During a period of 5.5 years, examinations of bone marrow for proven or suspected malignant disorders were supplemented with screening for parvovirus B19 DNA with a qualitative PCR. Positive samples were then analyzed with the quantitative PCR [1]. Informed consent to participate in the study was obtained from the children or their guardians. The study was approved by the ethical committee at Karolinska Institutet (Stockholm, Sweden).

A total of 229 bone marrow samples from 123 children who underwent bone marrow examinations were collected. Overall, 9 (7%) of 123 patients were positive for B19 DNA, and 8 of those 9 had test results positive for B19 DNA at the time of diagnosis of the underlying disease. No additional underlying immunodeficiency or previous blood transfusion was recorded. Consecutive samples were available from 4 of the B19 DNA–positive patients (2–7 samples per patient), and the outcomes were recorded for 5–32 months. B19 DNA was, in one instance, persistently detected for 24 months after diagnosis of the underlying disorder, all but 2 of the B19 DNA–positive patients experienced multiple episodes of fever and severe long-standing cytopenias that required multiple blood transfusions (range, 5–60 transfusions).

Except for studies involving children with ALL, little information is available on the influence and persistence of B19 infection among children with malignancies [1–6]. In the present study, 7% of children with malignant or hematological disorders were found to be B19 DNA positive and this infection likely contributed to some of the severe cytopenic periods observed. Viral load was detected in high titers, and some children had prolonged periods of detectable B19 DNA. Owing to the multiplicity of these underlying diagnoses, no statistical comparison was possible for B19-infected versus uninfected individuals, as was done in our previous study involving children with ALL [4]. However, that study served as the basis for our contention that screening with PCR for B19 DNA in bone marrow samples is clinically important for all children with malignancies, not only for early detection and treatment of the infection but also for limiting the effects of associated complications. Future studies will hopefully clarify the clinical relevance of viral load levels in different patient categories, at which levels to initiate antiviral treatment, and whether analyses of serum samples is as sensitive as analysis of bone marrow samples. Considering the notable number of B19 DNA–positive children in our relatively small but significant study, we suggest that quantitative PCR testing is a useful differential diagnostic tool in these patient categories.

Acknowledgments

Financial support. The Stockholm City Council/Karolinska Institutet, Swedish Children’s Cancer Foundation, and the Tobias Foundation. Potential conflicts of interest. All authors: no conflicts.

References

children undergoing intermittent hemodialysis (HD). Contrary to the recommendation from Robson et al [2] to dose after alternate HD sessions [2], we suggest to dose oseltamivir in children (age, >1 year) after each HD session (7.5 mg for children weighing ≤15 kg, 10 mg for children weighing 16–23 kg, 15 mg for children weighing 24–40 kg, and 30 mg for children weighing >40 kg).

We have based this recommendation on 2 main arguments. First, dosing after alternate dialysis sessions leads to a low plasma concentration of oseltamivir carboxylate from the first HD session after the dosing until the next dosing, which is a period of ∼48 h. Even though the total area under the curve is appropriate, the plasma concentration during this latter 48 h may be suboptimal. Second, safety analysis of oseltamivir has shown that high plasma concentrations are generally well tolerated [3] and may even be more effective than low concentrations [4].

To test our dosing schedule, plasma concentrations of oseltamivir carboxylate were measured using a validated liquid chromatography tandem mass spectrometry (LC-MS/MS) method (PRA International) in 3 children undergoing HD with suspected H1N1 infection. Blood samples, obtained from patients after a median of 2 days treatment, were taken just before and after an HD session to define extracorporeal elimination.

Results from the analysis are presented in Table 1. All patients recovered well, and none of the patients experienced any adverse effects as a result of the treatment.

Our data show that plasma concentrations are attained at the lower end of an adult reference population [2] and that extracorporeal elimination is higher than expected (>80%).

We present the first data on oseltamivir dosing in children undergoing HD [5]. These data illustrate the appropriateness of our dosing schedule, and the high extracorporeal elimination indicates the need to supply a dose of oseltamivir after each HD session to prevent subsequent subtherapeutic exposure [2, 5]. Obviously, 3 patients are not enough to provide adequate evidence for our schedule, but in the clinical setting, we are confronted with children undergoing HD who need adequate and safe oseltamivir treatment. This forces us to define a dosing schedule on the basis of sparse data. We hope that more data will become available to define the best oseltamivir dosing schedule for this vulnerable patient cohort.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

Michiel F. Schreuder,1,*
Michiel van der Flier,2,3 Noël B. Knops,4
Linda Koster-Kamphuis,1 and Roger J. Bruigemmann4

1Department of Pediatric Nephrology, 2 Department of Pediatrics, Infectious Diseases and Immunology, 3Nijmegen Institute for Infection, Inflammation and Immunity, and 4Department of Clinical Pharmacy, Radboud University Nijmegen Medical Centre, Nijmegen, and 5Clinical Study Group Nephrology, Medicines for Children Research Network, Amsterdam, the Netherlands; and 6Department of Pediatric Nephrology, University Hospital Leuven, Leuven, Belgium

References


Timely Administration of Antivirals for Pandemic (H1N1) 2009 Influenza

To the Editor—As part of a study on pandemic (H1N1) 2009 in patients hospitalized at our institution from 1 May through 30 June 2009, we evaluated antiviral prescribing practice and its timeliness. All study patients had positive test results for pandemic (H1N1) 2009 with use of an in-house reverse transcription polymerase chain reaction (RT-PCR), and