Simplified treatment of sick infants at risk of possible serious bacterial infection

Worldwide, approximately 2.6 million newborns died in 2016, or 7,000 each day. Five countries record half of all newborn deaths: the Democratic Republic of Congo (DRC), Ethiopia, India, Nigeria, and Pakistan. Premature birth, asphyxia, and neonatal infections are the main causes of mortality. Neonatal sepsis alone is responsible for 26% of all newborn mortality.¹ In the DRC, the mortality burden is 28 per 1,000 live births².

To treat infections in newborns and young infants (age 0 to 59 days), WHO recommends transferring them to a hospital and administering a regimen combining two injectable antibiotics, namely, penicillin or ampicillin, plus gentamicin for seven to ten days. In the DRC, national policy recommends hospitalization with a curative treatment containing a triple combination of injectable broad-spectrum bactericide antibiotics: injectable ß-lactamine (ampicillin) combined with an aminoside (gentamicin) and a third-generation cephalosporin (cefotaxim); in the event of any suspected anaerobe germs, metronidazol is added by intravenous injection.³ Implementation of this recommendation poses operational challenges because of the poor availability of organized and geographically accessible health facilities with integrated health services that can provide quality care to newborns.

¹ Ranjeva SL, Warf BC, Schiff SJ. Economic burden of neonatal sepsis in sub-Saharan Africa, 2018; http://dx.doi.org/10.1136/bmjgh-2017-000347
To find alternatives to the standard treatment protocol, several clinical trials involving simplified antibiotic regimens were conducted simultaneously in the DRC, Kenya, and Nigeria. The studies were wide in scope, including separately controlled and randomized trials. They compared therapeutic regimens in newborns and infants (0 to 59 days) who showed signs of infection and whose parents did not accept medical care at the referral level or were not able to transfer the infant. These trials found management of a possible serious bacterial infection (PSBI) in young infants in Africa is effective at the health center level when families do not accept referral to the hospital.

On the basis of these studies, WHO implemented a new directive that does not replace the management of PSBI patients in the hospital setting but that can be recommended for the treatment of infants who show signs of serious infection in settings where resources are limited or families either do not accept or are unable to access referral care. This directive allows for use of simple, safe, and effective antibiotic regimens for ambulatory treatment of serious clinical infections and rapid breathing problems (pneumonia) in children between 0 and 59 days old.

After adoption of the treatment protocol by DRC’s Ministry of Health (MOH), it was recommended that a demonstration site be set up before large-scale extension. The USAID-funded Integrated Health Project Plus (IHPplus), the Kinshasa School of Public Health (KSPH), WHO, and the Division Provinciale de Santé (DPS, or provincial health division) of Sud Kivu collaborated to test the application at 10 sites to manage neonatal infection when referral is not possible and to identify best practices, needs, and challenges before scale up.

**Approaches and Levels of Intervention**

The intervention takes place at the following levels:

**Community level:** Community health workers (CHWs) provide two home visits during pregnancy (in the first and third trimesters) to provide advice on hygiene and nutrition of pregnant women and three post-natal home visits on the first, third, and seventh day following birth to screen for signs of trouble in sick infants and direct those cases to health centers.

**Health center:** A nurse decides if the infant should be urgently referred or can be treated at the health center. If the child is referred, and if the referral is refused or is not possible, the nurse should reassess and reclassify the case and determine the appropriate treatment. Very sick infants should be monitored on the second day.

**Health zone central office:** The health zone management team is responsible for monitoring, monthly supervision, and provision of drugs.

**Steps to implementation**

At the national level, IHPplus held orientation meetings in coordination with the MOH and WHO to share the results of new studies and the new WHO guideline. These meetings led to the revision of two standard tools: the Integrated Management of Childhood Illness (IMCI) 0–2 months chart booklet and the case reporting form for infants with classifications based on WHO’s new guidelines.

**Identifying health zones and health areas**

Sud Kivu Province was selected because of its high rate of neonatal mortality (47 per 1,000 live births) and because of the presence of active Champion Communities in the IHPplus-supported Katana and Walungu health zones. In each health zone, the five health areas that reported the highest number of births were selected.

**Implementation at the Operational Level**

IHPplus provided technical and financial support to complete the following activities:

1. Train nurses in clinical IMCI for infants 0–2 months old, which incorporates the new guidelines for treatment of neonatal infection at the health center if referral is not possible
2. Provide drugs and medical supplies for infants
3. Train CHWs to make home visits to pregnant women and newborns to detect signs of trouble, orient patients on health care facilities, and promote good practices in nutrition and hygiene of newborns and pregnant women
4. Monitor and supervise trained staff through health zone management teams and DPS staff

**Training service providers**

Staff members of the national IMCI program and DPS, in collaboration with the KSPH and IHPplus, facilitated a three-day training of health center nurses. The nurses were trained in clinical IMCI for infants 0 to 2 months, of which the basic module contained the following elements:

- Assessment and classification of infants for PSBI or a very serious illness
- Determination of whether infants must be urgently referred to the hospital or could be treated at the health center level
- If referral is refused or not possible, the case is reassessed and reclassified and the appropriate treatment is determined

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*Tshefu A., Lokangaka A, Ngaima S, et al. Simplified antibiotic regimens compared with injectable procaine benzyl penicillin plus gentamicin for treatment of neonates and young infants with clinical signs of possible serious bacterial infection when referral is not possible: a randomized, open label, equivalence trial. Lancet 2015, 385(9979):1767-76*
In each health center, two service providers were trained to treat sick infants; four supervisors from the health zone central office monitored the training to be able to provide support to the service providers during supervision visits.

- The DPS team, supported by facilitators from the national level, facilitated a four-day community outreach training for registered nurses. The nurses took the training to better understand the roles and responsibilities of community outreach.

**Material and medicines**

WHO and IHPplus provided materials, such as gloves, the “neo-Natalie” mannequin, syringes, absorbent cotton, denatured alcohol, timers, thermometers, and baby-weighing scales. The project also supplied medicines, such as dispersible 250 mg amoxicillin and injectable 80 mg/2 ml gentamycin, to all facilities on a monthly basis.

**Supervision and monitoring**

The health zone central office conducts monthly supervision. The DPS team and service providers provided monitoring on a quarterly basis. IHPplus supported the MOH, which developed a monitoring and supervision guide for the community- and health-center levels to monitor integration and any challenges.

**Methodology of the Assessment**

The project conducted an assessment to understand what would be necessary to integrate PSBI activities into the minimum package of activities of the health center; it focused on two main study questions.

1. Are PSBI activities compatible with the minimum package of activities offered at the health center?
2. What do the community health workers, nurses in the health centers, and health zone central office staff members need to do their work better?

This descriptive analysis used a mixed approach (qualitative and quantitative). Data collection took place from April 26 to May 3, 2018, in six health centersrationally selected for their optimal accessibility relative to the Central Office: Ihimbi, Kabushwa, and Mugheri in the Katana health zone, and Bideka, Mulamba, and Nyanza in the Walungu health zone.

WHO guidelines for treatment of neonatal sepsis were compared with the guidelines of the DRC contained in the IMCI treatment manual and the IMCI chart booklet for the 0–2 month age range.

Information concerning qualitative data in relation to the number of infants with infections, and treatment was systematically examined in the log books of medical consultations and the case report forms of infants in the six health centers, starting from a framework. Data relative to live births were collected from the DHIS2.

Data about knowledge, attitudes, and practices were gathered for each health center from the nurse and CHWs present during the assessment team’s visit. Individual interviews were conducted using a guide designed for that purpose by one representative each from the DPS and the project. The data collected were organized, tabulated, and compared with live births.

**Results**

**Comparison of WHO Recommendations with DRC Guidelines**

Generally, the guidelines for the simplified management of sick infants at risk for PSBI when referral is not possible in the DRC are in conformity with those of the WHO. However, the DRC guidelines include home visits with pregnant women and add details about the frequency of visits. The dosage of amoxicillin was revised upward in the DRC guidelines (from 50 mg/kg for WHO to 75 mg/kg). For infants aged 0 to 59 days with a serious clinical infection, the DRC has chosen WHO option 2 and reiterates the basic concepts for the preparation of gentamicin.

<table>
<thead>
<tr>
<th>WHO recommendations</th>
<th>DRC guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Community outreach and home visits for prenatal and postnatal care</strong></td>
<td>CHWs perform two antenatal care home visits for the mothers, three postnatal care visits for term babies, or five visits for low birthweight babies. During home visits, CHWs provide advice to families on hygiene and nutrition for pregnant women and on detecting danger signs during pregnancy; they must examine infants for signs of potential illness and encourage and assist the search for appropriate care.</td>
</tr>
</tbody>
</table>
Option 1 is the preferred option, but in situations where the health system does not allow its implementation, option 2 can be considered. The Guidelines Development Group (GDG) felt that option 2 probably would be easier to offer, more equitable in terms of access, easier to monitor, easier to obtain, and with the same efficacy. It is expected that each country will adapt those recommendations to its own social, cultural, and economic context. Countries are encouraged to hold debates to inform decision makers on the use and introduction of recommendations into the national programs.

### Experience and Results of Implementation

Table 2. Data on the treatment of neonatal infections in six health facilities in Sud Kivu from January to March 2018

<table>
<thead>
<tr>
<th>Health zone</th>
<th>Health center</th>
<th>Number of live births</th>
<th>Number of infants with infections admitted to the health center</th>
<th>Number of parents accepting referral</th>
<th>Number treated according to simplified protocol at the health center</th>
<th>Number adhering to treatment at the health center</th>
</tr>
</thead>
<tbody>
<tr>
<td>Katana</td>
<td>Ihimbi</td>
<td>304</td>
<td>11</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Katana</td>
<td>Kabushwa</td>
<td>92</td>
<td>8</td>
<td>1</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Katana</td>
<td>Mugheri</td>
<td>63</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Walungu</td>
<td>Bideka</td>
<td>92</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Walungu</td>
<td>Mulamba</td>
<td>293</td>
<td>23</td>
<td>0</td>
<td>22</td>
<td>20</td>
</tr>
<tr>
<td>Walungu</td>
<td>Nyandja</td>
<td>47</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>891</td>
<td>62</td>
<td>1</td>
<td>60</td>
<td>57</td>
</tr>
</tbody>
</table>

All six health facilities use the simplified ambulatory therapeutic regimen for infant infection when referral is not possible. For the first quarter of 2018, the 6 health facilities registered 891 live births; 62 of them showed signs of neonatal infections and were brought to the health center; only one accepted referral; and 97% of the infants were treated with the aid of the IMCI 0 to 2 months forms and the chart book (which was called the “faithful friend” at the health-center level). Adherence to the treatment sought in the case report forms was 95%. No deaths were recorded among the infants treated at the health center; however, the child who was referred to the hospital was taken instead to a house of prayer and later died.

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1. Option 1 is the preferred option, but in situations where the health system does not allow its implementation, option 2 can be considered. The Guidelines Development Group (GDG) felt that option 2 probably would be easier to offer, more equitable in terms of access, easier to monitor, easier to obtain, and with the same efficacy. It is expected that each country will adapt those recommendations to its own social, cultural, and economic context. Countries are encouraged to hold debates to inform decision makers on the use and introduction of recommendations into the national programs.
When nurses were asked about providing care according to the new approach, they unanimously said that the new guidelines for treatment of neonatal infections at the health-center level have benefited them in their work; they had already been caring for these sick infants because referral is rarely accepted, but there were no support protocols and the results were not satisfactory.

“We are happy with the new orientation on infant care; in the past, the prescriptions were limiting, and we were forced to resort to referrals to the hospital; many parents went to the prayer houses and we lost many children. Now, if a mother does not accept referral to the hospital because of the distance and cost, we provide ambulatory care with simple drugs in precise doses; we recorded no deaths related to infant infection since implementation of the approach in our health area.”

Heath center nurse

The proportion of refusals for referrals is influenced by the fact that parents know that there are alternatives to treatment at the health center; they also fear separating the newborn from its mother and the challenges related to transport of the new parents in rural areas.

“It is difficult for parents to send women and children away from the village because they need someone to take care of the birth mother in the hospital, feed them, etc., and often they neglect the newborn if it is only the latter who is the problem.”

CHW

Discussion

The incidence of neonatal infection in the visited health areas is 70 per 1,000 live births (62 cases per 891 newborns); this rate is below the estimates of the expected incidence of infections in newborns and infants up to 60 days old for developing countries, which is 170 per 1,000 live births based on clinical diagnosis. This low rate reportedly is linked to the insufficient number of CHWs available to cover the entire health area; medical records not indicating the age of the child; and poor classification of case report forms, which explains why not all the forms were found. However, nurses estimate that they are receiving more and more cases of infection in newborns from CHWs compared to the time prior to those staff receiving training.

The proportion of parents who refused referral to the hospital (more than 98%) is significantly higher than that recorded by IHPplus, which is 18% for referred adult patients and children. According to interviews, it is possible that more parents refuse if they know there is an alternative at the health center.

However, it seems that parents are more aware of the signs of serious infection and the potential consequences.

The prenatal care home visits proposed in the DRC guidelines reinforce the link between the woman and the community through CHWs who are accepted by the family and can, confidently look for signs of trouble and infection in the newborn. The effectiveness of this approach is evidenced by the improvement in detection of cases and adherence to treatment.

Use of the protocol for simplified treatment of sick infants at risk of PSBI when referral is not possible is compatible with integration in the minimum packages of activities at the health-center level, specifically in the IMCI program. It does not require any additional tasks by nurses; however, monthly supervision visits are required to train the nurse to master this approach.

The program requires the continuous availability of the IMCI case report form for the 0 to 59 month age range, as well as the IMCI chart booklet in the consultation room.

Management tools and IMCI forms for the 0 to 59 month age group are available in all health facilities; antibiotics (250 mg dispersible amoxicillin and injectable gentamicin) were available in all health facilities, except in the Kabushwa health center, which ran out of dispersible amoxicillin 250 mg a week before the assessment team visited.

Quantification of commodities, such as dispersible amoxicillin, gentamycin, syringes, distilled water syringes, timers, thermometers, baby-weighing scales, etc., should be based on actual data from neonatal and other infections, including pneumonia, to account for actual demand for these commodities. Each village should have community outreach for monitoring; the number of CHWs should be based on the population, that is, one CHW per 1,000 inhabitants or 48 newborns per year, or one CHW per village, which permits the latter to cover all infants.

Recommendations

- Revise the required frequency of home visits for infants by CHWs with the elimination of the visit on the first day of birth because the newborn is still in the health facility
- Revise the National Health Information System and medical records by integrating the elements of data on infection of newborns
- Increase the number of CHWs to reduce their workload to 40 pregnant women per year
- Integrate the IMCI training package of 0 to 2 months with that of 2 months to 5 years and supply case report forms

“ Our health center serves more than 15,000 people and is located in a pretty hard to reach area. IHPplus training on detecting and treating sepsis has been particularly helpful. Thanks to the updated protocol we follow, we also know which cases can be treated safely at the health center and which cases should be sent to the hospital. …I think there is a good relationship between our health center and the CHWs. Following the IHPplus training, I ran a campaign with CHWs from the local villages to provide information to community members about the importance of coming to the health center for treatment. I’ve also trained CHWs in the signs of sepsis that they need to recognize. They know that when they see these signs, they should urge their clients to go to the community health center for treatment… When I first arrived three years ago, people would go to the traditional healers rather than rely on modern medicine from the health center. Now, their first impulse is to come to our health center for treatment. I’m so happy how this training has made me better at the work I do to support the community I serve!”

Ignace Koko Wanduma
Nurse, Mulamba health center, near Walungu