Letter to the Editor

Relative Efficacy of Trimethoprim-Sulfamethoxazole and Nalidixic Acid for Acute Invasive Diarrhea

An epidemic of bacillary dysentery caused by multiply resistant Shigella dysenteriae type 1 swept through all the districts of West Bengal in 1984 (S. C. Pal, Letter, Lancet 1:1462, 1984), providing us the opportunity to evaluate the efficacy of two drugs in the treatment of invasive diarrhea, particularly shigellosis. Male patients over 5 years of age admitted to the Infectious Diseases Hospital, Calcutta, with blood-mucus diarrhea between June 1984 and December 1985 were randomly assigned to one of the two treatment groups, viz., trimethoprim-sulfamethoxazole (TMP-SMX) or nalidixic acid (NA). One of the investigators, who had no knowledge of the drug administered, recorded the different clinical parameters of response. Fresh stool samples from all the patients included in this study were bacteriologically screened by previously described methods (2) for Shigella spp., Campylobacter spp., Vibrio parahaemolyticus, and enteroinvasive Escherichia coli. The susceptibility of Shigella spp. isolated in this study to various drugs was determined by the Kirby-Bauer disk method (1).

The 60 cases (30 patients in each treatment group) investigated in this series were classified according to the severity of illness as severe (stool frequency, ≥15/day), moderate (stool frequency, 8 to <15/day), and mild (stool frequency, <8/day). In the NA group, 13 cases were severe, 11 were moderate, and 6 were mild, while in the TMP-SMX group there were 12, 9, and 9 severe, moderate, and mild cases, respectively. The patients in the two groups were comparable on admission with respect to age, duration of illness, stool frequency, fever, abdominal pain, tenesmus, anorexia, and vomiting.

Of the 60 patients, 18 were positive for Shigella spp. (12 were positive for S. dysenteriae type 1, 5 were positive for S. flexneri, and 1 was positive for S. boydii). There were 10 positive cases of shigellosis in the NA group and 8 in the TMP-SMX group. Shigella isolates from the 10 patients administered NA were found to be uniformly susceptible to the drug. There was no failure in this group. In contrast, among the eight Shigella-positive patients in the TMP-SMX group, five excreted strains resistant to the drug. Two of these patients, whose illness was severe, failed to respond to the drug and were subsequently successfully treated with NA. Despite excreting strains resistant to TMP-SMX, the three remaining patients (one each with mild, moderate, and severe illness) recovered when treated with this drug. In such cases, the drug possibly did not assist recovery at all, since mild-to-moderate cases of shigellosis are generally self-limiting; perhaps other body mechanisms play an important role in modifying in vivo drug action. However, mention deserves to be made that recovery in the severe case was delayed. The antimicrobial susceptibility pattern of the Shigella strains isolated in this study was: nalidixic acid, 100%; TMP-SMX, 38.9%; gentamicin, 83%; furazolidone, 77.7%; ampicillin, 38.8%; streptomycin, 0%; tetracycline, 0%; and chloramphenicol, 0%.

The responses to therapy with both drugs were compared according to the severity of illness. Patients with severe illness belonging to the NA group had significantly shorter duration of fever (1.7 versus 2.7 days; \(P < 0.001\)), abdominal pain (2.2 versus 2.8 days; \(P < 0.01\)), and presence of blood (2.6 versus 3.6 days; \(P < 0.01\)) and mucus (3.3 versus 4.1 days; \(P < 0.01\)) in the stool than those receiving TMP-SMX. There was, however, no significant difference in these parameters among patients with mild and moderate illness in both the study groups. Based on the results of this study, it appears that NA is a superior alternative to TMP-SMX in the treatment of shigellosis, especially in situations in which TMP-SMX-resistant isolates are widely prevalent. However, we recommend the use of NA only for the treatment of severe cases of shigellosis. Indiscriminate use is likely to foster emergence of NA-resistant strains.

LITERATURE CITED


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