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Evidence-based commentaries on women's reproductive health

ABSTRACT & COMMENTARY

New Treatment Option for Women at Risk of Fragility Fractures

By Jeffrey T. Jensen, MD, MPH, Editor

Leon Speroff Professor and Vice Chair for Research, Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland

Dr. Jensen reports that he is a consultant for and receives grant/research support from Bayer, Abbvie, ContraMed, and Merck; receives grant/research support from Medicines 360, Agile, and Teva; and is a consultant for MicroChips and Evofem.

SYNOPSIS: A randomized trial demonstrated a reduced risk of fragility fractures in high-risk women with osteoporosis treated monthly with the monoclonal antibody romosozumab compared with weekly alendronate.

SOURCE: Saag KG, Petersen J, Brandi ML, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. *N Engl J Med* 2017;377:1417-1427.

Fragility fractures that occur in women with osteoporosis lead to significant morbidity, and prevention of fractures represents the primary reason for treatment. This recent publication from the *New England Journal of Medicine* presents results from a multicenter, international, randomized, double-blind trial comparing standard therapy with weekly oral alendronate (70 mg) to monthly subcutaneous romosozumab (210 mg) for 12 months. After completion of this first year of study, all subjects entered an open-label observation period for an additional 12 months during which they received weekly oral alendronate (70 mg). Subjects also received oral vitamin D (600 to 800 IU) and calcium (500 to 1,000 mg) daily. The study enrolled postmenopausal women aged 55 to 90 years who were at high risk for fragility fracture defined as: 1) bone mineral density T score of -2.5 or less at the total hip or femoral neck and at least one moderate/severe vertebral fractures or two mild vertebral fractures; or 2) T score of -2.0 or less at the total hip or femoral neck and either two or more moderate or severe vertebral fractures or a fracture of the proximal femur sustained 3 to 24 months before randomization. Subjects underwent bone density screens and lateral X-rays of the spine every 12 months to assess incidence of new fractures. Women < 75 and

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≥ 75 years of age were randomized in separate groups.

The primary trial endpoints were the cumulative incidence of new vertebral and other clinical fractures at 24 months. Key secondary endpoints included bone mineral density at the lumbar spine, total hip, and femoral neck at 12 and 24 months and the incidence of nonvertebral fractures (including hip). The sample size had sufficient power to detect a 30% lower risk of clinical fracture in the romosozumab-to-alendronate group than in the alendronate-to-alendronate group at 24 months.

A total of 4,093 women underwent randomization, with 3,654 (89.3%) completing 12 months of the trial and 3,150 (77.0%) completing the 24-month primary analysis period. Dropout between the treatment groups was non-differential. The study enrolled a high-risk group; the mean age of participants was 74.3 years, 99.0% had a previous osteoporotic fracture, 96.1% had a prevalent vertebral fracture, and the mean bone mineral density T scores were -2.96 at the lumbar spine, -2.80 at the total hip, and -2.90 at the femoral neck.

After 24 months, subjects randomized to treatment with romosozumab followed by alendronate showed a 48% lower risk of new vertebral fractures than those receiving alendronate alone (6.2% vs. 11.9%; hazard ratio [HR], 0.52; 95% confidence interval [CI], 0.40-0.66), and a 27% lower risk of clinical fracture (9.7% vs. 13%; HR, 0.73; 95% CI, 0.61-0.88). Significantly fewer hip fractures occurred in the romosozumab-to-alendronate group (2% vs. 3.2%; HR, 0.62; 95% CI, 0.42-0.92). Women who received romosozumab also showed greater improvement in bone mineral density from baseline at all measured sites and at all time points. Romosozumab treatment increased levels of the bone-formation marker P1NP and decreased levels of the bone-resorption marker β-CTX within 12 months. In contrast, treatment with alendronate alone decreased both P1NP and β-CTX.

Although the incidences of adverse events and serious adverse events were similar overall between the two treatment groups, serious cardiovascular adverse events occurred more frequently in the romosozumab group (2.5% vs. 1.9%; significance not provided in the paper) during the 12-month randomization interval. The authors concluded that the results support the use of romosozumab in women at high risk of fragility fractures, with a decrease in fracture risk compared to bisphosphonate therapy alone.

■ COMMENTARY

Because of concerns regarding postmenopausal hormone replacement therapy, in the future we may find more women presenting with osteoporosis and vertebral fractures. How to best manage these women remains controversial. While effective at preventing bone loss, bisphosphonates do not stimulate bone formation, and concerns over atypical femoral fractures and osteonecrosis of the jaw have reduced the enthusiasm for their use. Rapid bone loss occurs at menopause due to the absence of estrogen-regulated modulation of bone remodeling. In addition to direct effects on bone, estrogen also has important effects on vitamin D metabolism, and the intestinal absorption and renal excretion of calcium.[1] We have level 1A evidence that postmenopausal estrogen replacement therapy does prevent hip and other fractures.[2,3] Although women using raloxifene had a reduction in spinal compression fractures, this important reduction in hip fracture was not observed.[4,5] A reduction of nonvertebral fracture also has been reported with bazedoxifene, but the absolute number of hip fractures seen in the study was small and not different from placebo or raloxifene.[6] Bisphosphonates have been shown to reduce vertebral and non-vertebral fracture risk, but the data are less convincing[7] for primary prevention of hip fracture. This leads me to conclude that women at risk for fracture without contraindications to estrogen therapy should be strongly counseled to consider this benefit for primary prevention. Women with osteoporosis or prevalent fractures require enhanced therapy.

Romosozumab, a monoclonal antibody that binds to and inhibits sclerostin, increases bone formation and decreases bone resorption. The development of romosozumab is a triumph of molecular biology. Scientists investigating sclerosteosis, a rare genetic disorder with high bone mass, determined that a mutation in SOST, the gene that encodes sclerostin caused of the disorder. Sclerostin is produced by osteocytes and inhibits bone formation and enhances bone resorption. Romosozumab promotes bone formation and slows resorption by blocking sclerostin activity.

In the placebo-controlled, Phase III, randomized Fracture Study in Postmenopausal Women with Osteoporosis (FRAME), one year of monthly romosozumab treatment increased bone mineral density at the lumbar spine by 13% and decreased the risk of new vertebral fracture by 73%.[8] The study by Saag et al extends these observations by focusing on a group of women at extremely high risk of fracture. Although the results were impressive, the significance is blurred by the assessment of the primary endpoint at 24 months, after one year of use of alendronate. Still, the reduction in fracture incidence is impressive and deserves attention.

All new therapies carry the potential for risk and benefit. Our > 50-year experiment with estrogen and progestogen therapy leaves us well acquainted with these trade-offs. A major concern with romosozumab is the twofold increase in the risk of cardiovascular complications at one year. This increase was not seen in the placebo-controlled study. Although some evidence of a protective effect of alendronate exists, a potential mechanism for harm exists as sclerostin is expressed in vascular smooth muscle and may promote remodeling in vascular tissue.[9] We also can expect that the cost associated with this injectable monoclonal antibody treatment to be significant. As is typical in medicine, there are no panaceas. ■

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ABSTRACT & COMMENTARY

Trends in OB/GYN Malpractice Litigation

By Rebecca H. Allen, MD, MPH

Associate Professor, Department of Obstetrics and Gynecology, Warren Alpert Medical School of Brown University, Women and Infants Hospital, Providence, RI

Dr. Allen reports she is a Nexplanon trainer for Merck, and has served as a consultant for Bayer and Pharmanest.

SYNOPSIS: In this review of medicolegal claims data from 2005-2014, obstetric and gynecologic surgery had the second highest average indemnity payment compared to other specialties, topped only by neurosurgery. Of the 10,915 claims identified, the majority (60%) were dropped, withdrawn, or dismissed; 31.1% of claims were paid by the defendant (90% before trial); and 7.5% were successfully defended by the physician.

SOURCE: Glaser LM, Alvi FA, Milad MP. Trends in malpractice claims for obstetrics and gynecologic procedures, 2005 through 2014. *Am J Obstet Gynecol* 2017;217:340.e1-340.e6.

This is a retrospective study from January 1, 2005, to December 31, 2014, of medical liability claims using the Physician Insurers' Association of America (PIAA) data-sharing project. The PIAA is an insurance trade association representing multiple medical professional liability insurance companies and other entities. This de-identified medical liability database was created to identify medical professional liability trends across specialties using claims from 20 private insurance carriers. A "claim" was defined as any written or oral demand for compensation. "Closed claims" were defined as resolved either with or without payment, and "paid claims" as those resolved with any payment to the plaintiff. Claims data from general obstetrics and gynecology were examined and included all types of deliveries and gynecologic surgical procedures, both in the hospital and in the office. Claims factors examined included average indemnity payments, single largest indemnity payments, and the paid-to-closed ratios of all claims for each specialty.

During the study period, 10,915 claims were identified. Although the majority (60%) of claims were dropped, withdrawn, or dismissed, 31.1% of claims were paid by the defendant (90% before trial), and 7.5% were successfully defended by the physician. The average

Table 1: Procedures Associated With OB/GYN Closed Claims					
Procedure	**Closed Claims**	**Paid Claims**	**% Paid to Closed**	**Total Indemnity**	**Average Indemnity**
Operative procedures on uterus	943	262	27.8	$73,198,625	$279,384
Cesarean delivery	879	287	32.7	$158,741,223	$553,105
Vaginal delivery	730	261	35.8	$136,706,000	$523,778
Operative procedures on tubes and ovaries (exclusive of sterilization)	278	96	34.5	$27,728,721	$288,841
Vacuum delivery	145	69	47.6	$30,536,872	$442,563

indemnity for all paid claims was $423,250; indemnity was $417,518 for claims settled prior to trial and $750,791 for claims given a verdict in favor of the plaintiff. Over time, average indemnity decreased 10% when comparing 2005-2009 and 2010-2014. When compared with other medical specialties, the average indemnity for obstetrics and gynecology procedures ($423,250) was 27% higher than the average indemnity for all medical specialties combined ($330,940). When ranked by medical specialty, obstetrics and gynecology procedures had the second highest average indemnity payment of 28 specialties after neurosurgery. The most common procedure associated with claims was operative procedures on the uterus. (*See Table 1.*)

■ COMMENTARY

The authors of this study sought to report on trends in obstetrics and gynecology medicolegal claims, a subject of interest to every OB/GYN physician. The paper would have been improved with more analysis on trends over time (e.g., number of claims). In addition, using ICD-9 codes and unique PIAA codes hampered a greater understanding of which procedures most commonly were involved in claims. For example, the following procedures were not included in Table 1 because the description was not informative: prescription of medication; general physical examination; diagnostic interview, evaluation, or consultation; and miscellaneous manual examinations and nonoperative procedures. Nevertheless, the comparison with other specialties provides interesting information. I suppose it is not surprising that obstetrics and gynecologic surgery was the second highest specialty in average indemnity paid for medical claims given the stakes involved. Similarly, pediatrics was also one of the top 5, which also included nonsurgical neurology and anesthesiology.

In 2015, the American College of Obstetricians and Gynecologists reported on its survey of its members regarding professional liability issues.[1] A total of 4,294 OB/GYN physicians responded to the survey out of 32,425 fellows and junior fellows (13% response rate). Most respondents (74%) reported that at least one liability claim was filed against them during their professional career. The average number of claims per physician was 2.6. The most common obstetric claim was neurologically impaired infant (27.4%) followed by stillbirth or neonatal death (15%). The most common gynecologic claim was major patient injury (27.9%), followed by minor patient injury (23.4%) and "delay in or failure to diagnose" (21.5%). Of the "delay in or failure to diagnose" claims, the most frequent claims involved failure to diagnose cancer, with breast cancer being the most common type. Respondents reported that because of fear of litigation, 23.8% decreased the number of high-risk obstetric patients they saw, 13.4% stopped performing vaginal birth after cesarean delivery, 19.7% decreased the number of gynecologic surgeries, and 7.7% stopped performing major gynecologic surgery.

The authors speculated that one reason gynecologic surgery had higher numbers of claims was because of volume issues. They maintained that OB/GYN physicians have to stay competent in so many different types of procedures that it is difficult to maintain adequate procedural volume and technical competence. That is an issue, but the paid-to-closed claim ratio for obstetric and gynecologic surgery was 31.2, compared to 29.4 in general surgery. This is not very different, and general surgeons also perform a number of varied procedures. Overall, our field is known to have high liability costs not because of gynecologic surgery but rather because of obstetric procedures. Vacuum delivery was highlighted by the authors because it represented 8.3% of all delivery-related claims, but it only occurs during 2.8% of births. Maintaining operative vaginal delivery skills is a weakness in our field but, by definition, a delivery that requires forceps or vacuum already is higher risk and may be more likely to result in litigation. Unfortunately, there is no easy answer to adequately training our residents in vacuum and forceps delivery given decreasing volume of these procedures. ■

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ABSTRACT & COMMENTARY

Hormone Replacement: Have We Made Progress Since WHI?

By Molly Brewer, DVM, MD, MS

Professor and Chair, Department of Obstetrics and Gynecology, Division of Gynecologic Oncology, University of Connecticut Health Center, Farmington

Dr. Brewer reports no financial relationships relevant to this field of study.

SYNOPSIS: Vaginal estrogen may improve vaginal symptoms of menopause and does not increase the risk for endometrial cancer, stroke, or cardiovascular disease.

SOURCE: Crandall CJ, Hovey KM, Andrews CA, et al. Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. *Menopause* 2017; Aug 14. doi: 10.1097/GME.0000000000000956. [Epub ahead of print.]

Since the Women's Health Initiative (WHI) first was published in 2002, women have been reluctant to use any type of hormone replacement therapy (HRT). In my practice, women routinely refuse both systemic HRT and vaginal HRT because of their fear of cancer, primarily breast cancer. In this recent study in *Menopause*, Crandall et al reported that the risk of breast and endometrial cancer and cardiovascular events was not elevated in postmenopausal women using vaginal estrogen. This observational study, which was a subset of the original WHI study, ran from 1993 to 2005, and included 45,663 postmenopausal women aged 50-79 years. One-third of these women had a hysterectomy and the remainder had an intact uterus. The authors calculated the global index event (GIE), which is the time to first coronary heart disease (CHD), breast cancer, stroke, pulmonary embolism, hip fracture, colorectal cancer, endometrial cancer, or death, and the hazard ratios (HR) ranged from 0.69-0.76, depending on which confounders were included in the model (95% confidence interval [CI], 0.59-0.81, 0.64-0.91). Death, CHD, stroke, colorectal cancer, hip fracture, and pulmonary embolism/deep vein thrombosis all had HRs < 1, but CHD and hip fracture were the only two outcomes that were statistically significant, with HRs of 0.52 (95% CI, 0.31-0.85) and 0.40 (95% CI, 0.64-0.91).

When the authors analyzed based on hysterectomy status, women without a uterus had no statistically significant difference in outcomes; women with an intact uterus tended toward an increased risk of developing endometrial cancer, but this was not statistically significant. However, these women did have a statistically significant difference in GIE (HR, 0.68; 95% CI, 0.55-0.86), death (HR, 0.62; 95% CI, 0.41-0.93), CHD (HR, 0.30; 95% CI, 0.19-0.78), and hip fracture (HR, 0.40; 95% CI, 0.16-0.96). For the outcomes listed above in the women without a uterus, the number of events was so low that there was inadequate statistical power to determine definitively that the risk was lower with vaginal estrogen. However, we can conclude that the trend was lower for these outcomes except for endometrial cancer.

Several other studies have addressed the risk of cancer, CHD, and stroke with vaginal estrogen. Two studies did not find an increase in risk of endometrial hyperplasia with atypia or cancer.[1,2] However, a Danish study found a relative risk of 1.96 (95% CI, 1.77-2.17) with vaginal estrogen. It was not clear in the study if some of the women also were taking systemic estrogen or a higher dose of vaginal estrogen than was used in this study.[3]

■ COMMENTARY

So where are we with HRT? Since 2002 when the first WHI study was published, there has been a significant fear of HRT by patients.[4] The WHI study created such controversy that most women on HRT in 2002 stopped their HRT without understanding the real findings in the study.[5] A follow-up publication in 2013 by some of the same authors continued to support the notion that "Menopausal [hormone therapy] is not suitable for long-term prevention of CHD given risks of stroke, venous thromboembolism, and breast cancer (for estrogen plus progestin therapy) found in both clinical trials and in observational studies."[6] Other studies have disagreed. In a recent publication, Langer et al stated, "The WHI was not intended, and was not statistically powered, to evaluate the common clinical use of MHT (menopausal hormone therapy) initiated near menopause." They considered that it was inappropriate to use WHI data from the 70% of the enrolled cohort that was more than 10 years postmenopausal to make decisions about HRT in younger women transitioning into menopause. In addition, their findings were not adjusted for age or risk of chronic disease. The women in the WHI trial had a mean age of 63 years, were approximately 12 years beyond menopause, and should not have been included with the younger patients who are most likely to have menopausal symptoms and require HRT. Langer et al went on to state: "Unfortunately, the USPSTF has consistently made this error in its consideration of the

evidence."[7] Finally, the effect of the WHI study was that most women stopped using HRT because of their fears resulting from the widespread publicity of this flawed study.

So how do we counsel our patients? The use of both systemic and vaginal estrogen around the time of menopause is safe and reduces symptoms. Patients with breast cancer or a family history of breast cancer should be counseled more carefully than those without a strong personal or family history of breast cancer. However, we can counsel our patients, even those with breast cancer, that vaginal estrogen is safe and may be beneficial for more than just vaginal symptoms. Those women with an intact uterus using vaginal estrogen had a lower risk of death, cardiovascular disease, and hip fractures while those who have had a hysterectomy will not suffer harm from vaginal estrogen. However, I have many patients who are deathly afraid of any hormone and will not even use vaginal estrogen. They suffer with many quality-of-life issues and, potentially, an increased risk of CHD because of the misconceptions around hormone replacement treatment. ■

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SPECIAL FEATURE

Update on Postpartum Hemorrhage

By Rebecca H. Allen, MD, MPH

Associate Professor, Department of Obstetrics and Gynecology, Warren Alpert Medical School of Brown University, Women and Infants Hospital, Providence, RI

Dr. Allen reports she is a Nexplanon trainer for Merck, and has served as a consultant for Bayer and Pharmanest.

Postpartum hemorrhage (PPH) traditionally has been defined as estimated blood loss in excess of 500 mL after vaginal delivery and in excess of 1,000 mL after a cesarean delivery. The newest definitions from the American College of Obstetricians and Gynecologists' (ACOG) reVITALize program defines PPH as estimated blood loss ≥ 1,000 mL or blood loss accompanied by signs and symptoms of hypovolemia within 24 hours of birth (including intrapartum loss) regardless of route of delivery.[1] In the United States, hemorrhage accounts for 11.4% of maternal deaths, the fourth most common cause after cardiovascular diseases, non-cardiovascular diseases, and infection; worldwide, it is the leading cause of maternal mortality.[2] The rate of PPH increased in the United States from 2.3% in 1994 to 2.9% in 2006.[3] This 26% increase primarily was the result of an increase in uterine atony.

Management of PPH involves a team approach, and ACOG recommends that all hospitals have standardized processes in place, including a massive transfusion protocol.[4] Risk factors for PPH should be assessed upon admission. (*See Table 1.*) Primary causes of PPH that occur within the first 24 hours of birth include uterine atony, lacerations, retained placenta, placenta accreta/increta/percreta, acquired or inherited coagulation defects, and uterine inversion. Secondary causes of PPH that occur more than 24 hours after delivery and up to 12 weeks postpartum include subinvolution of the placental site, retained products of conception, infection, and inherited coagulation defects. For prevention of primary PPH, ACOG recommends oxytocin at the time of delivery, either 10 units intramuscular injection or a dilute intravenous solution (bolus dose 10 units).[4]

Table 1: Risk Factors for Postpartum Hemorrhage

- Prolonged use of oxytocin
- High parity
- Chorioamnionitis
- General anesthesia
- Overdistended uterus, e.g., multiple gestation, polyhydramnios, macrosomia
- Fibroid uterus
- Operative vaginal delivery (lacerations)
- Previous uterine surgery (malplacentation)
- Amniotic fluid embolism

The management of PPH depends on the cause, with uterine atony comprising 70-80% of the cases. Management of uterine atony includes uterine massage, removal of intrauterine clots, and emptying the bladder to allow the uterus to contract. Oxytocin should be given and, typically, a second uterotonic, such as methylergonovine, 15-methyl prostaglandin F2a, or misoprostol, is necessary. Of note, tranexamic acid is a new agent that has entered the field for the treatment of PPH. Tranexamic acid reduces bleeding by inhibiting the enzymatic breakdown of fibrinogen and fibrin by plasmin.[4] OB/GYNs will be familiar with the oral form of tranexamic acid (brand name Lysteda), which is used for the treatment of heavy menstrual bleeding. The intravenous formulation of tranexamic acid has been studied outside of pregnancy and was found to be effective in decreasing mortality in trauma patients with hemorrhage.[5]

Based on the data in trauma patients, the WOMAN (World Maternal Antifibrinolytic) trial was conducted in 193 hospitals in 21 countries (both developed and developing nations) to evaluate tranexamic acid for treatment of PPH.[6] The study was a randomized, double-blind, placebo-controlled trial in women 16 years of age and older who had a clinical diagnosis of PPH after vaginal birth or cesarean delivery. Subjects were assigned randomly to receive 1 gram of tranexamic acid or placebo intravenously. If bleeding continued after 30 minutes or bleeding stopped and restarted within 24 hours, a second dose was permitted. The primary outcome was a composite of death from all causes or hysterectomy within 42 days of randomization. Secondary outcomes included deaths due to bleeding, thrombotic events, surgical interventions, and other complications.

Between March 2010 and April 2016, 20,060 women were randomized to tranexamic acid (n = 10,050) or placebo (n = 10,009). Of the 483 maternal deaths, 346 (72%) were due to bleeding. The risk of death due to bleeding was reduced in the tranexamic acid group compared to the placebo group (155 [1.5%] vs. 191 [1.9%]; relative risk [RR], 0.81; 95% confidence interval [CI], 0.65-1.00; $P = 0.045$). Deaths due to other causes, such as preeclampsia, pulmonary embolism, and sepsis, did not differ. The tranexamic acid was effective in reducing death due to hemorrhage if given within three hours of birth but not if given after more than three hours. Of the 709 women who underwent hysterectomy, 608 (86%) were on the day of randomization and 191 (27%) within 1 hour of randomization. The risk of hysterectomy was not reduced with tranexamic acid (358 [3.6%] vs. 351 [3.5%]; RR, 1.02; 95% CI, 0.88-1.07; $P = 0.84$). The risk of thrombosis and other adverse outcomes was no different between the two groups. The authors of the WOMAN study concluded that tranexamic acid is effective in reducing deaths due to PPH and is most effective the earlier it is started. No effect was found on hysterectomies, likely because many clinicians in the study already had decided to perform hysterectomy at the time of randomization. This makes sense in the context of life-threatening hemorrhage that multimodal treatments would be initiated simultaneously. The authors concluded that tranexamic acid should be given alongside uterotonics because it is safe, effective, and there were no adverse effects. In its recent practice bulletin, ACOG concluded that 1 gram IV tranexamic acid should be considered for PPH when initial medical therapy fails.[4] The dose may be repeated if bleeding persists after 30 minutes or restarts within 24 hours. However, most experts currently believe that using tranexamic acid for the prevention of PPH is still investigational.

Other techniques to control PPH after medical therapy include intrauterine tamponade with balloon systems (e.g., Bakri), 60 mL Foley catheter, or uterine packing. Ultimately, surgical intervention may be required including uterine artery embolization, vascular ligation, uterine compression sutures, or hysterectomy. One critical component of PPH management is early transfusion therapy. Maternal tachycardia and hypotension often occur only after significant blood loss in the healthy women for whom we care. One lesson learned from past maternal deaths is that inadequate early resuscitation leads to consumptive coagulopathy and other complications. Therefore, as soon as estimated blood loss approaches 1,500 mL, ACOG recommends preparing for blood transfusion, including packed red blood cells, fresh frozen plasma, and platelets.[4] The current recommended initial ratio for transfusion in the setting of anticipated massive transfusion is 1:1:1 of packed red blood cells:fresh frozen plasma:platelets.[7] Ultimately, treatment of PPH is a team effort and hospitals should prepare themselves by having an organized multidisciplinary response that is reinforced with hemorrhage drills and/or team training exercises. It is heartening that we have one more tool — tranexamic acid — to use to treat PPH. This agent may well play a role in reducing significant maternal morbidity and mortality in the United States. ■

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CME/CE QUESTIONS

1. Compared to alendronate alone, treatment of women at high risk for fragility fracture with romosozumab for one year followed by alendronate resulted in:
a. a reduction in non-vertebral and vertebral fractures.
b. an increase in bone mineral density.
c. an increase in cardiovascular complications
d. All of the above

2. From 2005 to 2014, average indemnity payments for obstetric and gynecologic procedures increased.
a. True
b. False

3. Which of the following is true regarding vaginal estrogen?
a. It does not increase the risk of coronary heart disease.
b. It increases the risk of stroke.
c. It decreases the risk of endometrial cancer.
d. All of the above

4. When should tranexamic acid for the treatment of postpartum hemorrhage be started?
a. As soon as hemorrhage is identified and uterotonics fail to control the bleeding
b. One hour after excessive bleeding starts
c. Two hours after excessive bleeding starts
d. At the time of hysterectomy

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- Explain the latest data regarding diagnosis and treatment of various diseases affecting women;
- Discuss new data concerning prenatal care, neonatal health, and complications arising in pregnancy and the perinatal period; and
- Discuss the advantages, disadvantages, and cost-effectiveness of new testing procedures in women's health.

[IN FUTURE ISSUES]

What Do the Urinary Microbiota and Incontinence Have To Do With Each Other?