

## Outpatient treatment for neonates and young infants with clinically suspected severe infection



The reduction in mortality in children younger than 5 years over recent decades has been impressive, but shortfalls still exist in achievement of the MDG4 targets.<sup>1</sup> Acceleration of progress for child survival would need increased emphasis on quality care at and around birth, and timely and efficacious treatment for neonatal infections, diarrhoea, and pneumonia in regions where these causes contribute substantially to mortality in children younger than 5 years. The challenge in provision of standard care is increased wherever health systems are weak, socioeconomic conditions are suboptimum, and settings are remote and inaccessible. Innovative implementation research is being widely promoted to provide solutions that improve equitable delivery of established interventions without compromising safety or effectiveness. This type of research is challenging and often complex.

In *The Lancet Global Health*, Abdullah Baqui and colleagues<sup>2</sup> report their findings from a large equivalence trial in Bangladesh, in which two antibiotic regimens were compared with the standard regimen (intramuscular injections of procaine benzylpenicillin and gentamicin once per day for 7 days) for treatment of clinically suspected serious infection in young infants (aged 0–59 days) who were treated in an outpatient setting after their parents sought help but refused hospital admission.

The two alternative regimens assessed were: intramuscular gentamicin once per day and oral amoxicillin twice per day for 7 days; and intramuscular procaine benzylpenicillin and intramuscular gentamicin once per day for 2 days, followed by oral amoxicillin twice per day for 5 days. Thus, compared with the 14 injections in the reference treatment, these regimens had reduced numbers of injections (seven and four, respectively). The primary outcome was a composite measure of treatment failure by day 8 of enrolment based on several individual indicators, and deaths were also carefully recorded.

The risk of treatment failure was 8% in each of the two alternative regimens, compared with 10% in the standard treatment group.<sup>2</sup> Risk of death by day 15 of follow-up was 2% in all treatment groups. This result was similar to the number of deaths in infants

who opted for hospital admission (2% in hospital and another 1% within one week of discharge). We believe that the equivalence of these regimens for the primary outcome was satisfactorily established in the type of patients enrolled. The case fatality rates were low overall and consistent with the similar failure rates across treatment arms.

What are the implications of these findings for child health programmes? In an ideal world, serious infections in neonates and young infants would be treated in medical facilities. However, the barriers to such care are overwhelming for millions of families in Asia and Africa. Facilities can be far away, often the services provided are of poor quality, and families might not be able to afford the related direct and indirect costs of care. Therefore, simplified outpatient treatment regimens in settings close to home make for a strong programmatic rationale for treatment of serious infections in young infants whose caregivers are unwilling or unable to accept hospital admission. Widespread acceptance of such a strategy needs rigorous and conclusive evidence for its feasibility, efficacy, and safety. In this respect, Baqui and colleagues should be complimented for designing and undertaking a high quality study that paves the way for adoption of this approach in health programmes.

Some limitations of the study, however, should be noted. The trial was not masked for practical reasons. The trial enrolled fewer infants younger than 7 days than older infants, and this subgroup might differ in terms of causes and outcomes. The study individuals were young infants whose families sought care but did not accept admission to hospital; the infants in the study might therefore represent a group with milder disease than that of those who accepted hospital admission.

In this efficacy trial, high compliance was achieved for all regimens, which were delivered at home through regular physician visits. Regardless of the regimen, compliance with treatment and monitoring might be better in hospitals than at home in real-life programmes. Our view is that referral and hospital admission should be promoted for sick neonates and young infants. The study results do, however, provide good evidence that when hospital admission is not feasible, and if simplified

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regimens can be delivered in outpatient settings, complications rates would be low and similar to those in hospitals.

Community-based management of infections in young infants that includes intramuscular injections every day for 7 or more days, given by trained health workers, has been studied and reported to be effective.<sup>3-5</sup> Regimens with reduced numbers of injections could be easier to deliver and have a substantial effect on young infant mortality. However, in many countries or subregions, even these simplified regimens might be challenging. The questions of who should give injections in primary care and outpatient settings, and at what level in the health-care system, remain unsettled in many developing countries.

Growing realisation exists that primary health centres need to be upgraded to become effective treatment facilities. The health-care providers deployed to them should be able to assess young infants whose parents seek care, arrange referral for hospital admission for those with possible serious infections, and when that is not acceptable to the families, they could offer ambulatory treatment using one of the study regimens in Baqui and colleagues' study.<sup>2</sup> The treatment provider could be a doctor (as in the study, but often not feasible), or an effectively trained health assistant, nurse, or auxiliary nurse midwife. This approach could particularly help female infants whose care-seeking is differentially undermined in many societies. For outpatient treatment to be effective, frontline treatment centres need to be predictably open and accessible to families, and have adequate supplies. The

interface between home and the treating health centre, and between the treatment provider and the hospital doctor, will need to be optimised and supported. Safety margins in care can be enhanced further through mobile phone communication wherever possible.

Overall, the innovative findings of the trial<sup>2</sup> are a valuable contribution, and a vital part of a whole solution in which other components must fall into place to have a noticeable effect on mortality in neonates and young infants. Studies such as these should motivate reflection and action.

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VKP was a member of the data safety monitoring board in Baqui and colleague's study. MKB declares no competing interests.

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