



Photo Credit: Bobby Neptune/GHSC-PSM

Ensuring Uterotonic Quality in Liberia

SUMMARY: In Liberia, oxytocin is the preferred medicine for prevention and treatment of postpartum hemorrhage (PPH); however, due to its heat sensitivity, ensuring its quality throughout the supply chain remains a challenge. In collaboration with the USAID Global Health Supply Chain Program-Procurement and Management (GHSC-PSM) project, Liberia's Ministry of Health aims to ensure oxytocin quality through integration of oxytocin into the vaccine cold chain and expanded use of misoprostol for PPH in settings without available cold storage options. This model may be useful for other countries with limited cold storage infrastructure.

OXYTOCIN QUALITY CHALLENGES

PPH—or excessive bleeding after childbirth—is the leading cause of maternal mortality worldwide.¹ The World Health Organization (WHO) estimates that approximately 303,000 maternal deaths occur each year with nearly 20% of those resulting from PPH.¹ PPH is both preventable and treatable with inexpensive medicines that are widely available.² Oxytocin injection remains a preferred medicine for prevention and treatment of PPH; however, other uterotonic—including oral misoprostol—may be used for PPH prevention and treatment where oxytocin is not available or its quality cannot be ensured.³

In most low- and middle-income countries (LMICs), oxytocin is preferred for PPH management. Oxytocin's effectiveness is widely recognized; however, challenges to maintain its quality are prevalent. In a recent systematic review, 36% of tested oxytocin samples from 15 LMICs did not meet quality standards as defined by the authors.⁴ Quality deficiencies may occur due to poor adherence to Good Manufacturing Practices (GMP) and/or due to long-term exposure to higher than acceptable temperatures.⁵

GLOBAL RECOMMENDATIONS TO ENSURE UTEROTONIC QUALITY AND AVAILABILITY

To improve oxytocin quality in LMICs, WHO, the United Nations Population Fund (UNFPA), and the United Nations International Children's Fund (UNICEF) provide clear guidance on oxytocin storage and management and suggest strategies to support their recommendations. In 2015, WHO and UNICEF released a joint statement to clarify that oxytocin may be stored in the vaccine cold chain as long as all temperature-sensitive products are clearly labeled and good storage practices are observed.⁶ In 2019, WHO, UNFPA, and UNICEF released a second joint-statement that clarifies storage requirements for oxytocin, stating that oxytocin should be labeled for storage between 2 and 8°Celsius (C) and managed in a cold chain of 2 - 8°C for storage and distribution.⁷



Photo Credit: Jennifer Chavez/GHSC-PSM

Additionally, WHO's updated 2018 guidance on PPH prevention further clarifies that where oxytocin's quality cannot be guaranteed, oral misoprostol—which does not require cold storage—is a recommended uterotonic option.³



MATERNAL HEALTH AND UTEROTONIC OPTIONS IN LIBERIA

While maternal survival has increased in Liberia since 2000, Liberia's maternal mortality ratio remains elevated at 661 maternal deaths per 100,000 live births.⁸ In 2016, Liberia's institutional delivery rate was high at 76 percent, which indicates that quality of maternal health care services may be low.⁹ Given the high prevalence of poor quality oxytocin in neighboring African countries, quality of oxytocin in Liberia is of concern.^{4,10}

Currently, oxytocin injection is the uterotonic of choice in Liberia, and the supply chain is set up for oxytocin procurement and supply management. Liberia's National Standard Therapeutic Guidelines and

Essential Medicines List includes oxytocin and misoprostol for prevention and treatment of PPH;¹¹ however, in practice oxytocin is the preferred medication. UNFPA provides the majority of Liberia's oxytocin and misoprostol and sources only quality-assured, appropriately labelled oxytocin (i.e. for storage at 2 - 8 °C).

Procurement of quality-assured oxytocin is one component of ensuring the availability of quality oxytocin at service delivery points; however, oxytocin's degradation profile necessitates end-to-end cold chain storage throughout the supply chain. Excessive exposure to high temperatures results in more rapid degradation and shorter product shelf life, which increases the risk that the product may not be effective when it is administered to the patient. Recent survey data indicates that the availability of working refrigerators in Liberian health facilities may be limited with the implication that oxytocin may not always be stored under refrigeration and may be exposed to high ambient temperatures. In October 2019, Liberia's Deputy Minister of Health/Chief Medical Officer issued a statement calling on health facilities and supply chain managers to store oxytocin in vaccine refrigerators or stock and use oral misoprostol for PPH in facilities without any available refrigerators as a strategy to mitigate potential quality risks.¹²

PLANNING FOR LIBERIA'S UTEROTONIC SUPPLY CHAIN

In January 2020, GHSC-PSM co-hosted an engagement session with the Liberia Ministry of Health (MOH), Family Health Division (FHD) on uterotonic quality. During the session, best practices and recent oxytocin quality evidence were shared and discussed amongst meeting stakeholders to clarify and support global recommendations and national strategies to ensure the availability of quality uterotonics. Meeting stakeholders co-generated the following points of clarification:

- Because oxytocin degrades more rapidly when it is exposed to high ambient temperature, warehouses and facilities that do not have functional cold chain facilities are inappropriate storage facilities for oxytocin.
- Where possible, efforts to integrate oxytocin into the vaccine cold chain should move forward in accordance with the Deputy Minister/Chief Medical Officer's statement. Where integration is not immediately possible, other products—e.g. misoprostol for PPH—should be used.
- In warehouses and facilities without functional cold chain, misoprostol may be used instead of oxytocin. Broader use of misoprostol for PPH will need to be reflected in quantification, procurement, supply planning, and storage needs.

PROGRESS TO-DATE AND NEXT STEPS

As of June 2020, the MOH and partners remain committed to their efforts to ensure the availability of quality uterotonics. Liberia's most recent national quantification (March 2020) included additional quantities of misoprostol for PPH to reflect expanded use in all the health facilities in Liberia and especially those without cold storage. Presently, based on the supply plan developed during the national quantification exercise, additional misoprostol is being ordered by UNFPA.

The FHD is working closely with the West African Coast Initiative (WACI) supported by West African Health Organization to develop Liberia's PPH guidelines and provide a foundation for the implementation of interventions that have been shown to be effective in reducing the burden of PPH. The FHD has strongly adhered to the recommendations from GHSC-PSM to use both misoprostol and oxytocin in the management of PPH.

GHSC-PSM will continue to collaborate with the MOH and other stakeholders to advocate for continuous supply of lifesaving uterotonics in health facilities. The project will work with technical committees in Liberia to prioritize activities around commodity selection, forecasting, and supply planning. By conducting consistent supply plan reviews and forecasting, GHSC-PSM will be well positioned to advocate for long-term procurement needs of uterotonics.

Finally, GHSC-PSM will collaborate with partners to support integration of oxytocin into the vaccine cold chain and increased use of misoprostol for PPH. The project will use the End-Use Verification survey to monitor the integration of oxytocin into the Expanded Program on Immunization (EPI) cold chain to ensure that facilities are able to maintain oxytocin's quality. Additionally, GHSC-PSM will pilot a new set of survey questions to glean more information on oxytocin storage conditions at health facilities and to monitor further progress. Data from the survey will be used to identify gaps and propose recommendations for improving the availability of quality-assured uterotonics in Liberia.

* UNFPA, UNICEF, the Pharmacy Division, the Montserrado County Health Team, Clinton Health Access Initiative, the Supply Chain Management Unit, Jhpiego, Last Mile Health, the Liberia Nursing and Midwifery Board, World Health Organization, the National Public Health Institute of Liberia, DKT, Partners in Health, and the Liberia Midwifery Association

REFERENCES

1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller A-B, Daniels J, et al. Global causes of maternal death: a WHO systematic analysis. *Lancet Glob Health*. 2014 Jun 1;2(6):e323–33.
2. Jhpeigo. Business Case: Investing in Production of High-Quality Oxytocin for Low-Resource Settings [Internet]. Baltimore, MD: Jhpiego; 2014 Dec [cited 2017 May 30]. Available from: http://www.conceptfoundation.org/wp-content/uploads/2015/06/BusinessCase_Oxytocin_web.pdf
3. World Health Organization. WHO Recommendations: Uterotonics for the Prevention of Postpartum Haemorrhage [Internet]. Geneva, Switzerland: World Health Organization; 2018 [cited 2019 Feb 14]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/277276/9789241550420-eng.pdf?ua=1>
4. Torloni MR, Gomes Freitas C, Kartoglu UH, Metin Gülmezoglu A, Widmer M. Quality of oxytocin available in low- and middle-income countries: a systematic review of the literature. *BJOG Int J Obstet Gynaecol*. 2016 Dec;123(13):2076–86.
5. Lambert P, McIntosh MP, Widmer M, Evans L, Rauscher M, Kuwana R, et al. Oxytocin quality: evidence to support updated global recommendations on oxytocin for postpartum hemorrhage. *J Pharm Policy Pract*. 2020 May 15;13(1):14.
6. WHO, UNICEF. WHO/UNICEF Joint Statement: Temperature-Sensitive Health Products in the Expanded Programme on Immunization Cold Chain [Internet]. [cited 2017 Nov 8]. Available from: [https://www.unicef.org/health/files/EPI_cold_chain_WHO_UNICEF_joint_statement_A4_rev2_5-14-15_\(3\).pdf](https://www.unicef.org/health/files/EPI_cold_chain_WHO_UNICEF_joint_statement_A4_rev2_5-14-15_(3).pdf)
7. World Health Organization, UNICEF, UNFPA. WHO/UNICEF/UNFPA Joint Statement on Appropriate Management of Oxytocin - a Key Commodity for Maternal Health [Internet]. 2019 [cited 2019 Jun 17]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/311524/WHO-RHR-19.5-eng.pdf?sequence=1&isAllowed=y>
8. World Health Organization. Trends in Maternal Mortality 2000-2017: Estimates by WHO, UNICEF, UNFPA, World Bank Group and the United Nations Population Division [Internet]. Geneva, Switzerland; 2019. Available from: <https://www.who.int/reproductive health/publications/maternal-mortality-2000-2017/en/>
9. National Malaria Control Program (NMCP) [Liberia], Ministry of Health (MOH), Liberia Institute of Statistics and Geo-Informational Services (LISGIS), ICF. Liberia Malaria Indicator Survey 2016 [Internet]. Monrovia, Liberia: MOH, LISGIS, and ICF; 2017 [cited 2020 Jun 29]. Available from: <https://dhsprogram.com/pubs/pdf/MIS27/MIS27.pdf>
10. Lambert P, Nguyen T-H, McEvoy C, Minhas RS, Wright P, Deadman K, et al. Quality of oxytocin ampoules available in health care facilities in the Democratic Republic of Congo: an exploratory study in five provinces. *J Glob Health [Internet]*. [cited 2020 May 7];8(2). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6126516/>
11. Ministry of Health, Liberia. National Standard Therapeutic Guidelines and Essential Medicines List, Liberia - 2017 [Internet]. 2017 [cited 2020 Mar 17]. Available from: <http://moh.gov.lr/wp-content/uploads/Liberia-NSTG-EML-2nd-Edition-2017.pdf>
12. Francis N. Kateh, Deputy Minister and Chief Medical Officer. Memorandum: Authorization of New Routine for Essential Reproductive Health Medicines. 2019.