analogues in patients with advanced HIV disease who have previously undergone treatment with multiple RT inhibitors. Further studies are needed to confirm this observation. Alternative agents, such as the new protease inhibitor indinavir, seem to be more potent than lamivudine, causing a more pronounced decline in the viral load and a greater increase in the CD4+ cell count. Changes in these parameters within a short time after beginning therapy have been associated with a reduced risk of clinical progression using other antiretroviral drugs (4, 5). Differences in the activity of indinavir and lamivudine, which target different viral enzymes, might be markedly increased in patients with previous heavy exposure to RT inhibitors. In such patients conformational changes induced in the RT viral enzyme by the accumulation of aminoacid substitutions secondary to mutations causing drug resistance could further decrease the inhibitory activity of new RT inhibitors (so-called convergent therapy). In this situation, the addition to the treatment regimen of new drugs targeting other viral enzymes, such as protease inhibitors, should be more effective (so-called divergent therapy).

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References


Survey on Rotavirus Infections in a German Pediatric Hospital

Rotavirus is the most common cause of infectious diarrhea in children worldwide. Especially in developing countries, rotavirus infections contribute considerably to morbidity and mortality in young children (1). One-third of all deaths in children younger than 5 years of age in these countries are diarrhea-related. Epidemiological data from developed countries, e.g., the USA, Canada and Great Britain (2-4), indicate that diarrhea plays an important role regarding not only mortality but morbidity as well. Reliable data on rotavirus infections in Europe are available from only a few countries (4-6). Since an effective rotavirus vaccine is available (7) and introduction of the product in the European Union is under consideration, further epidemiological data from European countries are needed. In order to add to the limited existing data from Germany, we performed a retrospective hospital-based analysis.

Charts and laboratory journals from the University Children’s Hospital Freiburg were screened for infectious diarrhea and Salmonella and rotavirus etiology from July 1994 through June 1996. The hospital is a tertiary care center that serves an urban and rural population of roughly 400,000 inhabitants. The charts of hospitalized patients were checked for the ICD-9 coded diagnosis of gastroenteritis as a first or second diagnosis on admission and on discharge. In patients with more than one hospitalization for infectious diarrhea, only the first episode was evaluated. The laboratory journals were checked for stool specimens positive for rotavirus antigen (Pathfinder; Kallestadt, USA) or Salmonella spp. Standard bacteriological procedures were used to detect salmonellae. The duration of hospitalization in days was recorded for all patients with diarrhea and was analyzed separately according to rotavirus or Salmonella etiology.

During the investigation period, a total of 10,966 children had been hospitalized, 925 (9%) of them for infectious diarrhea. Children under 4 years of age accounted for 37% of all hospitalized children and for 75% of children with gastroenteritis. Rotavirus was the etiological agent in 51% of cases in children under 1 year of age and
in 41% of children under 4 years of age. *Salmonella* spp. accounted for 1 and 4%, respectively (Figure 1). No death due to rotavirus infection was recorded. There was a higher prevalence of both gastroenteritis and rotavirus etiology during the winter months, especially in children under 1 year of age. In the first winter season, December and January were the peak months. In the following winter season, most rotavirus-associated cases were recorded during February and March. The median duration of hospitalization for patients with gastroenteritis was four days (mean 4.7); for those with rotavirus-associated diarrhea, five days (mean 5.5); and for those with *Salmonella*-associated diarrhea, five days (mean 5.3). Rotavirus-associated diarrhea in infants caused a median hospital stay of six days (mean 5.8 days); in children between 1 and 2 years of age, five days (mean 4.9 days); in children between 2 and 4 years of age, four days (mean 4.3 days); and in children over 4 years of age, four days (mean 5.1 days). Altogether, rotavirus gastroenteritis accounted for 3350 hospital days during the two-year period.

Our data indicate that infectious diarrhea is a significant cause of morbidity in Germany, especially in children under 4 years of age. Rotavirus is the predominant pathogen in this age group, accounting for the vast majority of hospitalizations due to diarrhea with a defined etiology. In all age groups it outnumbered other etiologies like *Salmonella* spp., the most frequent bacterial pathogen, by a wide margin. This is in accordance with data from other developed countries (8, 9). The incidence of rotavirus infection is actually higher than the number of hospitalized cases, with the additional cases being treated as outpatients by general practitioners. These patients are, in most cases, cared for by one parent who must then be absent from work. Thus, the disease burden of rotavirus gastroenteritis in terms of economic loss is even higher than that estimated by the hospitalization data. In addition, since the inclusion criterion for our study was the diagnosis of diarrhea on admission as well as on discharge, it is likely that a relevant cohort of hospitalized patients who acquired a nosocomial rotavirus infection during their hospital stay were missed. In such cases, hospitalization is supposed to be prolonged, causing additional morbidity, especially in young infants (10). In conclusion, the data regarding the frequency and duration of hospitalization of children with rotavirus-associated diarrhea obtained from a tertiary care center in Germany, leads us to believe that a rotavirus vaccine is of medical and economic interest. However, to obtain a more reliable basis for calculations in Germany, a prospective multicenter study is required.

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References