CORRESPONDENCE

PROPHYLACTIC HEPARIN IN APL

To the Editor:

In a recent article, Goldberg and colleagues presented the Brigham and Women’s Hospital and Dana Farber Cancer Institute’s experience in managing acute promyelocytic leukemia (APL) without heparin. They also analyzed historical data and concluded “that the coagulopathy associated with APL can be successfully managed with intensive chemotherapy and blood product support” and that “the necessity for the inclusion of prophylactic heparin therapy into the remission induction regimens of all patients with APL has not been proven.”

Although the benefit of prophylactic heparin in APL is unproven, the thrust of the article made a case against the use of heparin and by its title (“Is heparin administration necessary during induction chemotherapy for patients with acute promyelocytic leukemia?”) suggested the exclusion of heparin in the management of these patients. Because of flaws in the study and in the authors’ analysis of previous studies, however, one can make no conclusion about the use of heparin in patients with APL based on this article.

In presenting their own data, the authors demonstrate a complete remission rate comparable to that of series that have included heparin in conjunction with anthracycline-based chemotherapy. This, they state, suggests the exclusion of heparin in the management of these patients. Because of this, it is difficult to compare their data with the literature.

To support their conclusions, the authors present a series of data from eight studies. They state that their comparison was limited to anthracycline-based protocols, yet 13 of 60 patients treated by Kantarjian and colleagues did not receive anthracyclines. Four additional hemorrhagic deaths among patients treated without heparin were not included in the analysis when that stipulation was applied to another study.

Furthermore, nine deaths included among the hemorrhagic deaths of patients treated with heparin occurred during aplasia, at which time the heparin should have been discontinued. The data from Cunningham and co-workers were incorrectly reported. Correcting for these discrepant values (Table 1) gives a hemorrhage-related death rate of 15% in patients treated with heparin and of 29% in patients managed without heparin during induction therapy.

Although we agree that no definite evidence shows heparin to be a necessary component in the treatment of APL, heparin clearly has not been shown to be deleterious in this setting, despite the authors’ legitimate concern regarding the administration of heparin to “thrombocytopenic, critically ill patients.” Confirmation of risk factors predicting for a hemorrhagic diathesis, such as absolute blast count or α2-plasmin inhibitor level, as has recently been suggested, could identify those patients most in need of treatment of their coagulopathy with heparin and/or epsilon-aminocaproic acid.

We agree with the authors’ final conclusion that a prospective randomized trial is required. Only by this type of analysis can the optimal management of acute promyelocytic leukemia be determined.

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REFERENCES


Table 1. Effect of Heparin on Incidence of Hemorrhagic Deaths in Adults with APL During Induction Chemotherapy

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total Patients</th>
<th>With Heparin</th>
<th>Without Heparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drakpin et al</td>
<td>34</td>
<td>20 (60%)</td>
<td>14 (40%)</td>
</tr>
<tr>
<td>Ruggero et al</td>
<td>10</td>
<td>5 (50%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Daly et al</td>
<td>10</td>
<td>5 (50%)</td>
<td>5 (50%)</td>
</tr>
<tr>
<td>Collins et al</td>
<td>7</td>
<td>4 (57%)</td>
<td>3 (43%)</td>
</tr>
<tr>
<td>Bernard et al</td>
<td>13</td>
<td>7 (54%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Cordonnier et al</td>
<td>57</td>
<td>35 (61%)</td>
<td>22 (39%)</td>
</tr>
<tr>
<td>Cunningham et al</td>
<td>50 (54)</td>
<td>28 (56%)</td>
<td>22 (44%)</td>
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<td>Kantarjian et al</td>
<td>31</td>
<td>16 (52%)</td>
<td>15 (48%)</td>
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<tr>
<td>Goldberg et al</td>
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<td>2 (100%)</td>
</tr>
</tbody>
</table>

Total 175 26 (15%) 124 36 (29%)
Prophylactic heparin in APL [letter]

AP Venook, MA Shuman and L Corash