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New Research on Community Management of Severe Neonatal Infections

An Overview

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Efforts by developing countries, backed by international support, are helping achieve a steady decline in under-5 mortality. Recent estimates suggest that under-5 deaths fell from 9.6 million to 6.9 million between 2000 and 2011, with the under-5 mortality rate falling from 73 to 51 per 1000 live births.[1] This progress, though slower than hoped in some countries, nevertheless gives cause for optimism. Of note, as postneonatal mortality has declined, an increasing proportion of under-5 deaths are occurring in the neonatal period, underscoring the importance of prevention of neonatal mortality to overall infant and under-5 mortality. Research must focus on the design of innovative solutions that are both efficacious and effective for preventing neonatal deaths.

Prematurity and clinical infections are major causes of neonatal deaths. Neonatal infections, including pneumonia, sepsis and meningitis, are estimated to cause over 700,000 deaths each year.[2] Until recently, neonatal deaths associated with clinical infections were considered difficult to address, but several advances are paving the way for the design of a concrete strategy and action plan to address infectious causes of neonatal mortality.

WHAT ARE THESE ADVANCES?

Institutional delivery rates are increasing in some countries through incentives such as conditional cost transfers and expansion of neonatal services. In large parts of the developing world, however, most deliveries still occur at home. Skilled supervision of birth is an unmet challenge for those born at home, as is the promotion of essential newborn care, recognition of illness and access to treatment of clinical infections for both home and facility births in the neonatal period and in early infancy. The concept of home visitation during the neonatal period, pioneered by Abhay Bang, has provided a tool for prevention and early detection of clinical infection.[3] Furthermore, a number of simple, yet reliable, classification and treatment algorithms for young infants (0 to 2 months) and those who are older (2 months to 5 years) have been developed and validated. The transformative nature of these assessment tools is underappreciated because access to treatment of sick, young infants with clinical infection is still not readily available, thus limiting impact on neonatal mortality. The research under discussion in this special issue addresses this vital issue.

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Several large randomized clinical trials have demonstrated the effect of community/home-based newborn care intervention packages on reduction of neonatal mortality.[4–7] The common feature of these intervention packages is home visitation in the neonatal period, treatment of sick neonates and young infants by community healthcare workers and, when possible, facilitation of referral for sick neonates. There are several challenges to our ability to scale-up community care of neonates and young infants with clinical infection. The first relates to lack of consensus on who among the healthcare providers in rural communities can and should be allowed to provide treatment to neonates with clinical infection, and secondly, what are the efficacious and deployable treatment regimens that are acceptable to all stakeholders. Finally, who among the many sick newborns must be referred to higher level institutions for care, and how can we systematically enable the desired referral. It is important to note that to be credible, referral facilities must be capable of providing appropriate, affordable care without the current unacceptably high rates of hospital-acquired infections.

The World Health Organization (WHO) guideline for treatment of probable sepsis in young infants recommends a combination of injectable penicillin and gentamicin for 10 days.[8] This recommendation is for young infants who are deemed to have clinical infection, either pneumonia or probable sepsis, and covers the entire spectrum of severity of neonatal clinical infection.

In most communities in the developing world, sick young infants are assessed by trained healthcare providers in addition to physicians and classified as suffering from possible serious bacterial infection.[9] Application of current WHO guidelines requires referral of all these infants to a health facility for inpatient care. In effect, in less developed parts of the world, where referral may be either unaccessible or unacceptable to families, this leads to a situation where many young infants die without any or with delayed treatment. This poses an ethical dilemma. Moreover, it is unclear whether the current WHO regime is truly required for the treatment of neonatal infections of all severity. When neonates are assessed closer to home, the spectrum of severity includes many more with milder infections than is the case for those who present at facilities. The treatment regimens must be linked to these severity-based subcategories, so as to achieve the best balance between efficacy and deliverability.

An expert consultation on community-based approaches for neonatal sepsis management was held in London in 2007 to, "identify research that could accelerate the availability and use of safe, effective, affordable, simple and feasible community-based approaches for neonatal sepsis/infection among families with no or limited access to facility based care."[10] The London consultation and the subsequent interagency reviews concluded that more focused and large-scale clinical trials are required to achieve consensus on optimal treatment guidelines for neonatal clinical infections that make treatment accessible with little loss of efficacy, if any. Customization of treatment to the categories of fast breathing alone, the presence of any sign of systemic infection, and the critically ill infant all need to be explored.

This special issue describes the details of the several community-based regimens being evaluated through randomized controlled trials in South Asian and African countries.

WHAT ARE THE KEY FEATURES OF THIS NEW RESEARCH?

The regimens being evaluated represent consensus among researchers and practitioners from developed and developing countries. Interestingly, some of the trials are focused on young infants with only fast breathing, whereas others include sick infants with at least 1 danger sign suggesting severe clinical infection. The common objective is to establish equivalence with current WHO-recommended treatment regimens. A large trial size to provide precise estimates of efficacy is a common and valued feature of these trials. Given the policy implications of the research, it is important that the details of design, implementation, planned analysis, ethics as well as trial oversight by data safety monitoring boards be widely disseminated before analysis of results and their publication. This should contribute to a correct interpretation of the trial results as they become available and generate the required credibility so essential for consensus building and policy formulation.

There are several features of this research that merit recognition. The proposed regimens under evaluation are backed up with sound scientific rationale and set rigorous standards for demonstrating equivalence with the current best regimens. The innovation, though incremental, is important. The simplification in regimens has the potential to hugely increase compliance with community care. Finally, several lead agencies are working together and have adopted a remarkably democratic approach to consensus building, and to generating robust evidence through high-quality trials by experienced investigator groups of world class quality. The location of trial sites in multiple countries should ensure wide generalizability of findings. Finally, the oversight by the WHO will add to the credibility of the research.

The studies described in this issue are important and should extend and complement the pioneering innovations of home care, health worker assessment and classification tools and the recent availability of large numbers of trained community health workers in developing countries. We are optimistic that a well-orchestrated onslaught on the most important cause of neonatal death, clinical infection, is on the horizon.

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