Rectal Delivery of Magnesium Sulfate

Health need

Preeclampsia and eclampsia (PE/E) are among the leading causes of maternal death and disability worldwide and account for at least 14% of maternal deaths in low-resource settings. The risk that a woman in a developing country will die of PE/E is approximately 300 times greater than that for a woman in a developed country. The World Health Organization (WHO) has identified magnesium sulfate ($MgSO_4$) as the most effective, low-cost anticonvulsant for the treatment of severe PE/E, yet this intervention is widely underused. This can partially be attributed to the current regimen for $MgSO_4$—requiring either intravenous (IV) or intramuscular (IM) administration and a complex calculation of dilution and dosing—as a key barrier to widespread use. In order to address these challenges to use and increase uptake of $MgSO_4$, PATH is developing a rectally administered gel which is simple to use for the sustained delivery of $MgSO_4$.

Technology solution

Rectally administered $MgSO_4$ could simplify delivery and improve access to $MgSO_4$ treatment in low-resource settings. Use of the rectal route of delivery is well established for many pharmaceutical products. The introduction of a $MgSO_4$-releasing retention enema could have the advantage of reducing the need for complex dilution and variable dosing regimens, eliminating use of sharps and painful IM injections, while addressing health providers' concerns about the risk of magnesium toxicity. Building on PATH's research experience in mucosally delivered vaccines and rectally administered microbicides, we are developing a $MgSO_4$ formulation that is safe, easy to administer, and can consistently deliver magnesium at rates and doses comparable to those obtained using the current IV/IM delivery regimen. A gel containing $MgSO_4$ will be developed that can be delivered through the rectum to the lower gastrointestinal tract of a patient using a simple, low-cost enema bulb. An enema of approximately 60 mL to 250 mL will be formulated to optimize retention and distribution to the mucosal surfaces of the digestive tract. Bioavailability and pharmacokinetic modeling will be used to help ensure that the formulation provides safe and therapeutic levels of magnesium in the serum consistent with the WHO-recommended anticonvulsant treatment for PE/E.

Current status and results

PATH has conducted extensive background research on magnesium uptake and rectal administration of pharmaceuticals. This research provides us guidance for product development and for outlining the parameters for a safe and therapeutic rectally administered product for PE/E. We held stakeholder interviews to assess the need, acceptability, and barriers for this innovation with experts in maternal health care, pharmaceutical development, and manufacturing. PATH is currently conducting laboratory studies of potential enema formulations to define the lead formulation. A preclinical bioavailability study in an appropriate model is planned for 2014 to determine the uptake of magnesium from this lead formulation.

PATH/Patrick McKern

Enema bulb with gel containing magnesium sulfate.

"The majority of respondents felt that rectal administration of an MgSO4 gel would fill an unmet need and offer an option for care of women with PE/E to providers in low-resource settings."

PATH. *Summary Report on Stakeholder Input*. May 2014. [unpublished]

Availability

For more information regarding this project, contact Elizabeth Abu-Haydar at eabuhaydar@path.org.

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