EDITORIALS

Early Detection and Bundled Treatment for Postpartum Hemorrhage

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Postpartum hemorrhage is the leading cause of maternal death in developing regions, accounting for 20% of maternal deaths, most of which are preventable.[1] This opportunity for prevention is evident by the decrease over time in the contribution of postpartum hemorrhage to maternal death in developed regions, where it accounts for 8% of maternal deaths.[1]

Bleeding after childbirth is normal and part of the physiologic transition that occurs in the postdelivery period. However, the transition to abnormal bleeding can be swift. Postpartum hemorrhage, which is traditionally defined as blood loss of more than 500 ml, can develop within minutes and can escalate rapidly, with severe sequelae, including disseminated intravascular coagulation, multiorgan dysfunction, and death.[2]

Active management of the third stage of labor (including the administration of oxytocin, uterine massage, and, with signs of placental separation, umbilical-cord traction) has been a cornerstone in the prevention of postpartum hemorrhage for several decades.[2,3] Although uterine massage and umbilical-cord traction are no longer considered to be essential in the most recent World Health Organization (WHO) recommendations[2] for the prevention and treatment of postpartum hemorrhage, guidelines continue to recommend oxytocin, a heat-sensitive uterotonic agent, as the most effective tool for prevention and treatment.[2,3] In 2019, carbetocin, a heat-stable oxytocin analogue, and tranexamic acid, an antifibrinolytic agent, were both added to the core list of medicines for reproductive health in the 21st edition of the *WHO Model List of Essential Medicines*.[4] Carbetocin was shown to be noninferior to oxytocin for the prevention of blood loss of at least 500 ml or the use of additional uterotonic agents in women undergoing vaginal delivery.[5] Recommendations call for the use of carbetocin if oxytocin is not available, if a cold chain to maintain the stability of oxytocin is hard to achieve, or if the cost of carbetocin in that area is similar to that of other uterotonic agents.[6] In another large trial, tranexamic acid reduced the risk of death due to bleeding among women with postpartum hemorrhage and is recommended as an addition (within 3 hours after birth) to standard treatments for postpartum hemorrhage.[7,8] However, despite this growing list of tools with documented benefit, a lack of consistent implementation in resource-poor settings translates to many preventable deaths from postpartum hemorrhage.[9]

In this issue of *the Journal*, Gallos et al.[10] report findings from the E-MOTIVE trial, an international, cluster-randomized trial of early detection and treatment of postpartum hemorrhage after vaginal delivery. The trial targeted two challenges: a delay in the recognition and diagnosis of postpartum hemorrhage and a delayed and inconsistent use of interventions for management of postpartum hemorrhage. The intervention included early detection, with the use of a calibrated drape, combined with a treatment bundle that was applied in parallel, rather than sequentially, and that included uterine massage, oxytocin, tranexamic acid, intravenous fluids, and examination and escalation as needed. The intervention was supported by several implementation strategies: training (simulation-based and peer-assisted), provision of a trolley or carry case containing all medicines and devices, local cham-

pions (midwives and doctors), and monthly auditing and feedback to provide data on rates of detection, bundle use, and rates of outcome measures. The primary outcome was a composite of severe postpartum hemorrhage (blood loss, ≥1000 ml), postpartum laparotomy for bleeding, or maternal death from bleeding.

Across four countries (Kenya, Nigeria, South Africa, and Tanzania), 80 hospitals were randomly assigned to the intervention or usual standard care; data from 78 hospitals were available, and outcomes in 206,455 patients were analyzed. A primary-outcome event occurred in 1.6% of the patients in the intervention group and in 4.3% of those in the usual-care group (risk ratio, 0.40; 95% confidence interval, 0.32 to 0.50; P<0.001), a result that was driven mostly by a lower risk of severe postpartum hemorrhage in the intervention group. Results for the key secondary implementation outcomes correspondingly favored the intervention group; postpartum hemorrhage was detected in 93.1% of the patients in the intervention group and in 51.1% of those in the usual-care group, and adherence to the treatment bundle was documented in 91.2% and 19.4%, respectively.

The E-MOTIVE trial sought to target postpartum hemorrhage by improving detection and implementing bundled, rather than sequential, treatment. The scalability of the trial intervention is supported by the use of components that can be administered by a midwife and are accessible in facilities with fewer resources and by the local procurement of oxytocin and tranexamic acid. However, important questions remain regarding the ability to scale up this intervention, given the current variability in implementation of many of its components despite availability and recommendations for their use.[2,3,9] This trial was supported by a robust implementation strategy, which included training, champions, auditing, and feedback. More work will be needed to understand the contribution of these components to the success of this approach and the cost and infrastructure needed to sustain them and to identify and disseminate an effective framework for broad implementation.

In summary, the E-MOTIVE trial showed that the early detection and a bundled treatment for postpartum hemorrhage with the use of readily available and recommended medicines and intervention strategies substantially reduced the risk of severe outcomes from postpartum hemorrhage. The next challenge will be to achieve widespread adoption and implementation at scale in resource-limited environments.

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