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ABSTRACT & COMMENTARY

Tranexamic Acid for the Prevention of Obstetric Hemorrhage

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SYNOPSIS: In this prospective, cohort, pharmacokinetic-pharmacodynamic (PKPD) dose-finding study by Ahmadzia and colleagues, 30 pregnant women (10 women in each study arm) received 5 mg/kg, 10 mg/kg, or 15 mg/kg doses of tranexamic acid for the prevention of postpartum hemorrhage. Advanced PKPD modeling demonstrated that 600 mg of tranexamic acid was the optimal dose to use in the prevention of postpartum hemorrhage.

SOURCE: Ahmadzia HK, Luban NL, Li S, et al. Optimal use of intravenous tranexamic acid for hemorrhage prevention in pregnant women. *Am J Obstet Gynecol* 2020; Nov 26. doi: 10.1016/j.ajog.2020.11.035. [Online ahead of print].

Postpartum hemorrhage is a critical public health problem and accounts for a major cause of maternal morbidity and mortality in developing and developed countries.[1] Although the majority (70% to 80%) of causes for postpartum hemorrhage are related to uterine atony, a smaller percentage are the result of abnormalities in blood coagulation.[2] In uncomplicated pregnancies, the platelet count normally decreases consistently throughout gestation, with the largest physiological decrease occurring at term.[3] However, several other clotting factors in the intrinsic and extrinsic pathways of the clotting cascade are increased 10- to 1,000-fold during pregnancy. Hence, pregnancy is said to be a "hypercoagulable state."[4] Thus, control of normal postpartum blood loss is dependent on uterine contractions and activation of the coagulation cascade.

Tranexamic acid is an anti-plasmin synthetic analog of the amino-acid lysine that is valuable for the management of postpartum hemorrhage through its action on the coagulation cascade.[5] When given parenterally, tranexamic acid inhibits fibrinolysis by preventing plasminogen activation to plasmin, thereby inhibiting the formation of fibrin degradation products (FDPs). Tranexamic acid for the treatment of postpartum hemorrhage received

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global attention after the publication of the World Maternal Anti-fibrinolytic (WOMAN) trial. The trial recruited more than 20,000 women with a clinical diagnosis of postpartum hemorrhage after a vaginal birth or cesarean delivery to evaluate the effects of tranexamic acid on treatment of postpartum hemorrhage, maternal death, and surgical interventions for postpartum hemorrhage.[6] Data from the WOMAN trial demonstrated that tranexamic acid reduced maternal mortality from postpartum hemorrhage by about one-third (31%), with no evidence of serious adverse effects.[6] Although 1 g was used in the WOMAN trial as well as in many other tranexamic acid studies, there are limited data on the optimal dose of tranexamic acid to use in postpartum hemorrhage and whether dosing recommendations need to be adjusted based on a patient's clinical characteristics, such as renal function and body mass index (BMI). This study by Ahmadzia et al aimed to determine if lower doses of tranexamic acid can prevent postpartum hemorrhage.[7]

This study was an open-label, pharmacokinetic/pharmacodynamic (PKPD) dose-finding study, conducted primarily at George Washington University. Inclusion criteria were pregnant women with a singleton gestation, 18 to 50 years of age, who were scheduled for cesarean delivery and at ≥ 34 weeks of gestation, with serum creatinine of < 0.9 mg/dL. Women were excluded if they had a history of or active thrombotic or thromboembolic disease, inherited thrombophilia or preexisting conditions that predisposed them to thromboembolic events, a subarachnoid hemorrhage, an acquired defective color vision, history of seizure disorder, hypersensitivity to tranexamic acid or anti-fibrinolytic therapy, or a history of liver dysfunction.[7]

The primary outcome was a combination of both pharmacokinetic and pharmacodynamic parameters. The pharmacokinetic primary outcome target plasma concentration was > 10 ng/mL of tranexamic acid on high-performance liquid chromatography mass spectrometry (HPLC/MS), while the primary pharmacodynamic outcome target was pharmacodynamic activity < 17% maximum lysis (ML) on modified rotational thromboelastometry (ROTEM). Secondary outcomes included safety and clinical endpoints.[7]

The authors enrolled 30 women into three different study arms (based on doses of tranexamic acid administered): 5 mg/kg, 10 mg/kg, or 15 mg/kg, with a sample size of 10 women in each arm. The intravenous tranexamic acid dose was administered only once at the time of umbilical cord clamping, followed by serial sparse pharmacokinetic blood sampling at pre-dose, 10 minutes, 30-60 minutes, one to three hours, four to six hours, seven to eight hours, and 24 hours post-dose. Pharmacodynamic measurements (clotting and fibrinolytic activity) were done with ROTEM using tissue plasminogen activator (tPA). Advanced PKPD modeling was used to determine the optimal dose of tranexamic acid to use in postpartum hemorrhage prevention.

The average maternal age was 33 years (23-41 years) and the mean maternal weight was 87 kg (59.5-147.5 kg). The participants were from a diverse ethnic background: 11 Caucasians (37%), 16 Black/African Americans (53%), one Hispanic (3%), one Asian (3%), and one other participant whose ethnicity was classified as "other." The mean hematocrit concentration prior to administration of tranexamic acid was 34% (27.8% to 41.9%), and the mean platelet count was 210,000 (93,000-408,000). All participants achieved the pharmacokinetic target of > 10 ng/mL of tranexamic acid in plasma, and the concentrations were sustained for at least 45 minutes after infusion of tranexamic acid in all three groups, with an average time to achieve pharmacokinetic threshold of three minutes (range, 1.8-6.6 minutes). The average ± standard deviation (SD) of doses for tranexamic acid administered to participants was 447.7 mg (87.1 mg), 831.8 mg (158.8 mg), and 1,000 mg (0 mg) for arms 1, 2, and 3, respectively. Advanced PKPD modeling demonstrated that 600 mg was the optimal dose of tranexamic acid to use in the prevention of postpartum hemorrhage. The 600 mg dose achieved the > 10 ng/mL target in 97% of the participants over a 60-minute time interval. Furthermore, the ML was maintained below 17% for 30 minutes in 87% of the patients at the 600 mg

dose. The pharmacokinetics of tranexamic acid were independent of body weight, maternal age, serum creatinine, and creatinine clearance.

■ COMMENTARY

Tranexamic acid has been studied extensively in trauma and general surgery (CRASH-2 randomized clinical trial).[8] It began to be used extensively in obstetrics for the treatment of postpartum hemorrhage after a vaginal or cesarean delivery because of the impressive data from the WOMAN trial. Although it has been used for the treatment of postpartum hemorrhage, its use as a prophylactic therapy has been studied in two major randomized clinical trials in obstetrics: the Tranexamic Acid for the Prevention of Blood Loss after Vaginal Delivery trial (TRAAP-1) and Tranexamic Acid for the Prevention of Blood Loss after Cesarean Delivery trial (TRAAP-2).[9,10] In 2018, the TRAAP-1 multicenter, double-blind, randomized, controlled trial evaluated the effect of 1 g of tranexamic acid after vaginal delivery for the prevention of postpartum hemorrhage. Women who were ≥ 35 weeks of gestation and with a singleton live fetus and who were in labor after a scheduled vaginal delivery were randomized to receive 1 g of intravenous tranexamic acid or placebo in addition to prophylactic oxytocin within two minutes of delivery.

TRAAP-1 demonstrated that tranexamic acid was associated with a lower risk of postpartum hemorrhage (defined by blood loss ≥ 500 mL) than placebo, without increased risk of severe adverse events within three months after delivery. In 2021, the TRAAP-2 multicenter, double-blind, randomized, controlled trial similarly evaluated the influence of 1 g of tranexamic acid vs. placebo before cesarean delivery at ≥ 35 weeks of gestation for the prevention of postpartum hemorrhage. The primary outcome was blood loss > 1,000 mL or a red blood cell transfusion by day 2 after delivery. TRAAP-2 demonstrated that women undergoing cesarean delivery who received prophylactic uterotonics and tranexamic acid had a significantly lower rate of postpartum hemorrhage and blood transfusions than placebo, but they did not have reduced hemorrhage-related secondary clinical outcomes. Although these two randomized clinical trials demonstrate some efficacy of tranexamic acid in the prevention of postpartum hemorrhage in obstetrics, tranexamic acid still is not currently used widely prophylactically in obstetrics. It also is important to note that tranexamic acid has been shown to be cost-effective.[11]

In several randomized clinical trials, researchers have studied the efficacy of tranexamic acid for the prevention and treatment of hemorrhage when used as fixed doses (1 g) or as body-weight adjusted doses.[9,10] Because of the physiologic changes during pregnancy, and different maternal body mass indexes of pregnant women who experience postpartum hemorrhage, it is important to determine the lowest effective dose of tranexamic acid to use in both prevention and treatment of postpartum hemorrhage to avoid sub-therapeutic or supra-therapeutic dosing (with the potential for multiple adverse effects). The study by Ahmadzia et al demonstrated that the 600 mg dose (rather than 1 g dose) of tranexamic acid is optimal in preventing postpartum hemorrhage.

Although Ahmadzia and colleagues have recommended 600 mg, all the preventive and therapeutic trials in obstetrics (WOMAN, TRAAP-1, and TRAAP-2 trials) used the 1 g intravenous dose. Therefore, until data from ongoing trials are completed and available, clinicians should continue to use the 1 g intravenous dose of tranexamic acid for treatment of postpartum hemorrhage. As recommended by the American College of Obstetricians and Gynecologists, if bleeding continues after 30 minutes of tranexamic acid administration, or if bleeding stops and restarts within 24 hours after the first dose, a second intravenous dose of 1 g of tranexamic acid could be given.[2] ■

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ABSTRACT & COMMENTARY

Does Maternal BMI Influence the Success of Trial of Labor After Cesarean?

By Jeanine Mikek, MSN, RN, RNC-NIC, CEN

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SYNOPSIS: In this retrospective cohort study between May 2007 and April 2016, women undergoing a trial of labor after cesarean (TOLAC) were analyzed to determine if pre-pregnancy or delivery obesity status made an impact on TOLAC success. Overall, maternal body mass index did not have a significant effect on TOLAC success rates.

SOURCE: Mei JY, Havard AL, Mularz AJ, et al. Impact of obesity class on trial of labor after cesarean success: Does pre-pregnancy or at-delivery obesity status matter? *J Perinatol* 2019;39:1042-1049.

Cesarean births have become more prevalent in recent years and now account for nearly one-third of deliveries in the United States.[1] Although not all women meet the criteria for an optimal trial of labor, choosing a vaginal birth after cesarean (VBAC) has gained attention and can lead to fewer complications. Maternal obesity as a whole can lead to several complications for both vaginal and cesarean deliveries. Although most studies in the past focus on pre-pregnancy weight, this study analyzed maternal weight at the time of delivery as well.

The authors analyzed delivery data from UCLA Medical Center between May 2007 and April 2016 to find 657 women who attempted trial of labor after cesarean (TOLAC) and had less than two prior cesarean deliveries. Six hundred fourteen women met the inclusion criteria and were categorized into four groups based on their body mass index (BMI) pre-pregnancy and at the time of delivery. In this study, 22.8% of the studied women were considered obese pre-pregnancy and 50.7% were obese at the time of delivery. Chi-squared analyses and Fisher's tests were used to calculate statistically significant *P* values set at < 0.05. The overall TOLAC success rate was 72.3% and the average BMI at the time of delivery was 30.7 (class I obesity).

A higher obesity class, both pre-pregnancy and at the time of delivery, was found to be correlated with elevated blood pressure by the time of delivery ($P < 0.001$). Despite this complication, VBAC success rates were not affected greatly by maternal BMI, either pre-pregnancy or at delivery (rates of 71.4% to 81.8% prior to pregnancy with $P = 0.91$; rates of 65.9% to 74.4% at time of delivery with $P = 0.75$). Maternal morbidity markers and perinatal outcomes, including indications for repeat cesarean deliveries; appearance, pulse, grimace, activity, and respiration (APGAR) scores; uterine rupture; and postpartum hemorrhage also were assessed. None of these measures were greatly affected by maternal BMI at any point, since *P* values ranged from 0.151-0.970.

■ COMMENTARY

Although this study encompassed nine years of data, it was only performed at a single center, which negatively affects the ability to generalize the results because of demographic and socioeconomic variances throughout the country. Despite the fact that more than one-quarter of the women who were not obese pre-pregnancy met obesity classification at the time of delivery, there still was low representation of women who attempted a TOLAC in class II and class III (13.7% and 5.5%, respectively). There are individual variances in every labor and delivery that may not be controlled, but TOLAC success rates may be more accurate if closer to an equal amount of women were categorized in each of the four BMI classes at the time of delivery.

Obesity should not be a deciding factor when discussing the potential of a TOLAC vs. a repeat cesarean, since it has no significant difference in TOLAC success rates. TOLAC still is a safer alternative to cesarean delivery for obese women, especially when considering the additional risks of surgical complications, wound infections, and venous thromboembolisms. Women should be offered the same delivery options regardless of their BMI. However, providers should emphasize individualized care and the potential complications for the mother and fetus in the antenatal period as well as at the time of delivery. For example, gestational weight gain above recommendations made by the Institute of Medicine can lead to higher rates of cesarean birth, gestational hypertension, infant macrosomia, and a risk of shoulder dystocia.[2] Measures to reduce BMI or to achieve healthy lifestyle habits should be discussed at appointments prior to confirmation of a pregnancy if possible. This recommendation may be complicated by individual barriers that would limit annual provider visits, including but not limited to finances, transportation, and scheduling. However, preventive care has more patient and financial benefits compared to reactive care for an acute or chronic issue. ■

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ABSTRACT & COMMENTARY

Anticholinergic Use for Three Months or More Increases Dementia Risk

By Chiara Ghetti, MD

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SYNOPSIS: There is a significant increase in dementia risk associated with the use of anticholinergic medications for three months or longer.

SOURCE: Dmochowski RR, Thai S, Iglay K, et al. Increased risk of incident dementia following use of anticholinergic agents: A systematic literature review and meta-analysis. *Neurourol Urodyn* 2021;40:28-37.

The main objective of this study was to determine the effect of three or more months of anticholinergic use and, specifically, medications used to treat overactive bladder (OAB) on the risk of dementia, mild cognitive impairment, and change in cognitive function. This was a systematic literature review and meta-analysis performed according to PRISMA guidelines and registered in the PROSPERO database. PubMed, Embase, and Cochrane Library databases were searched for English-language articles published before August 2019. Studies eligible for this review included full-text articles of primary publications of randomized controlled trials (RCTs), and cohort and case-control studies. Studies were reviewed by two reviewers and eligible if studies examined the effect of anticholinergic drug use for ≥ 3 months on dementia or cognitive function in adult patients and contained an adequate description of the methods used. Studies were excluded if they assessed only serum anticholinergic activity, used a combined scale of drug burden that did not specify the risk for exposure to anticholinergic agents only, or examined acute outcomes, such as delirium or acute cognitive dysfunction. Studies assessing anticholinergics used to treat OAB were considered for a separate meta-analysis.

Of the initial 2,092 articles identified on search, 1,990 were screened based on title and abstract. Of these, 316 were assessed by full text and 21 met inclusion criteria and underwent qualitative analysis. An increased cognitive impairment risk was reported in the studies evaluated using a variety of endpoints (incident dementia, Alzheimer's disease, mild cognitive impairment, and change in cognitive function). Only the incident dementia category had sufficient studies (six of nine studies) to perform a meta-analysis. These comprised three case-control and three cohort studies and collectively included data from 645,865 patients. The six studies used varying anticholinergic exposure and dementia definitions. The authors reported an average relative risk for incident dementia using these six studies of 1.46 (95% confidence interval, 1.17-1.81; 95% prediction interval, 0.70-3.04) and ranged from 1.05 to 2.63. Clinically, this translates into an average increased risk of dementia of 46% with use of anticholinergics compared to nonuse. Three of these studies reported anticholinergic dosing data; using these studies, any anticholinergic exposure was associated with increased incident dementia when compared to no anticholinergic exposure. Two studies specifically examined the role OAB medications had on dementia. In these two studies, the risk of dementia from OAB medications appeared higher than the overall risk across all anticholinergic agents for most levels of exposure (adjusted odds ratios ranged from 1.21 to 1.65).

■ COMMENTARY

Urinary incontinence is defined as the involuntary loss of urine and it affects more than 50% of women.[1,2] Despite this being a very common condition that affects women, urinary incontinence remains frequently undertreated. Urgency incontinence, or OAB, is associated with a strong urge to void that is difficult to defer.[1] Although the evaluation of urinary incontinence is similar for all types, treatment options vary by diagnosis.

Guidelines for the evaluation of urinary incontinence consistently recommend characterization of symptoms, history, physical exam, and testing for urinary tract infection as well as an assessment of post-void residual, but guidelines vary in specific details and in testing recommendations.[1] Treatment

for urge incontinence should begin with behavioral and lifestyle modification, and often simple, conservative measures can improve symptoms dramatically. Behavioral and lifestyle modifications include fluid management; limiting bladder irritant consumption (diet beverages, in particular), carbonated beverages, and caffeine; addressing and managing constipation, smoking cessation, and weight loss; and treating vaginal atrophy. In addition, pelvic floor physical therapy and pelvic floor exercises have been shown to be effective strategies in the treatment of urge incontinence.[3] Pharmacotherapy can be used concomitantly with these measures or used as the next step in women in whom conservative options have not fully resolved symptoms. Other treatments for urge incontinence include intradetrusor botulinum toxin injections, percutaneous tibial nerve stimulation, and sacral neuromodulation. It should be noted that some insurance plans require a trial of pharmacotherapy prior to authorizing some of these additional procedural treatments.

Antimuscarinics are the most commonly prescribed medications to treat urge urinary incontinence. These include darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, and trospium. Modest improvements have been seen in pharmacotherapy when compared to placebo.[4] Combined therapy with behavior modification has been shown to be more successful than medication alone.[5] Antimuscarinic agents are contraindicated in patients with untreated narrow angle glaucoma and supraventricular tachycardia. Nearly 50% of patients taking these medications have side effects; most commonly, these medications have peripheral anticholinergic effects, including dry mouth and constipation. As a result of these side effects, discontinuation is common. It is important to keep in mind that these medications have additive side effects with other medications, and patients often are on other medications with significant anticholinergic properties.

Importantly, the study by Dmochowski et al further adds to the growing literature linking anticholinergic drug use with the risk of dementia. Cognitive impairment is a significant public health issue. One in nine U.S. adults experience symptomatic cognitive decline.[6] There are an estimated 6 million people living with dementia in the United States today, and this number is projected to increase to 14 million by 2060.[7] Worldwide, more than 50 million people have dementia and 10 million new cases are added annually.[8] One of the studies included in the systematic review noted earlier is a nested case control study from the United Kingdom by Coupland et al.[9] This study included 58,769 patients with a diagnosis of dementia and 225,574 matched controls. The authors found a significant dementia risk in patients with exposure to several types of strong anticholinergic drugs, including antimuscarinics. They found 50% increased odds of dementia with an exposure equivalent to three years of daily use of a sole strong anticholinergic medication and estimated that 10% of dementias could be attributable to this exposure.

As obstetrician gynecologists and as urogynecologists, we must strongly consider these associations prior to prescribing antimuscarinics. Although we may be most familiar with antimuscarinic bladder medications, frequently our patients come to us taking other anticholinergic medications, such as antiarrhythmic medications, antihistamines, antidepressants, antiepileptics, antiemetics, antiparkinson agents, and antipsychotics. Alongside becoming more familiar with the broader class of anticholinergic medications, screening women for signs of cognitive changes and assessing their family history of dementia prior to prescribing antimuscarinics may aid us in better understanding the risks and benefits of pharmacologic therapy for our patients. We should strive to maximize nonpharmacologic management of urge incontinence with behavioral and lifestyle modification and then refer for nonpharmacologic treatment with intradetrusor botulinum toxin injections or neuromodulation. As women's health providers, we are in the unique position to affect the long-term well-being of women and can help educate patients and colleagues as we work toward deprescribing antimuscarinic medications for the management of urge incontinence. ■

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ABSTRACT & COMMENTARY

Is a Vacuum-Induced Device Effective for Control of Postpartum Hemorrhage?

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SYNOPSIS: In this multicenter study across 12 centers in the United States, a vacuum-induced intrauterine device successfully treated 94% of participants who experienced a postpartum hemorrhage with a median time of three minutes to control of bleeding.

SOURCE: D'Alton ME, Rood KM, Smid MC, et al. Intrauterine vacuum-induced hemorrhage-control device for rapid treatment of postpartum hemorrhage. *Obstet Gynecol* 2020;136:882-891.

Postpartum hemorrhage is a significant cause of maternal morbidity and a majority of cases may be preventable.[1] The use of uterotonic agents or intrauterine devices such as the Bakri balloon, and the administration of blood products are in standard protocols for most obstetric facilities and are recommended by the American College of Obstetricians and Gynecologists and the California Maternal Quality Care Collaborative.[2,3] Although balloon tamponade devices have demonstrated efficacy in controlling hemorrhage in more than 80% of atony-related cases (95% confidence interval [CI], 84% to 90%), the mechanism of outward pressure seems counterintuitive if the end goal is uterine compression and contraction.[4] This study aimed to evaluate the clinical effectiveness of a modern intrauterine device that relies on vacuum suction in contrast to the balloon tamponade method.

The vacuum-induced device is comprised of a silicone loop with 20 vacuum pores that is placed into the uterine cavity after a manual sweep to check for retained placental products. Upon placement, 60 mL to 120 mL of sterile fluid fills the cervical seal to prevent displacement, and the device is hooked to wall suction at 80 mmHG to 100 mmHg to contract the uterine myometrium. The collection of expelled or vacuumed blood can be measured accurately in the suction canister. The device remains in place, with vacuum applied, for at least one hour after hemorrhage is controlled. Once control is established, the vacuum is discontinued and the cervical seal emptied, but the device remains in place for an additional 30 minutes during close observation for further atony or bleeding.

A prospective, observational study was performed at 12 medical centers throughout the United States between February 2018 and January 2020. Inclusion criteria included 34 weeks gestation or later, normal uterine anatomy, and atony-related pre-device placement estimated blood loss (EBL) of 500 mL to 1,500 mL after vaginal delivery or 1,000 mL to 1,500 mL after cesarean delivery. Most facilities were not using quantitative blood loss (QBL) at this time. Consent was obtained by more than 7,500 women prior to delivery in the event a postpartum hemorrhage occurred and the vacuum device could be used. In total, 106 women received treatment with the vacuum-assisted device to control postpartum bleeding.

The majority of women were white (57%) and primiparous (33%), and most deliveries were performed vaginally (85%). Uterine atony was noted as the primary cause of postpartum bleeding in these women with a median EBL of 870 mL for vaginal delivery and 1,300 mL for cesarean delivery. The success rate for the vacuum-induced device was 94% (100/106; 95% CI, 88% to 98%) with a median time of three minutes to control of bleeding. Forty of the women (38%) still required blood products, with the majority (35/40 participants) receiving one to three units. However, evacuated blood when the device was in place was able to be measured and remained a low amount at a median of 110 mL, further supporting the device's ability to contract the uterus and prevent additional uncontrolled bleeding. Five participants required more significant intervention after the vacuum failed to adequately control bleeding, including uterine balloon tamponade (n = 2), B-Lynch compression suture (n = 1), B-Lynch compression suture followed by hysterectomy (n = 1), and hysterectomy (n = 1).

■ COMMENTARY

Overall, a vacuum-assisted device was deemed to be effective in controlling postpartum hemorrhage. Enrollment of this study was limited to participants with less than 1,500 mL of blood loss, and, therefore,

the effectiveness of the device in potentially reducing the need for blood products is questioned. Although the vacuum-assisted device is newer than the balloon tamponade devices and more research with severe cases of postpartum hemorrhage is needed, results thus far are promising if bleeding control can be achieved in a matter of minutes. The median time of vacuum treatment was 144 minutes in the study, which included 60 minutes with the device in place and 30 minutes for observation with the vacuum disconnected from suction. A tamponade device, such as the Bakri balloon, can stay in place for no more than 24 hours. Logically, the less time a device is left in place in a body cavity the lower the risk for infection, so a vacuum-assisted device would be preferable in this aspect.

One concern that would warrant individual facility investigation is the potential cost of a balloon tamponade device (Bakri) vs. the vacuum-induced device (Jada). For example, upon my own inquiry, I found it would be nearly six times more expensive to stock Jada on the unit and could be nearly four times the amount billed to the patient compared to the Bakri balloon. Since every hemorrhage can be affected by several factors or can respond differently to treatment, it can be difficult to generalize if one device reduces the amount of blood products administered or the need for surgery over the other. However, the cost should not deter facilities from trialing new products that are found to be effective and lifesaving. The Jada device is available to facilities at this time, and I await further information from a local hospital that has it stocked. At the time of this writing, it has not yet been used at the facility, since the need has not been warranted in a postpartum hemorrhage. ■

REFERENCES

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CME/CE QUESTIONS

1. **Which of the following was *not* an outcome measure in the study by Ahmadzia and colleagues?**
   a. Achieving a target plasma concentration of > 10 ng/mL of tranexamic acid on high-performance liquid chromatography mass spectrometry (HPLC/MS) was a pharmacokinetic primary outcome.
   b. Achieving a target plasma concentration of > 10 ng/mL of tranexamic acid on HPLC/MS was a pharmacodynamic primary outcome.
   c. Attaining < 17% maximum lysis on modified rotational thromboelastometry was a pharmacodynamics outcome.
   d. The need for blood or platelet transfusion was a safety outcome.
2. **Which of the following is true regarding maternal body mass index (BMI) status and the success rate of a trial of labor after cesarean (TOLAC) delivery?**
   a. Only pre-pregnancy BMI has an effect.
   b. Only delivery BMI has an effect.
   c. There is no significant difference between BMI categories.
   d. TOLAC success rates did not vary, but perinatal outcomes did.
3. **Based on the study by Dmochowski et al, anticholinergic medications:**
   a. do not increase the risk of dementia in older patients.
   b. prescribed for bladder symptoms are not associated with cognitive impairment.
   c. should be prescribed after careful consideration of both the benefits and risks of developing dementia.
   d. can be prescribed safely without concern for dementia risk.
4. **Despite a median time of three minutes to control postpartum bleeding, what percentage of women in the study by D'Alton et al still required the administration of blood products?**
   a. 42%
   b. 31%
   c. 29%
   d. 38%