特別企画　“ウイルス性下痢症の予防を考える”（5）

Randomized placebo-controlled clinical trial of immunoglobulin Y as adjunct to standard supportive therapy for rotavirus-associated diarrhea among pediatric patients

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This study aims to evaluate the effect of hyperimmune immunoglobulin Y (IgY) against human rotavirus (HRV) among pediatric patients receiving standard supportive treatment for rotavirus-associated diarrhea mostly with an enteric non-cholera co-pathogen in a hospital setting. Two natural HRV reassortant clinical strains ATCC VR 2273 and ATCC VR 2274 were used as mixed immunizing antigens in poultry hens to generate anti-HRV IgY (Rotamix IgY). The control or placebo IgY was prepared using tissue culture medium from mock-infected MA104 cell line as antigen. In vitro, Rotamix IgY exhibited multi-serotypic cross neutralization activities along with synergistic effects against major global serotypes G1, G2, G3, G4 and other human or animal rotavirus strains when compared with mono-specific IgY. Suckling mice pre-treated orally once with Rotamix IgY and then challenged with rotavirus 3 hr later showed a significant dose-dependent reduction in frequency ($P<0.05$) and duration ($P<0.05$) of diarrhea compared to placebo IgY-treated mice. Out of 114 children aged between 3 and 14 months and with diarrhea upon admission in a Myanmar hospital, 54 dehydrated and rotavirus-positive children were randomized into Rotamix IgY group and placebo IgY group. Of these, only 52 children had complete data with n=26 children per study group. Ninety-two percent of patients in each of these groups were positive for co-infecting enteric pathogen. The patients were monitored for volume and duration of oral rehydration fluid (ORF) and intravenous fluid (IVF) intake, daily stool frequency, overall duration of diarrhea, frequency and duration of rotavirus shedding. Compared to placebo IgY group, the Rotamix IgY group had statistically significant reduction in mean ORF intake ($p=0.004$), mean duration of intravenous fluid administration ($p=0.03$), mean duration of diarrhea from day of admission ($p<0.01$) and mean duration of rotavirus clearance from stool from day of admission ($p=0.05$). Overall, our novel approach using oral Rotamix IgY for rotavirus-infected children mostly with non-cholera enteric pathogen co-infection appears to be a promising, safe and effective adjunct to management of acute diarrhea in pediatric patients.