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positive PCR results were suspected of harboring B19 infection on the basis of clinical assessments [1]. Yet, retrospective review showed that the B19-associated cytopenias significantly prolonged periods of unwanted interruption of chemotherapy, necessitated more blood transfusions, and compelled more bone marrow examinations. Our purpose here was to extend those findings by studying children with other malignancies or hematological disorders.

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, and viral loads consisted of up to \(8.7 \times 10^7\) copies/mL. According to a review of medical records, none of the B19 infections were suspected on clinical grounds, and the infections were not clustered during any given time of year or epidemic period. Serum samples that had been collected at the time of the first bone marrow sample collection were available from 27 of these children. Of these 27 children, 13 (48%) were B19 immunoglobulin G positive, whereas only 1 was B19 immunoglobulin M positive. During the 6 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.

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Potential conflicts of interest. All authors: no conflicts.

References


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Oseltamivir Dosing in Children Undergoing Hemodialysis

To the Editor—With the advent of the new influenza A (H1N1) virus, the need for antiviral treatment has increased, especially in vulnerable patients, such as patients undergoing dialysis [1]. For adult patients, Robson et al [2] have provided a guideline for dosing of oseltamivir, whereas for children undergoing dialysis, such data are lacking.

On the basis of data from Robson et al [2], we formulated a dosing schedule for
children undergoing intermittent hemo-
dialysis (HD). Contrary to the recom-
mendation 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 chil-
dren weighing 16–23 kg, 15 mg for chil-
ren weighing 24–40 kg, and 30 mg for chil-
dren weighing >40 kg).

We have based this recommendation on
2 main arguments. First, dosing after al-
ternate dialysis sessions leads to a low
plasma concentration of oseltamivir car-
boxylate 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 anal-
ysis of oseltamivir has shown that 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 ad-
equate evidence for our schedule, but in
the clinical setting, we are confronted with
children undergoing HD who need ade-
quate evidence for our schedule, but in
the clinical setting, we are confronted with
children undergoing HD who need ade-
quate 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.

Our data show that plasma concentrations
are attained at the lower end of an adult
reference population [2] and that extrac-
orporeal elimination is higher than ex-
pected (>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 ade-
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Timely Administration
of Antivirals for Pandemic
(H1N1) 2009 Influenza

To the Editor—As part of a study on
pandemic (H1N1) 2009 in patients hos-
pitalized at our institution from 1 May
through 30 June 2009, we evaluated an-
tiviral prescribing practice and its timeli-
ness. 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

Table 1. Characteristics of 3 Children undergoing Hemodialysis (HD) and Treated with Oseltamivir

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, years</th>
<th>Sex</th>
<th>Body weight, kg</th>
<th>Diagnosis</th>
<th>Endogenous creatinine clearance, mL/min/1.73 m²</th>
<th>HD treatment</th>
<th>Oseltamivir carboxylate plasma concentration before HD session, ng/mL</th>
<th>Oseltamivir carboxylate plasma concentration after HD session, ng/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>3</td>
<td>M</td>
<td>15</td>
<td>Denys-Drash syndrome, bilateral nephrectomy</td>
<td>0</td>
<td>For 3 h 4 times per week; Fresenius F4HPS dialyser; effective bloodflow, 100 mL/min</td>
<td>660</td>
<td>133</td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>M</td>
<td>24</td>
<td>Posterior urethral valves</td>
<td>5</td>
<td>For 3 h 3 times per week; Fresenius FXS dialyser; effective bloodflow, 100 mL/min</td>
<td>207</td>
<td>37.3</td>
</tr>
<tr>
<td>C</td>
<td>11</td>
<td>F</td>
<td>34</td>
<td>Interstitial nephritis</td>
<td>2</td>
<td>For 4 h 3 times per week and for 3 h 1 time per week; Fresenius FX5 dialyser; bloodflow, 225 mL/min</td>
<td>419</td>
<td>60.7</td>
</tr>
</tbody>
</table>