROUND:
Minimizing time to HIV viral suppression is critical in pregnancy. Integrase strand transfer inhibitors (INSTIs), like raltegravir, are known to rapidly suppress plasma HIV RNA in nonpregnant adults. There are limited data in pregnant women.

OBJECTIVE:
We describe time to clinically relevant reduction in HIV RNA in pregnant women using INSTI-containing and non-INSTATI-containing antiretroviral therapy (ART) options.

STUDY DESIGN:
We conducted a retrospective cohort study of pregnant HIV-infected women in the United States from 2009 through 2015. We included women who initiated ART, intensified their regimen, or switched to a new regimen due to detectable viremia (HIV RNA >40 copies/mL) at ≥20 weeks gestation. Among women with a baseline HIV RNA permitting 1-log reduction, we estimated time to 1-log RNA reduction using the Kaplan-Meier estimator comparing women starting/adding an INSTI in their regimen vs other ART. To compare groups with similar follow-up time, we also conducted a subgroup analysis limited to women with ≤14 days between baseline and follow-up RNA data.

RESULTS:
This study describes 101 HIV-infected pregnant women from 11 US clinics. In all, 75% (76/101) of women were not taking ART at baseline; 24 were taking non-INSTATI containing ART, and 1 received zidovudine monotherapy. In all, 39% (39/101) of women started an INSTI-containing regimen or added an INSTI to their ART regimen. Among 90 women with a baseline HIV RNA permitting 1-log reduction, the median time to 1-log RNA reduction was 8 days (interquartile range [IQR], 7-14) in the INSTI group vs 35 days (IQR, 20-53) in the non-INSTATI ART group (P < .01). In a subgroup of 39 women with first and last RNA measurements ≤14 days apart, median time to 1-log reduction was 7 days (IQR, 6-10) in the INSTI group vs 11 days (IQR, 10-14) in the non-INSTATI group (P < .01).

CONCLUSION:
ART that includes INSTIs appears to induce more rapid viral suppression than other ART regimens in pregnancy. Inclusion of an INSTI may play a role in optimal reduction of HIV RNA for HIV-infected pregnant women presenting late to care or failing initial therapy. Larger studies are urgently needed to assess the safety and effectiveness of this approach.

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KEYWORDS:
HIV; integrase inhibitors; pregnancy

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A universal mid-trimester transvaginal cervical length screening program and its associated reduced preterm birth rate.

Son M, Grobman WA, Ayala NK, Miller ES.

Abstract

BACKGROUND:

Mid-trimester transvaginal cervical length assessment can identify women who are at risk of preterm birth and afford opportunities for preterm birth prevention. However, the incidence of a short cervix is low, and some physicians have questioned whether a universal screening program among women without a previous preterm birth would be beneficial.

OBJECTIVE:

The purpose of this study was to examine whether the introduction of a universal transvaginal cervical length screening program is associated with a reduction in the preterm birth rate.

STUDY DESIGN:

This is a cohort study of women with singleton gestations and without any previous preterm births who underwent an obstetric sonogram at 18-24 weeks of gestation and who had their delivery at a single tertiary institution from January 2007 to January 2014. In July 2011, a program was implemented in which all pregnant women who had a sonogram at 18-24 weeks of gestation were to receive a transvaginal cervical length measurement. The preterm birth rates were compared before and after the implementation of the universal cervical length screening program. Multivariable analysis was used to identify whether the universal cervical length screening program was associated independently with the frequency of preterm birth. The Breslow-Day test for homogeneity was used to assess whether any interaction existed in the association based on parity.

RESULTS:

Of 64,207 eligible women, 46,598 underwent their mid-trimester sonogram before the universal cervical length screening program, and 17,609 underwent a sonogram after implementation of the program. Of the 17,590 women (99.9%) who agreed to cervical length measurement, 157 (0.89%) had a measurement of ≤25 mm. The introduction of the cervical length program was associated with a significant decrease in the frequency of preterm birth at <37 weeks of gestation (6.7% vs 6.0%; adjusted odds ratio, 0.82 [95% confidence interval, 0.76-0.88]), <34 weeks of gestation (1.9% vs 1.7%; adjusted odds ratio, 0.74 [95% confidence interval, 0.64-0.85]), and <32 weeks of gestation (1.1% vs 1.0%; adjusted odds ratio, 0.74 [95% confidence interval, 0.62-0.90]). This reduction in frequency of preterm birth primarily was due to a change in spontaneous (and not medically indicated) preterm births. The effect size for the reduction in preterm birth was similar in nulliparous and multiparous women with previous term births.

CONCLUSION:

The introduction of a universal transvaginal cervical length screening program in women without a history of preterm birth is associated with a reduction in the frequency of preterm birth.
Randomized Trial of Labor Induction in Women 35 Years of Age or Older.


Abstract

BACKGROUND:
The risk of antepartum stillbirth at term is higher among women 35 years of age or older than among younger women. Labor induction may reduce the risk of stillbirth, but it also may increase the risk of cesarean delivery, which already is common in this older age group.

METHODS:
We conducted a randomized, controlled trial involving primigravid women who were 35 years of age or older. Women were randomly assigned to labor induction between 39 weeks 0 days and 39 weeks 6 days of gestation or to expectant management (i.e., waiting until the spontaneous onset of labor or until the development of a medical problem that mandated induction). The primary outcome was cesarean delivery. The trial was not designed or powered to assess the effects of labor induction on stillbirth.

RESULTS:
A total of 619 women underwent randomization. In an intention-to-treat analysis, there were no significant between-group differences in the percentage of women who underwent a cesarean section (98 of 304 women in the induction group [32%] and 103 of 314 women in the expectant-management group [33%]; relative risk, 0.99; 95% confidence interval [CI], 0.87 to 1.14) or in the percentage of women who had a vaginal delivery with the use of forceps or vacuum (115 of 304 women [38%] and 104 of 314 women [33%], respectively; relative risk, 1.30; 95% CI, 0.96 to 1.77). There were no maternal or infant deaths and no significant between-group differences in the women's experience of childbirth or in the frequency of adverse maternal or neonatal outcomes.

CONCLUSIONS:
Among women of advanced maternal age, induction of labor at 39 weeks of gestation, as compared with expectant management, had no significant effect on the rate of cesarean section and no adverse short-term effects on maternal or neonatal outcomes. (Funded by the Research for Patient Benefit
A widespread epidemic of Zika virus (ZIKV) infection was reported in 2015 in South and Central America and the Caribbean. A major concern associated with this infection is the apparent increased incidence of microcephaly in fetuses born to mothers infected with ZIKV. In this report, we describe the case of an expectant mother who had a febrile illness with rash at the end of the first trimester of pregnancy while she was living in Brazil. Ultrasonography performed at 29 weeks of gestation revealed microcephaly with calcifications in the fetal brain and placenta. After the mother requested termination of the pregnancy, a fetal autopsy was performed. Micrencephaly (an abnormally small brain) was observed, with almost complete agyria, hydrocephalus, and multifocal dystrophic calcifications in the cortex and subcortical white matter, with associated cortical displacement and mild focal inflammation. ZIKV was found in the fetal brain tissue on reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay, with consistent findings on electron microscopy. The complete genome of ZIKV was recovered from the fetal brain.
To document associations between confirmed and suspected neonatal infection and motor, cognitive, educational, and mental health outcomes of very preterm (VPT)-born children at 9 years of age; to examine the potential intervening role of cerebral white matter abnormalities (WMAs) and structural development on term magnetic resonance imaging.

STUDY DESIGN:

A regional cohort of 110 infants born VPT in Christchurch, New Zealand were studied from birth to age of 9 years. Confirmed infection was defined as positive blood, cerebrospinal fluid or urine culture, and/or necrotizing enterocolitis ≥stage 2. Suspected infection was defined as ≥5 days of antibiotics with evidence of clinical correlates. At term gestational equivalence, infants underwent structural magnetic resonance imaging. At age 9 years, neuromotor function, IQ, educational achievement, and mental health were assessed.

RESULTS:

During hospitalization, 25% of VPT infants had confirmed and 23% had suspected infection. Longer-term neurodevelopmental impairments were largely confined to infants with confirmed infection (relative risk 1.4-3.1, vs uninfected). After accounting for other neonatal factors, these infants were at increased risk of severe motor impairment (OR 3.3, 95% CI 1.3-8), attention deficit hyperactivity disorder (ADHD) (OR 3.6, 95% CI 1.6-8), and IQ delay (OR 2.0, 95% CI 1.3). Cerebral WMAs contributed to associations between confirmed infection and motor and IQ impairments but not to ADHD (P = .005).

CONCLUSIONS:

Confirmed neonatal infection heightens VPT infants' risk for neurodevelopmental impairment. WMA appears to be an important intervening factor linking infection and severe motor and IQ impairments. Further analysis of the neurologic mechanism accounting for ADHD in infants with infection is needed.

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7.


Use of the Sequential Organ Failure Assessment score for evaluating outcome among obstetric patients admitted to the intensive care unit.

Jain S, Guleria K, Suneja A, Vaid NB, Ahuja S.

Abstract

OBJECTIVE:

To evaluate the prognostic value of the Sequential Organ Failure Assessment (SOFA) score among obstetric patients admitted to the intensive care unit (ICU).

METHODS:
A prospective study was conducted among 90 consecutive obstetric patients who were admitted to the ICU of Guru Teg Bahadur Hospital, Delhi, India, between October 6, 2010, and December 25, 2011. Maximum SOFA score was calculated for each of the six organ systems. Receiver operating characteristic curves were used to determine critical cutoff values for total, maximum total, and mean total SOFA scores at various time points.

RESULTS:

Total SOFA score at admission displayed an area under the curve (AUC) of 0.949, a cutoff value of at least 8.5, sensitivity of 86.7%, and specificity of 90.0%. Maximum total SOFA score had an AUC of 0.980, a cutoff value of at least 10.0, sensitivity of 96.7%, and specificity of 90.0%. Mean total SOFA score had an AUC of 0.997, a cutoff value of at least 9.0, sensitivity of 96.7%, and specificity of 96.7%.

CONCLUSION:

In terms of discriminatory power for predicting mortality among obstetric patients admitted to the ICU, total SOFA score at admission was the most relevant, simple, and accurate measure.

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KEYWORDS:

Critical illness; Intensive care unit; Near-miss cases; Obstetric cases; Prognostic score; Sequential Organ Failure Assessment score; Severe maternal morbidity

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8.

What is the role of the 11- to 14-week ultrasound in women with negative cell-free DNA screening for aneuploidy?

Reiff ES, Little SE, Dobson L, Wilkins-Haug L, Bromley B.

Abstract

OBJECTIVE:

This study aimed to examine the role of the 11- to 14-week ultrasound in women with negative cell-free DNA screening.

METHODS:

A retrospective cohort study of women at increased risk for aneuploidy based on age or medical history and negative cell-free DNA screening between March 2012 and March 2014 was conducted. Patients were included if they had an 11- to 14-week ultrasound and obstetrical care at our center(s). Primary
outcome was an unexpected finding at ultrasound. Imaging findings were compared with obstetrical outcome by medical record review.

RESULTS:

Study group was composed of 1739 patients. An unexpected finding was identified in 60/1739 (3.5%). An abnormal fetal finding occurred in 37 living fetuses (2.1%); 33 had a nuchal translucency (NT) ≥ 3 mm, including four 'isolated' cystic hygroma and three with a structural abnormality. Four fetuses had a structural anomaly without a thick NT. Karyotype confirmed euploidy in 98.7% of available cases. Pregnancy termination was chosen by 63.6% of those with cystic hygroma or anomaly at the 11- to 14-week scan. Unexpected multiples were identified in 13 (0.7%) women and a fetal demise in 10 (0.6%).

CONCLUSION:

Unexpected findings at the 11- to 14-week scan occur in 3.5% of patients with negative cell-free DNA. Recognition provides options for comprehensive testing, consultation, and management. © 2016 John Wiley & Sons, Ltd.

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9.


Association Between Hypertensive Disorders of Pregnancy and Later Risk of Cardiomyopathy.


Abstract

IMPORTANCE:

Women with hypertensive disorders of pregnancy, preeclampsia in particular, have an increased risk of cardiomyopathy during the peripartum period. Whether hypertensive disorders of pregnancy are also associated with cardiomyopathy later in life is unknown.

OBJECTIVE:

To determine whether hypertensive disorders of pregnancy are associated with cardiomyopathy beyond the peripartum period.

DESIGN, SETTING, AND PARTICIPANTS:

Nationwide register-based cohort study using Cox regression to compare rates of cardiomyopathy in women with and without a history of hypertensive disorders of pregnancy in a cohort of 1,075,763 women with at least 1 pregnancy ending in live birth or stillbirth in Denmark, 1978-2012, with follow-up through December 31, 2012.

EXPOSURES:
A hypertensive disorder of pregnancy (severe or moderate preeclampsia or gestational hypertension) registered in the National Patient Register.

MAIN OUTCOMES AND MEASURES:

Cardiomyopathy more than 5 months after delivery (outside the peripartum period) up to 34 years 7 months.

RESULT:

The women in the primary cohort had 2,067,633 eligible pregnancies during the study period, 76,108 of which were complicated by a hypertensive disorder of pregnancy. During follow-up, 1577 women (mean age, 48.5 years at cardiomyopathy diagnosis; 2.6% with multiple pregnancies) developed cardiomyopathy. Compared with women with normotensive pregnancies (18,211,603 person-years of follow-up; n = 1408 cardiomyopathy events, 7.7/100,000 person-years [95% CI, 7.3-8.2]), women with a history of hypertensive disorders of pregnancy had significantly increased rates of cardiomyopathy (in 173,062 person-years of follow-up among women with severe preeclampsia, n = 27 cardiomyopathy events; 15.6/100,000 person-years [95% CI, 10.7-22.7]; adjusted hazard ratio [HR], 2.20 [95% CI, 1.50-3.23]; in 697,447 person-years of follow-up among women with moderate preeclampsia, n = 102 cardiomyopathy events; 14.6/100,000 person-years [95% CI, 12.0-17.8]; adjusted HR, 1.89 [95% CI, 1.55-2.23]; in 213,197 person-years of follow-up among women with gestational hypertension, n = 40 cardiomyopathy events; 17.3/100,000 person-years [95% CI, 12.7-23.6]; adjusted HR, 2.06 [95% CI, 1.50-2.82]). These increases persisted more than 5 years after the latest pregnancy. Mediation analyses suggested that only about 50% of the association was an indirect association through postpregnancy chronic hypertension. In this cohort, 11% of all cardiomyopathy events occurred in women with a history of hypertensive disorders of pregnancy.

CONCLUSIONS AND RELEVANCE:

Women with a history of hypertensive disorders of pregnancy, compared with women without such a history, had a small but statistically significant increased risk of cardiomyopathy more than 5 months after delivery. Further research is necessary to understand whether there is a causal mechanism behind this association.

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10.


Number of prenatal visits and pregnancy outcomes in low-risk women.

Carter EB1, Tuuli MG1, Caughey AB2, Odibo AO3, Macones GA1, Cahill AG1.

Abstract

OBJECTIVE:

We investigated the association between number of prenatal visits (PNV) and pregnancy outcomes.
STUDY DESIGN:
A retrospective cohort of 12,092 consecutive, uncomplicated term births was included. Exclusion criteria included unknown or third trimester pregnancy dating, pre-existing medical conditions and common pregnancy complications. Patients with \( \leq 10 \) PNV were compared with those with >10. The primary outcome was a neonatal composite including neonatal intensive-care unit admission, low APGAR score (<7), low umbilical cord pH (<7.10) and neonatal demise. Secondary outcomes included components of the composite as well as vaginal delivery, induction and cesarean delivery. Logistic regression was used to adjust for potential confounders.

RESULT:
Of 7,256 patients in the cohort meeting inclusion criteria, 30% (N=2,163) had >10 PNV and the remaining 70% (N=5,093) had \( \leq 10 \), respectively. There was no difference in the neonatal composite between the two groups. However, women with >10 PNV were more likely to undergo induction of labor and cesarean delivery.

CONCLUSION:
Low-risk women with \( \geq 10 \) PNV had higher rates of pregnancy interventions without improvement in neonatal outcomes.


11.

Prolonged second stage of labour, maternal infectious disease, urinary retention and other complications in the early postpartum period.

Stephansson O, Sandström A, Petersson G, Wikström AK, Cnattingius S.

Abstract

OBJECTIVE:
To study the association between duration of second stage of labour and risks of maternal complications (infection, urinary retention, haematoma or ruptured sutures) in the early postpartum period.

DESIGN:
Population-based cohort study.

SETTING AND SAMPLE:
We included 72,593 mothers with singleton vaginal deliveries at \( \geq 37 \) weeks of gestation in cephalic presentation, using the obstetric database from the Stockholm-Gotland region in Sweden, 2008-12.

METHODS:
Logistic regression analysis. Odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated and adjustments were made for maternal age, body mass index, height, smoking, cohabitation, gestational age, labour induction, epidural analgesia and oxytocin augmentation.

RESULTS:

Rates of any complication varied by parity from 7.3% in parous women with previous caesarean section, 4.8% in primiparas and 1.7% in parous women with no previous caesarean section. Compared with a second stage <1 hour, the adjusted ORs for any complication (95% CI) in primiparas were for 1 to <2 hours 1.28 (1.11-1.47); 2 to <3 hours 1.54 (1.32-1.79), 3 to <4 hours 1.63 (1.38-1.93) and ≥4 hours 2.08 (1.74-2.49). The corresponding adjusted ORs for parous women without previous caesarean were 2.27 (1.78-2.90), 2.97 (2.09-4.22), 3.65 (2.25-5.94) and 3.16 (1.44-6.94), respectively. The adjusted ORs for women with previous caesarean were for 1 to <2 hours 1.62 (1.13-2.32); 2 to <3 hours 1.56 (1.00-2.43), 3 to <4 hours 2.42 (1.52-3.87), and ≥4 hours 2.31 (1.25-4.24).

CONCLUSIONS:

Risks of maternal complications in the postpartum period increase with duration of second stage of labour also after accounting for maternal, pregnancy and delivery characteristics. Special attention has to be given to parous women with previous caesarean deliveries.

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KEYWORDS:
Infectious disease; labour; postpartum; second stage; urinary retention

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excluded pregnancies missing outcome or exposure data. Our primary exposure was chorioamnionitis, defined by the clinical diagnosis of chorioamnionitis and a maternal fever greater than 100°F. Our primary outcome was a Bayley II Mental Developmental Index score less than 70 or Psychomotor Developmental Index score less than 70 assessed at age 2 years. We also assessed Mental Developmental Index or Psychomotor Developmental Index score less than 85. We conducted bivariate analyses and fit a log-linear regression model, adjusting for related to Mental Developmental Index or Psychomotor Developmental Index score less than 70 or less than 85 with a detectable effect size estimated at a relative risk of 1.5 or greater.

RESULTS:

Of 1,574 patients in our analysis, 194 (12%) had chorioamnionitis and 1,366 (87%) had preterm premature rupture of membranes. The mean gestational age at delivery was 29 3/7 weeks. There were no significant differences in Mental Developmental Index score less than 70 (37 [19.1%] compared with 233 [17%], P=.45) or Psychomotor Developmental Index score less than 70 (29 [15%] compared with 195 [14%] P=.76) for children born to mothers with or without chorioamnionitis, respectively. After adjusting for confounders, there remained no difference in the proportion of abnormal scores in either group. However, neonates diagnosed with sepsis were found to have significantly decreased Mental Developmental Index scores.

CONCLUSION:

Exposure to chorioamnionitis was not associated with neurocognitive defects as measured by abnormal Bayley II scores.

PMID: 26855093 [PubMed - in process]

13.


Abstract

BACKGROUND AND OBJECTIVE:

Several studies have shown the benefits of delayed cord clamping (DCC) in preterm and in healthy newborns at short and long term. Our objective was to evaluate the potentials benefits and risks of DCC in red cell alloimmunization.

METHODS:

This was a comparative before/after study of all living born neonates followed after fetal anemia requiring in utero transfusion. DCC was defined as cord clamping 30 seconds after birth.
RESULTS:

We included a continuous series of 72 neonates: 36 without DDC (group 1) and 36 with DDC (group 2). Hemoglobin at birth was lower in group 1 (10.2 vs 13.4 g/dL, P = .0003); 7 (25%) neonates in group 1 vs 24 (70.6%) in group 2 had no anemia at birth (P = .004). The rate of transfusion was similar between the 2 groups. Postnatal exchange transfusions were more likely performed in the group without DCC than in the group with DCC (47.2% vs 19.4%, P = .0124). Delay between birth and first transfusion was higher in group 2 (0 [0-13] vs 1 [0-21], P = .0274). The maximum level of bilirubin, the rate of intensive phototherapy, and the total duration of phototherapy were similar in the 2 groups.

CONCLUSIONS:

This study highlights a significant benefit of DCC in anemia secondary to red blood cell alloimmunization with a resulting decreased postnatal exchange transfusion needs, an improvement in the hemoglobin level at birth and longer delay between birth and first transfusion with no severe hyperbilirubinemia.

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