Paediatric oncology and intensive care treatments: changing trends

Isaac N Keengwe, Francesca Stansfield, Osborn B Eden, Nicholas D Nelhans, Oliver R Dearlove, Andrew Sharples

Abstract

Objectives—To review the outcome of patients with childhood malignancy requiring intensive care treatment and to assess whether there is any secular trend for improved outcome.

Design—Retrospective chart reviews of 74 consecutive admissions to a paediatric intensive care unit from a regional paediatric oncology centre between 1990 and 1997. During the same period there were 6419 admissions to the oncology unit, 814 of whom were new cases.

Results—The overall survival at discharge from the intensive care unit was 49 of 74. Patients with either systemic or respiratory infection requiring ventilation had the poorest survival (13 of 31) whereas postoperative patients had the best survival (15 of 15). However, patients with respiratory or systemic infection who required inotropic support with more than three agents all died compared with about one quarter of those needing no inotrope. All patients with systemic or respiratory infective illness were neutropenic and positive microbiological identification was possible in 13 of 21 and five of 18, respectively. Non-survivors had a higher mean acute physiology and chronic health evaluation system (APACHE-II) score than survivors (24.2 v 15.94, respectively) but no patient with a score of > 27 survived.

Conclusion—Compared with previous series, there has been a great improvement in survival of oncology patients admitted to the intensive care unit especially those with either systemic or respiratory infection needing ventilation. Full intensive care treatment should be provided for these patients.

Keywords: intensive care; oncology; haematology; inotropic support; ventilation; survival

Patients and methods

This is a retrospective review of all paediatric oncology patients who were admitted to the PICU at the Royal Manchester Children's Hospital between August 1990 and August 1997. This hospital offers both a regional oncology and intensive care service to the north west of England and some adjacent districts. The oncology unit is the third largest in the UK with about 120 new referred cases each year (10% of the UK total). During our study period there were 6419 admissions to the oncology unit 814 of which were new cases. Patients were admitted to the PICU for cardiovascular and/or respiratory support but occasionally for invasive monitoring. The diagnosis of systemic infection was made if fever, peripheral circulatory collapse, and signs of focal infection with or without bacteriological confirmation were present. The diagnosis of circulatory collapse was based on hypotension (mean arterial blood pressure < 2 SD below the mean for age), poor perfusion (cold, pale extremities, with capillary refill time of > 3 seconds), hypoxaemia (P_{aO2} < 60 mm Hg in 40% O_{2}), and persistent metabolic acidosis (pH < 7.3 with a base deficit of > 6). The oncologists ensured uniformity in the treatment provided by having standard policies...
for the management of all oncological malignancies and their complications. The list of oncology patients admitted to the PICU was obtained from the PICU admissions book. Data were collected from the hospital records, which detailed each patient’s personal details, diagnosis, previous treatment, reason for admission to the PICU, treatment received in the PICU, and outcome. One researcher (FS) collected all the data to minimise recorder bias. The worst physiological variables recorded during the first 24 hours of admission to the PICU were used to determine the acute physiology and chronic health evaluation system (APACHE-II) scores. Patients were categorised as non-survivors and survivors depending on the outcome at the time of leaving the intensive care unit. The Student’s t test was used to compare the mean APACHE-II scores between survivors and non-survivors. A result was considered as significant when p < 0.05.

Results

There were 74 oncology admissions to the PICU during our study period, comprising 42 boys and 32 girls, with a mean age of 5.4 years (range, 1 month to 16 years). These PICU admissions accounted for 1.2% of the total admissions, or 11% of new referrals, to the oncology unit over the same period.

Table 1 shows the underlying oncological diagnoses and survival rate and table 2 shows survival in relation to reason for admission. The overall survival at discharge from the PICU was 49 of 74. All patients admitted with infective illness (systemic or respiratory) were neutropenic. Positive identification of the causative organisms was possible in 13 of the 21 patients with systemic infection compared with five of the 18 patients with respiratory infection.

Twenty one patients had systemic infection, 13 of whom survived, whereas only eight of the 18 patients admitted with respiratory infection survived. Patients with infective illness requiring ventilation had the poorest survival rate (13 of 31) whereas postoperative patients had the best survival (15 of 15).

Inotropic support was required in 21 of the 34 patients with infective illness. None of the patients who required more than three inotropic agents survived in contrast to approximately one quarter of those in whom no inotrope was needed (fig 1).

Eleven patients had neurological disease (six intracranial tumours and five acute lymphoblastic leukaemia (ALL) associated with central nervous system involvement). Four out of the six survivors had subsequent neurological deficits related to either the primary disease or the immediate cause of admission to the PICU.

Tumour mass effect resulting in respiratory compromise was seen in four patients having the following diagnoses: non-Hodgkin’s lymphoma, neuroblastoma, yolk sac tumour, and teratoma. Other admissions included acute myeloid leukaemia (AML) with cardiac arrest, Hodgkin’s lymphoma with tumour lysis syndrome, and ALL with cardiac tamponade.

The mean (median) APACHE-II scores for survivors and non-survivors were 15.94 (16) and 24.2 (25), respectively (p < 0.001; 95% confidence interval (CI), 5.2 to 11.3).

Discussion

Over the past three decades the outlook for children with malignancy has improved dramatically so that 60–70% are now expected to be long term survivors.\(^4\)\(^5\) Such improvement has resulted from increasingly intensive and sustained chemotherapy. One of the most serious consequences of this is an increase in myelosuppression and immunosuppression, with a risk of life threatening infection. Over the past 15 years several groups have reported the outcome of patients with malignant disease admitted to intensive care units for treatment. Unfortunately, most of these studies were on adults\(^10\)\(^\text{-}12\) and only a few reports are on children.\(^4\)\(^7\) All of the paediatric studies were reported six or more years ago. Our study shows the use made of the PICU services by a regional oncology unit over the past seven years and highlights the changing pattern in outcome.

### Table 1 Survival after admission to paediatric intensive care unit in relation to underlying diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Cases</th>
<th>Survivors (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>26</td>
<td>16 (62)</td>
</tr>
<tr>
<td>AML</td>
<td>12</td>
<td>5 (42)</td>
</tr>
<tr>
<td>NHL</td>
<td>6</td>
<td>3 (50)</td>
</tr>
<tr>
<td>HD</td>
<td>1</td>
<td>1 (100)</td>
</tr>
<tr>
<td>Histiocytosis</td>
<td>1</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Solid tumours</td>
<td>28</td>
<td>24 (86)</td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>49 (66)</td>
</tr>
</tbody>
</table>

ALL, acute lymphoblastic leukaemia; AML, acute myeloid leukaemia; NHL, non-Hodgkin’s lymphoma; HD, Hodgkin’s disease.

### Table 2 Survival in relation to reason for admission

<table>
<thead>
<tr>
<th>Reason for admission</th>
<th>Ventilated</th>
<th>Patients</th>
<th>Total</th>
<th>Survived (%)</th>
<th>Not ventilated</th>
<th>Patients</th>
<th>Total</th>
<th>Survived (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic infection</td>
<td>21</td>
<td>15</td>
<td>7</td>
<td>(47)</td>
<td>6</td>
<td>6</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Respiratory infection</td>
<td>18</td>
<td>16</td>
<td>6</td>
<td>(38)</td>
<td>2</td>
<td>2</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td>11</td>
<td>9</td>
<td>6</td>
<td>(67)</td>
<td>2</td>
<td>1</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Postoperative</td>
<td>15</td>
<td>8</td>
<td>8</td>
<td>(100)</td>
<td>7</td>
<td>7</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Tumour mass effect</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>(100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After cardiac arrest</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>(100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic effects</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>(0)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>(100)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>57</td>
<td>33</td>
<td>(58)</td>
<td>17</td>
<td>16</td>
<td>(94)</td>
<td></td>
</tr>
</tbody>
</table>

Number of inotropes required

![Figure 1](http://adc.bmj.com/)
The overall survival in our series is higher than the 52% and 51% reported by Butt et al and Heney et al, respectively. In addition, the survival rate for ventilated patients in our study was twice that of Heney et al, who found an overall survival for ventilated patients of only 30%.

Patients with infective illness requiring ventilation had the lowest survival rate but this was an improvement on the results of Heney et al, who reported no survival for a similar category of patients. He advocated treatments other than ventilation for these children because of the very poor outcome. Similarly, Butt et al reported a low survival (≤16%) in patients with respiratory failure requiring ventilation. Therefore, our study shows a great improvement in the survival of oncology patients with infective illness who need ventilation and their chance of survival is nearing 50%.

Several factors may be responsible for this improved survival, including the development of paediatric intensive care units and an awareness by physicians of the improved long term survival of children with cancer, and the consequent need for acute support of these patients. Early management of sepsis using an aggressive antimicrobial, fluid, and inotropic policy, coupled with the use of granulocyte colony stimulating factor, might contribute to this improvement.

For those children with acute infective illness requiring inotropic support, survival fell greatly as the number of inotropic agents needed to maintain circulation increased. Requirement of multi-inotropic treatment after sepsis implies a greatly increased requirement of inotropic agents. We recommend aggressive intensive care management for such children to maximise the outcome.

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Case reports and case series have been used in the past in paediatric reports. Therapeutic approaches seem to be incapable of improving as the number of inotropic agents needed to improve improvement. Coupled with the use of granulocyte colony stimulating factor, might contribute to this improvement.

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Conclusion

There has been an improvement in the survival of oncology patients receiving intensive care treatment, especially those with acute infective illness requiring ventilation. We recommend aggressive intensive care management for such patients to maximise the outcome.

Patients needing more than three inotropes and those with high mean APACHE-II scores have a uniformly poor prognosis and informed advice and counselling should be given to their parents. Whether new experimental treatments will improve the outcome of such patients remains to be seen.

We thank the Manchester children's oncology and intensive care teams for tirelessly looking after the children whose data were used in this report, Professor JM Birch and her team at the CRC paediatric and familial cancer research group for allowing the use of data from the Manchester children's tumour registry; and D Kounali for statistical assistance.

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