

Prophylactic use of antibiotics and reduced case fatality in measles infection

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Measles is currently responsible for 1.4 million deaths per year.¹ Virtually all of these deaths occur in developing countries and are related to complications of the disease. Little is known about measles complication rates in the general population in developing countries. However, hospital studies have shown that pneumonia, diarrhea and laryngitis are very common in severe and fatal cases of measles.^{2,3} A considerable part of these complications is of bacterial origin. Hence an effective antibiotic prophylaxis against bacterial infections could potentially prevent a large number of measles-related deaths. Use of antibiotics in the absence of bacterial infections may cause many problems, including pneumonia caused by nosocomial infections³ and increased antibiotic resistance. Nonetheless our recent experience with prophylactic antibiotics for measles cases in Senegal suggests that such use may be beneficial and that further studies are needed.

METHODS

Between 1983 and 1986 in Niakhar, a rural area of Senegal, we found measles mortality to be high, around 7% (Table 1).⁴ In 1987 in connection with a measles immunization trial in this area,⁵ active case detection and home visits were introduced and it was decided that all children younger than 3 years of age seen within the first 2 weeks of the onset of measles symptoms should be treated with the antibiotic trimethoprim-sulfamethoxazole for 7 days irrespective of whether they had signs of bacterial infection at the time of clinical examinations. Antibiotics were provided for older children only if they had signs of respiratory complications. Fever, diarrhea, stomatitis and conjunctivitis were treated as needed. Treatment

of measles cases with vitamin A as recommended by the World Health Organization was introduced in the beginning of 1992. Between mid-1987 and 1991 when case detection and home treatment was instituted, 87% (564 of 650) of the reported cases in the study area were seen by a physician. Most of the measles cases not seen by a physician occurred during visits outside the study area.

RESULTS

As shown in Table 1, the case-fatality rates (CFRs) adjusted for age declined 2-fold (mortality ratio, 0.41 (95% confidence interval (CI) 0.21 to 0.81)) between 1983 and 1986 and between 1987 and 1991 when antibiotics were introduced for prophylaxis and treatment. Given the low CFR already attained from 1987 to 1991, the systematic use of vitamin A introduced in 1992 did not contribute significantly to further reduction in the case-fatality ratio (mortality ratio (1992/1987 to 1991), 0.72 (95% CI 0.22 to 2.38)).

This decline in CFR could be related to treatment with antibiotics or to other factors such as improved general medical care or improvements in socioeconomic status. Therefore we examined the effects of antibiotics in detail. Measles cases were detected through a systematic weekly morbidity surveillance in the whole study area of 26 000 people.⁵ Once cases were detected, homes were visited at least once a week. The prevalence of respiratory symptoms in children younger than 15 years of age was high in the second week after the onset of symptoms. Therefore we examined the effect of prior treatment with antibiotics on these symptoms (Table 2). Children younger than 3 years of age who had received prophylactic antibiotics during the first week were less likely to have respiratory symptoms than children of the same age group who had not received antibiotics and were seen for the first time on Days 8 to 15 of illness (relative risk, 0.37 (95% CI 0.15 to 0.94)). Among the older children for whom antibiotics were used only for treatment of complications, those treated during the first week did not have fewer respiratory symptoms at Days 8 to 15 compared with those not treated with antibiotics during the first week (relative risk, 1.39 (95% CI 0.70 to 2.76)) (Table 2).

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TABLE 1. CFRs in measles infection according to age and period

| Age (Years) | CFR (%) | | |
|-------------|----------------|--------------|-------------|
| | 1983-1986 | 1987-1991 | 1992-1993 |
| 0 | 11.5 (19/165)* | 2.2 (1/45) | 5.6 (2/36) |
| 1-2 | 12.1 (58/480) | 5.7 (5/87) | 0.0 (0/38) |
| 3-4 | 5.0 (16/321) | 0.0 (0/66) | 0.0 (0/39) |
| 5-9 | 1.2 (5/407) | 1.2 (3/257) | 0.0 (0/158) |
| 10+ | 0.0 (0/127) | 0.5 (1/195) | 2.2 (2/91) |
| Total | 6.5 (98/1500) | 1.5 (10/650) | 1.1 (4/362) |

* Numbers in parentheses, deaths/number of cases.

DISCUSSION

Even though this study is not an unbiased evaluation, it suggests that prophylactic use of antibiotics in young children might reduce respiratory complications in the later part of the acute phase at a time when these are likely to be a result of bacterial superinfections. Being seen by the physician in the first or only in the second week of infection could reflect a selection bias. However, it is more likely that the time of detection is a result of random events in the onset of measles, the timing of routine visits and reporting delays in the surveillance system. In the Niakhar study clinical events were counted from the onset of symptoms rather than from the onset of the rash; the first 4 days of symptoms of measles would correspond approximately to the prodromal period and Days 5 to 11 to the first week after the onset of rash. During the prodromal period many cases would not be detected by parents and the surveillance system. Thus it is only during Days 5 to 11 that all cases are likely to be detected by a routine weekly surveillance system. A similar beneficial tendency as reported in Table 2 was found when the analysis was limited to children younger than 3 years of age seen during the first week after the rash. Children treated with prophylactic antibiotics during the first 3 days (Days 5 to 7) had a lower frequency of respiratory complications at Days 8 to 11 (3 of 18) than the children seen for the first time at Days 8 to 11 (7 of 19) (relative risk, 0.45 (95% CI 0.14 to 1.49)).

TABLE 2. Frequency of respiratory complications seen in second week after onset of symptoms of measles according to age and the use of antibiotics during the first week of symptoms: Niakhar, 1987 to 1991

| Age (Years) | Antibiotics Given in First Week | No. with Respiratory Complications at Days 8-15 |
|-------------|---------------------------------|---|
| 0-2 | Yes* | 7 /62 (11.3)† |
| | No | 7 /23 (30.4) |
| 3-14 | Yes‡ | 8 /42 (19.1) |
| | No | 40/292 (13.7) |

* Given to all children seen.

† Numbers in parentheses, percent.

‡ Given only to those with signs of respiratory complications. Children were included only once even if seen several times during Days 8 to 15.

Hence prophylactic use of antibiotics may contribute to the prevention of severe and life-threatening respiratory disease in children with measles in developing nations. Because there is a need for improved management of the many cases of measles infection seen at the primary care level in developing countries, it seems warranted to conduct randomized trials to evaluate prophylactic use of antibiotics.

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