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OB/GYN Clinical [ALERT]

Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

Is Black Race Associated with Major Depression Following Early Pregnancy Loss?

By Maria F. Gallo, PhD

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SYNOPSIS: Reporting symptoms of having major depression one month after treatment for early pregnancy loss was about twice as common among Black women compared to non-Black women.

SOURCE: Shorter JM, Koelper N, Sonalkar S, et al. Racial disparities in mental health outcomes among women with early pregnancy loss. *Obstet Gynecol* 2021;137:156-163.

Early pregnancy loss (EPL) is common and can lead to psychological sequelae. Black women in the United States experience higher rates of pregnancy loss and perinatal depression than women of other racial groups. In a recent secondary analysis, Shorter et al evaluated whether Black women have more symptoms of major depression one month after being treated for EPL compared to non-Black women. To do this, they compared 120 women who self-identified as Black and 155 women who self-identified as non-Black. The latter group was comprised mostly of Hispanic (n = 72) women, followed by other (n = 36), white (n = 27), and Asian (n = 20) women. Participants in the parent trial (n = 300) were adults diagnosed with a nonviable intrauterine pregnancy at five to 12 weeks of gestation who were enrolled in a randomized trial in 2014-2017 to study the medical management of EPL.

For the present analysis, researchers diagnosed women as having symptoms of no, mild-moderate, or major depression one month after treatment using a common screening instrument, the Center for Epidemiological Studies-Depression scale (CES-D). This tool consists of 20 items that produce six subscales for the major dimensions of depression: depressed mood, feelings of guilt and worthlessness, feelings of helplessness and hopelessness, psychomotor retardation, loss of appetite, and sleep disturbance.

Participants also completed two other validated scales: the Perceived Stress Scale and the Adverse Childhood Experience (ACE) scale. The Perceived Stress Scale is a psychological tool for measuring perception of stress in the past month. Shorter et al included in their analysis participants from the parent study who completed the

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OB/GYN Clinical Alert Welcomes Maria F. Gallo, PhD

We are thrilled to welcome Maria F. Gallo, PhD, as an associate editor for *OB/GYN Clinical Alert*. Dr. Gallo is professor and chair of the Division of Epidemiology at the College of Public Health at The Ohio State University and also serves as the associate dean of research. Her primary research interests include contraception and abortion care. Prior to her tenure at Ohio State, Dr. Gallo worked in women's health and fertility at the Centers for Disease Control and Prevention. She brings a wealth of research experience to the evidence-based commentaries on women's health that *OB/GYN Clinical Alert* provides.

— Rebecca H. Allen, MD, MPH, Editor

CES-D and Perceived Stress Scale. Missing scale data seemed to be more common among white participants than those of other races.

Overall, 24% (65/275) of participants were classified as having symptoms of major depression one month after treatment for EPL. The fraction with symptoms of major depression was higher among Black women (31%; 37/120) compared to non-Black women (18%; 28/155). Black women had odds of having major depression symptoms 2.02 times than that of non-Black women (95% confidence interval [CI], 1.15-3.55). This difference persisted after the authors adjusted for parity, baseline depression, and ACE score; the adjusted odds ratio (OR) was 2.48 (95% CI, 1.28-4.81). The proportion of women who reported high perceived stress one month after EPL treatment did not differ between Black women (8%; 10/120) and non-Black women (5%; 8/155). The unadjusted OR was 1.67 (95% CI, 0.64-4.37), and the OR adjusted for parity, baseline depression, and ACE score was 1.09 (95% CI, 0.36-3.26).

Having had at least two adverse childhood experiences (classified as having a "high" ACE score) was more common among Black women (53%; 64/120) compared to non-Black women (40%; 62/155). Black women had an odds 1.71 times that of non-Black women (95% CI, 1.06-2.77) of having a high ACE score. Specifically, having experienced parental separation or divorce and criminal behavior in the household was more commonly reported by Black women compared to non-Black women. Having a high ACE score was associated with symptoms of major depression (OR, 2.51; 95% CI, 1.41-4.46) and high perceived stress (OR, 4.53; 95% CI, 1.45-14.1) one month after treatment. After adjusting for race, baseline depression, and parity, the association between a high ACE score and major depression did not hold (adjusted OR, 1.71; 95% CI, 0.89-3.27), but high ACE score did remain associated with high perceived stress (adjusted OR, 3.90; 95% CI, 1.08-14.0).

■ COMMENTARY

EPL, defined as a nonviable intrauterine pregnancy in the first trimester, sometimes is referred to as miscarriage or spontaneous abortion. EPL is a common occurrence, often taking place without the person even being aware of the pregnancy. EPL occurs in about 31% of pregnancies overall but only in 10% of pregnancies that are clinically recognized.[1] Shorter et al found that reporting symptoms of major depression was twice as common among Black women compared to non-Black women one month after receiving treatment for EPL. The non-Black category was heterogeneous in that it included women of Hispanic ethnicity, Asian race, and undefined "others." (Note: The authors did not explain how Hispanic Black women were categorized.) It is possible that the strength of the association between Black race and depression following EPL might vary widely depending on the composition of the non-Black comparison group.

Almost one-quarter of participants in the study reported symptoms of major depression post-treatment; however, the study design is not suitable for estimating the prevalence of major depression following treatment for EPL. Because the study population was not selected to be representative of an external population (but instead consisted of women consenting to enroll in a randomized trial to test medical treatment of EPL), we cannot generalize the frequency of the outcome to a general population. The authors did not find differences by race in perceived stress one month after treatment for EPL. However, because only 18 participants reported high perceived stress, the authors likely did not have enough power to assess the adjusted association between race and perceived stress. A general rule of thumb is that 10 events are needed for each predictor variable to avoid overfitting the regression model.[2] Thus, the authors would have needed at least 40 participants with high perceived stress for this analysis. As a result, we should consider the study findings to be uninformative as to the

association between Black race and high perceived stress following EPL. However, because so few women in the study reported perceived stress, the study findings tell us that either the scale was not a valid measure for this population or perceived stress does not commonly follow EPL.

A limitation of secondary analysis of data collected for another purpose is that the choice of measures might be less than ideal and important covariates might not have been collected. As the authors acknowledged, the ACE scale may have failed to capture important adverse experiences related to childhood exposure to racism and environmental conditions. In contrast, the scale used for measuring depression symptoms (CES-D) has been validated across racial groups. Another limitation was the lack of data on pregnancy intention. Evidence suggests that women who obtain an induced abortion have less anxiety following the procedure compared to those who are unsuccessful in obtaining a desired abortion.[3,4] Similarly, it is possible that women in the present study who had an unwanted pregnancy might have experienced relief at having the decision about continuing the pregnancy taken out of their hands. By not adjusting or otherwise controlling in the analysis for women's feelings about the pregnancy, the relationship between race and mental health following EPL might be confounded.

Women might experience negative emotions after a pregnancy loss because they, or their partner or family, believe they are to blame.[4] Clinicians can hold an important role in educating patients that EPL is common and might be accompanied by unfounded feelings of guilt or shame. Although the present study found an association between Black race and symptoms of major depression, this should not be used as an argument to target women for screening for depression based on their race. Given that major depression following EPL appears to be so common, and given that depression is a treatable condition, clinicians should be prepared to screen all patients with EPL, regardless of race or ethnicity, and, if necessary, to refer for timely mental health care.[5] ■

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ABSTRACT & COMMENTARY

Ketamine Use in the Prevention of Postpartum Depression Is Premature

By Nicole Cirino, MD, CST, IF

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SYNOPSIS: A double-blinded, randomized clinical trial of 134 low-risk pregnant women in Iran undergoing scheduled cesarean deliveries was conducted to address if a single dose of ketamine during anesthesia induction has a role in the prevention of postpartum depression. The authors reported that depression scores using the Edinburgh Postnatal Depression Scale at two and four weeks after the cesarean delivery were significantly lower in the ketamine group vs. the control group.

SOURCE: Alipoor M, Loripoor M, Kazemi M, et al. The effect of ketamine on preventing postpartum depression. *J Med Life* 2021;14:87-92.

The study population for this double-blinded, randomized controlled trial included low-risk pregnant women who were candidates for scheduled cesarean delivery at Rafsanjan University of Medical Sciences in Iran. The inclusion criteria included low-risk pregnancy, ages 18 to 35 years, being a candidate for a cesarean delivery, being American Society of Anesthesiologists (ASA) class 1 or 2 (not having any underlying diseases, such as ischemic heart diseases, diabetes mellitus, or hypertension), not having any contraindication to receiving ketamine, and absence of a history of drug abuse. Subjects with post-delivery hemorrhage requiring a blood transfusion were not included in the analysis. Participants were allocated randomly to two groups to induce anesthesia. In the intervention group, 1 mg/kg to 2 mg/kg of body weight of thiopental (Nesdonal) and 0.5 mg/kg of body weight of ketamine were used, and in the control group, 3 mg/kg to 5 mg/kg of body weight of thiopental was administered.

Data were gathered over the phone using the Edinburgh Postnatal Depression Scale (EPDS) at three time points: before the cesarean delivery, at two weeks after cesarean delivery, and at four weeks after cesarean delivery. The two studied groups were similar regarding the number of past

pregnancies, having a wanted or unwanted pregnancy, education, history of depression, and satisfaction with life.

In this study, the investigators measured depression using the EPDS, a validated screening tool. They used a score of 13 or higher as a cut-off to indicate the subject is "probably suffering from depression with various intensities, and they need further investigation to diagnose depression." They used 13 as the cut-off (as opposed to a lower value used in many studies), since its reliability of 0.70 has been studied specifically among the Iranian population. Results showed that median depression scores in both arms before intervention were positive (> 13) and roughly equivalent (13.79 in the control group vs. 13.78 in the treatment group). After the infusion, the ketamine arm showed significantly lower and descending depression scores: intervention vs. control group mean (± standard deviation) score was 11.82 ± 3.41 and 14.34 ± 4.29 ($P < 0.001$), respectively, two weeks after cesarean delivery and 10.84 ± 3.48 and 13.09 ± 3.79 ($P = 0.001$), respectively, four weeks after cesarean delivery. The depression mean scores in the intervention group also were below the EPDS cut-off point at two and four weeks after the cesarean delivery (11.82 and 10.84, respectively). The depression scores remained positive for the control group at two and four weeks (14.34 and 13.09, respectively).

The authors also used Apgar scores to measure neonatal outcomes. The mean Apgar score in the first minute after delivery was 7.30 ± 0.63 in the thiopental group and 7.82 ± 0.68 in the ketamine-thiopental group. The difference between the two groups was statistically significant ($P > 0.001$), but the authors concluded this was not clinically significant. Both groups received a score of 7 and had similar categorization regarding their need for resuscitation. The Apgar score of all the neonates in the fifth minute was 10. The authors concluded that "considering the reported advantageous effects of ketamine in the conducted studies, such as analgesia, analgesia during labor after cesarean [delivery] and vaginal delivery, safety during labor and cesarean [delivery], and its relatively known effect for the treatment of major depression, if its effect on preventing postpartum depression would be confirmed through another clinical trial, it would become a multipurpose appropriate option in gynecology and midwifery departments."

■ COMMENTARY

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist and has long been considered an inexpensive, accessible anesthetic medicine used in surgeries, including some cesarean deliveries. Over the past two decades, it has proven to be a novel and effective rapid treatment for treatment-refractory major depression and suicidality in adults.[1] This study adds to the small body of literature looking specifically at the use of ketamine in postpartum depression. This is the fourth randomized controlled trial published studying ketamine infusions in women receiving scheduled cesarean deliveries. In 2019, Jia-Hui et al conducted a large randomized controlled trial on 654 Chinese women undergoing cesarean deliveries with spinal anesthesia.[2] They administered ketamine (0.5 mg/kg of body weight) intravenously 10 minutes after delivery and through a patient-controlled intravenous analgesia device (PCIA). Jia-Hui et al reported positive findings with a reduction in depressive symptoms at four to six days and six to eight weeks postpartum.[2] Gao et al also found similar results in 2015 and reported the positive effect of ketamine on preventing postpartum depression.[3] In 2017, Xu et al used a lower dose of ketamine (0.25 mg/kg of body weight) and failed to find an effect on preventing postpartum depression.[4]

One of the barriers to using ketamine to treat major depression in non-perinatal patients is the requirement for intravenous infusion and monitoring outside the traditional outpatient mental health clinical setting. The scenario of a dual use of ketamine both for anesthesia/analgesia for cesarean deliveries and for postpartum depression prevention is promising. However, this study and the existing data have significant limitations. One of the limitations of this study is the generalizability of the data. In the United States, general anesthesia typically is not administered, particularly for low-risk pregnant women. All the studies on ketamine for postpartum depression, thus far, have looked at a specific demographic: the use of ketamine perioperatively during scheduled cesarean deliveries in hospital settings outside the United States. Another limitation of this study is that it does not address concerns about the effect of ketamine on infant neurobehavioral development. Although the Apgar scores were not reduced, other neurodevelopmental measures were not conducted. Animal models have shown apoptogenic action of ketamine at both the fetal and neonatal age, and an exposure duration of five hours is sufficient to induce a significant neuroapoptosis response at either age.[5]

The lack of both obstetric history and a validated clinical mental health interview in this study are of concern as well. We do not know the indication for cesarean delivery in the low-risk pregnant subjects nor important aspects of the mental health history obtained from a formal clinical interview (including diagnosis, active or recent treatment, and objective improvement). Although self-reported scores can be helpful, this is not the standard of care when evaluating a new pharmacologic intervention. Furthermore, the self-reported scores were elicited over the phone. Also, this study appears to capture a population with a high prevalence of self-reported active depression or other mental health conditions before treatment, since the average EPDS score at delivery before the infusion was > 13. However, without a proper assessment by a mental health professional, we do not know the current psychiatric condition of the subject, the current treatments being used, the other treatments offered in the postpartum period, or if clinical improvement has indeed occurred.

Clearly, more extensive clinical trials with a multidisciplinary team (pediatrics, obstetrician gynecologists, psychiatrists, anesthesiologists) still are needed in this area. Since ketamine is inexpensive and available in clinical settings in many countries where women are giving birth, this is an area that should be explored further. Remaining clinical questions

regarding the use of ketamine for postpartum depression include the timing and dose of ketamine (prior to or following delivery), the effect ketamine has on the neonate (including in lactation), the length of treatment effect, and if, indeed, ketamine is effective for the treatment or prevention of postpartum depression (and, if so, in which population of women at risk). It may be feasible that one day women who are candidates for a cesarean delivery and are at risk for postpartum depression may benefit from the protective role of a single ketamine infusion, but for now, both safety and efficacy need to be established first. ■

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ABSTRACT & COMMENTARY

Evaluation and Treatment of Women with Symptoms of Recurrent UTIs

By Chiara Ghetti, MD

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SYNOPSIS: Only 33% of women presenting to a urogynecology practice with symptoms of recurrent urinary tract infections met diagnostic criteria for recurrent urinary tract infections. The use of preventive strategies can be improved.

SOURCE: Dieter AA, Mueller MG, Andy UU, et al. Baseline characteristics, evaluation, and management of women with complaints of recurrent urinary tract infections. *Female Pelvic Med Reconstr Surg* 2021;27:275-280.

The main objective of this study was to characterize women who present to tertiary urogynecology care for symptoms of recurrent urinary tract infections (rUTIs) and to describe their evaluation and treatment. This study was a retrospective cohort study performed at five academic institutions. Subjects included new patients seen over a one-year period for referral, complaint, or diagnosis of recurrent or frequent UTIs. Patients were followed for one year from their initial visit. Exclusion criteria included: age younger than 18 years, any chronic catheter use, immunosuppression as the result of prior organ transplant, prior urinary tract reconstruction, and active malignancy or treatment for malignancy within last two years.

Culture-proven rUTIs were defined as three culture-proven UTIs (> 10,000 colony forming units [CFU] for catheterized specimen and > 100,000 CFU for voided specimens) in one year or two or more in six months. Outcomes included UTI occurrence as well as medical, surgical, and urogynecologic history, including history of lower urinary tract symptoms, urinary incontinence treatment, UTI evaluation, and treatments, including prevention. Prevention therapies included daily prophylactic antibiotics, post-coital antibiotics, vaginal estrogen, cranberry products, probiotics, D-mannose, methenamine, or other. Data also were recorded on advanced testing, including cystoscopy or radiologic imaging, as well as any change in clinical care resulting from testing. Of the 600 women included in the study, 193 (33%) met criteria for rUTI at the time of their initial visit and an additional 30 women (5%) met criteria at a follow-up visit. Women who met criteria for rUTIs were older (mean age 65 years, standard deviation [SD] 17 years) compared to women who did not meet criteria (mean age 56 years, SD 18 years). Women who did not meet criteria also were more likely to have had prior hysterectomy, to be postmenopausal, and to have a history of pelvic irradiation and gynecologic cancer and they were less likely to be sexually active than women who did not meet the criteria.

Urinary incontinence symptoms, as well as urinary symptoms, were similar in the two groups of women. The most commonly reported urinary symptoms were frequency, dysuria, and urgency. Women with culture-proven rUTI were significantly more likely to have dysuria compared to women who did not meet the criteria (59% vs. 40%, $P < 0.001$). More than one-third of women (234, 39%) underwent advanced testing. Clinical care was altered in only 21 (9%) of these women following testing. At the time of the first visit, one-quarter of women were using a preventive strategy, with approximately an additional 10% using more than one preventive strategy. Following the initial consultation, more than 40% of women were using one strategy and an additional 25% were using two or more strategies. The use of vaginal estrogen increased from 14% to 47% following the initial consultation. Forty-four percent of the women in the study were treated for a UTI in the

follow-up period. Of these, the majority of cultures (57%) were positive for *Escherichia coli* and 14% were positive for *Klebsiella*.

■ COMMENTARY

UTIs are very common, affecting 50% to 80% of women, and UTI symptoms are very bothersome. Studies have shown that having one infection may predispose up to 44% of women to UTI recurrence.[1,2] Women ages 18 to 34 years and ages 55 to 66 years appear to have the highest rates of rUTIs.[3] Guidelines for the evaluation and treatment of rUTI vary; however, UTIs are a frequent indication for referral to urogynecology subspecialists.[4]

Lower urinary tract symptoms associated with UTI include urinary frequency, urgency, dysuria, and suprapubic pain. However, other genitourinary symptoms can coexist and mistakenly can be attributed to a UTI and treated empirically. This study found that only 33% of women presenting with frequent UTI diagnosis or referral were, in fact, found to meet the clinical diagnosis of rUTI. Women who met clinical diagnosis were more likely to have dysuria. This finding supports prior work demonstrating that the presence of dysuria symptoms increases the likelihood of UTI diagnosis. Performing urine cultures for symptomatic patients prior to empiric treatment and avoiding routine urine testing in asymptomatic patients can decrease the treatment of asymptomatic bacteria. In addition, evaluating women for other coexisting conditions, such as urinary incontinence, genitourinary atrophy, and pelvic floor myofascial pain, which often contribute to overlapping symptoms, can help us better tease apart UTI-like symptoms from true UTIs.

Dieter et al found that a large portion of UTIs were caused by *E. coli* and more than half of UTIs were treated with nitrofurantoin. This is consistent with American Urogynecologic Society (AUGS) guidelines, which recommend the use of nitrofurantoin, fosfomycin, and trimethoprim-sulfamethoxazole as first-line agents when possible.[4] Guidelines for nitrofurantoin have changed, and it should be avoided in women with a creatinine clearance (CrCl) < 30 mL/min. Fluroquinolones are not considered first-line agents for the treatment for acute UTI. Fluroquinolones have high rates of adverse events and should be considered second-line agents alongside beta-lactam antibiotics. Vaginal estrogen therapy (VET) has been shown to prevent UTIs in postmenopausal women and is recommended by AUGS and American Urological Association/Canadian Urological Association/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction guidelines.[4,5] This study found that only 14% of women referred for rUTI symptoms had been prescribed VET prior to consultation, increasing to 47% after consultation. VET is a safe and effective therapy and can be initiated easily by primary providers and referring physicians alike as first-line prevention of rUTI in post-menopausal women. The findings of this study also highlight various society recommendations for judicious use of advanced imaging.[4,5] Although Dieter et al found that clinical care rarely was altered by advanced testing, referral for persistent UTI symptoms that do not respond to first-line measures is warranted. As OB/GYN providers, we can play an important role in the care of women with rUTIs and UTI symptoms. Although rUTIs may seem a challenging diagnosis to tackle initially, following a basic paradigm that involves a thorough assessment of symptoms to aid in careful diagnosis, thoughtful use of first-line antibiotic regimens, and implementation of initial prevention strategies, VET in particular, can improve our patients' urinary health dramatically. ■

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ABSTRACT & COMMENTARY

LMWH vs. UFH in Pregnant Women Undergoing Anticoagulation

By Ahizechukwu C. Eke, MD, PhD, MPH

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SYNOPSIS: In this retrospective cohort study of pregnant women treated with low-molecular-weight heparin (LMWH) alone compared to those switched to unfractionated heparin (UFH) in the peripartum period, the outcomes were similar in both groups.

SOURCE: Enakpene CA, Pontarelli KN, Della Torre M. Comparison of continuation of low-molecular-weight heparin versus switching to unfractionated heparin in the peripartum. *Am J Perinatol* 2020;37:304-312.

Despite the administration of prophylactic and therapeutic heparin to pregnant women with a current or past history of venous thromboembolism (VTE), VTE remains a major cause of maternal morbidity and mortality.[1] Although low molecular-weight-heparin (LMWH) has replaced the use of unfractionated heparin (UFH) during pregnancy to a great extent (because of its lower complication rate, predictable dosing, ease of administration, and greater reduction in thrombus size compared to UFH), a common practice is to switch pregnant women treated with LMWH to UFH approximately three to four weeks prior to the expected date of delivery (around 36 weeks of gestation for a planned term delivery), and continue UFH until after delivery.[2] This practice stems from the easy reversibility and short half-life of UFH and the need to balance efficient anticoagulation during pregnancy with the woman's desire for neuraxial analgesia in the event of spontaneous labor within 12 to 24 hours of administration of LMWH. However, some studies question the practice of switching LMWH to UFH during pregnancy as being inefficient.[3] Enakpene and colleagues designed this study to compare the continuation of LMWH to switching to UFH in the peripartum period.[3] This study was a retrospective cohort study conducted at the University of Illinois at Chicago Hospital and Health Sciences System (UI Health). Inclusion criteria were pregnant women who received prenatal care, were managed with LMWH, were switched to UFH during pregnancy, and delivered at ≥ 24 weeks of gestation at UI Health between 2005 and 2016.[3] Women were excluded if they delivered outside UI Health or if they delivered prior to 24 weeks of gestation. The outcomes of interest were peripartum anesthesia requirements based on the anticoagulant used, and significant peripartum bleeding complications (postpartum hemorrhage > 1,000 mL and severe bleeding complications resulting in hemoperitoneum). Demographics and maternal outcomes were analyzed using standard statistical tests.

From January 2005 to December 2016, 189 pregnant women who received LMWH anticoagulation met the inclusion criteria. Twenty-seven percent (51 women) were switched to UFH at some point during pregnancy, while 73% (138 women) continued LMWH until the time of delivery. The baseline characteristics were similar in both groups. However, women who delivered at < 34 weeks of gestation were five times more likely to be switched to UFH in the peripartum period ($P < 0.004$), with 82% (42 women) on prophylactic LMWH dosing and 18% (nine women) on therapeutic dosing.[3] The type of anticoagulation used (prophylactic vs. therapeutic) did not affect the kind of pain relief option women received (regional vs. general anesthesia). There were no statistically significant differences in peripartum anesthesia requirement and significant peripartum bleeding between women who continued LMWH and those who switched to UFH (82.4% vs. 79.7%, respectively; relative risk [RR], 1.20; 95% confidence interval [CI], 0.52-2.73; $P = 0.84$).

Composite bleeding complications were threefold higher in women who switched from LMWH to UFH compared to those who continued LMWH, and this was statistically significant (12% vs. 14%, respectively; RR, 2.7; 95% CI, 1.16, 6.40; $P = 0.030$). Postpartum hemorrhage (bleeding at the time of delivery > 1,000 mL) was similar in the two groups (6% vs. 10%; RR, 0.58; 95% CI, 0.17, 1.94; $P = 0.38$). In addition, the proportion of women who had re-exploration as the result of bleeding complications and hemoperitoneum after their primary surgery was similar in both groups (2.0% vs. 2.2%, respectively; RR, 0.90; 95% CI, 0.10, 8.48; $P = 0.930$). Among women who received anticoagulation < 24 hours prior to delivery, there were no statistically significant differences between the two groups after controlling for potential confounders (2.0% vs. 0.7%, respectively; RR, 0.33; 95% CI, 0.07, 1.65; $P = 1.000$). Similarly, among women who received their last dose of anticoagulant > 24 hours prior to delivery, multivariate analysis demonstrated there was no statistically significant difference between the groups (2.0% vs. 3.0%, respectively; RR, 0.5; 95% CI, 0.13, 2.0; $P = 0.33$).

■ COMMENTARY

The duration and type of anticoagulation (prophylactic vs. therapeutic) usually is dictated by the indication for anticoagulation. Therapeutic anticoagulation usually is indicated for current VTE or a history of high-risk thrombophilia. Generally, anticoagulation is commenced during pregnancy and continued until about six weeks postpartum (or longer, depending on risk factors and indication for anticoagulation), since the beneficial effects of anticoagulation in these settings outweigh its potential complications. The initial dosing of UFH is weight-based and typically is administered twice daily through the subcutaneous route. In this study by Enakpene and colleagues, the type of anticoagulation (prophylactic vs. therapeutic) did not affect the kind of anesthesia women received. Although composite bleeding complications were statistically significant between the two groups, postpartum hemorrhage, hemoperitoneum after primary surgery, and the proportion of women who had re-exploration as a result of bleeding complications were not different between both groups. Thus, based on the findings from this study, the authors at UI Health counsel their patients on the risks, benefits, and alternatives of continuing LMWH until delivery vs. switching to UFH, and patients make an informed decision. If patients choose to continue LMWH until delivery, they are counseled to hold their next LMWH dose until they are evaluated by their physician if they suspect they are in labor, have rupture of fetal membranes, and/or have vaginal bleeding.[3]

Heparin is considered safe during pregnancy since it does not cross the placenta.[4] Despite its inability to cross the placenta, monitoring of plasma/serum levels of therapeutic LMWH or UFH is critical, since the physiologic changes during pregnancy can affect LMWH/UFH concentrations. There are differences in how LMWH and UFH are monitored. UFH levels are monitored with activated partial thromboplastin time (aPTT) levels (goal 1.5 to 2.5 during pregnancy), while women on therapeutic LMWH are monitored with anti-Xa levels (with values of 0.6 to 1.2 being the therapeutic range). In addition, women treated with UFH usually require monitoring of platelet counts

during the first two to three weeks of therapy because of the small potential for heparin-induced thrombocytopenia (HIT), but the risk of HIT with LMWH is lower. Finally, the advantages of using UFH include the ease of rapid reversal with protamine sulfate, as well as lower cost when compared to LMWH. The potential risks of UFH include unpredictable pharmacodynamics (dose-response), severe bleeding complications, and the risk of HIT, which are all worse with UFH compared to LMWH. Despite these potential risks of UFH, most practitioners continue to switch pregnant women from LMWH to UFH in the third trimester because of the advantage of easy reversal of UFH with protamine sulfate and the short half-life of UFH compared to LMWH in the event of imminent delivery at term.

In conclusion, clinicians can consider continuing to treat pregnant women with both prophylactic and therapeutic doses of LMWH until the time of delivery after appropriate discussions of risks, benefits, and alternatives. However, the American College of Obstetricians and Gynecologists and other professional societies continue to recommend switching from LMWH to UFH, at doses of 10,000 international units of UFH, administered subcutaneously every 12 hours in the third trimester unless the aPTT is elevated, irrespective of indication (prophylactic or therapeutic use).[5] ■

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CME/CE QUESTIONS

1. **Shorter et al found which of the following associations between race and mental health outcomes following early pregnancy loss?**
   a. Black race was associated with higher frequency of symptoms of major depression.
   b. Black race was associated with higher frequency of perceived stress.
   c. Black race was associated with higher frequency of symptoms of major depression and perceived stress.
   d. Black race was associated with lower frequency of symptoms of major depression and perceived stress.

2. **The study by Alipoor et al claims that ketamine may prevent postpartum depression in which of the following scenarios?**
   a. Intravenous infusion in pregnant women prior to elective cesarean delivery
   b. Intranasal infusion of women with postpartum depression at two to four weeks postpartum
   c. Intravenous infusion in peripartum women immediately after elective cesarean delivery
   d. Intranasal infusion of pregnant women with a history of depression prior to vaginal delivery

3. **Which of the following statements regarding heparin in pregnant women is *false*?**
   a. Unfractionated heparin (UFH) levels are followed with activated partial thromboplastin time (aPTT) levels (with goal of 1.5 to 2.5 during pregnancy).
   b. Women treated with therapeutic low-molecular-weight heparin are monitored with anti-Xa levels (with values of 0.6 to 1.2 being the therapeutic range).
   c. Women treated with UFH are monitored with anti-Xa levels (with values of 0.6 to 1.2 being the therapeutic range).
   d. Patients treated with UFH usually require monitoring of platelet counts during the first two to three weeks of therapy because of the small possibility of heparin-induced thrombocytopenia.

4. **Based on the study by Dieter et al, which of the following statements is correct?**
   a. Most women with symptoms of recurrent urinary tract infections (UTIs) have true recurrent UTIs.
   b. Most women with symptoms of recurrent UTIs can benefit from preventive strategies, including vaginal estrogen.
   c. For most women with symptoms of recurrent UTIs, vaginal estrogen is not a useful prevention strategy.
   d. Most women with symptoms of recurrent UTIs should be evaluated with advanced imaging.