Evaluation of Dietetic Intervention in Children with Medulloblastoma or Supratentorial Primitive Neuroectodermal Tumors

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BACKGROUND. Malnutrition is a common complication of cancer treatment; it can affect energy levels and, as a consequence, quality of life. The goal of the current study was to evaluate the effect of dietetic intervention in a cohort of children treated for medulloblastoma and supratentorial primitive neuroectodermal tumors (PNET) over a 10-year period.

METHODS. A retrospective chart review (1992–2002) of newly diagnosed cases of medulloblastoma/supratentorial PNET was performed. Hospital records were reviewed for data, including demographic characteristics, patient heights and weights, and information on treatment modalities and the use of dietetic intervention. Percent changes in body weight were calculated at time points associated with particular stages of treatment or dietetic intervention.

RESULTS. One hundred three of 112 cases were evaluable. Treatment methods included surgery only (7.8%), surgery/radiotherapy (16.5%), surgery/chemotherapy (14.5%), and surgery/radiotherapy/chemotherapy (61.2%). There was no significant change in patient weight due to surgery (median change in body weight [MCBW], 0.35%) or radiotherapy (MCBW, 0.78%). In contrast, children experienced significant weight loss (MCBW, 4.35%; P < 0.0001) 3 months after starting chemotherapy. A dietician saw 53 of the 103 children in the study cohort. There were 84 dietetic interventions (oral, 36%; parenteral, 27%; enteral, 37%) among these 53 patients. Oral diets did not result in weight gain. Parenteral nutrition was associated with significant weight gain at 1 month (MCBW, 2.7%; P = 0.03), but not at 3 months. The use of enteral feeds resulted in significant weight gain at 1 month (MCBW, +4.8%; P = 0.006) and at 3 months (MCBW, +11.8%; P < 0.0001).

CONCLUSIONS. Current multimodality treatment of intracranial PNET results in significant nutritional morbidity, primarily due to the use of intensive chemotherapy regimens. Dietetic input for pediatric patients with medulloblastoma/PNET is essential, and the implementation of enteral feeding in these children can help to reverse their nutritional morbidity. Cancer 2003;98:1014–20.

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KEYWORDS: brain tumor, medulloblastoma, pediatric oncology, nutrition support, enteral nutrition, parenteral nutrition, gastrostomy tubes.

Medulloblastoma and primitive neuroectodermal tumors (PNET) are the most common types of malignant brain tumors in pediatric patients. For many years, surgery and radiotherapy have been the accepted standard treatment for all but children under 3 years. More recently, due to the contributions of pilot studies and multicenter cooperative randomized trials, chemotherapy has become part of the standard treatment regimen for both average-risk and high-risk
medulloblastoma.\textsuperscript{1-5} Five-year survival rates of up to 50–80\% (depending on risk factors) have been achieved with regimens that combine craniospinal radiation and chemotherapy. Most protocols currently include sequential chemotherapy after irradiation over a period of 8–12 months.\textsuperscript{6} Ongoing studies involving high-risk patients are investigating the feasibility of chemotherapy administered during radiotherapy and of high-dose chemotherapy administered after craniospinal irradiation.\textsuperscript{7} The ever-increasing role of chemotherapy is not without side effects. Infectious complications and renal and hearing toxicities represent the cost of introducing chemotherapy into the standard treatment regimens for medulloblastoma and PNET.\textsuperscript{5} One additional, often-overlooked side effect of chemotherapy is related to its nutritional consequences. Weight loss is a common complication of cancer treatment and can affect energy levels, physical condition, and, as a consequence, quality of life.\textsuperscript{8} The purpose of the current retrospective study was to evaluate the nutritional consequences of treatment and the effect of dietetic intervention in a cohort of children treated for medulloblastoma and supratentorial PNET over a 10-year period at a single institution. Specifically, the objectives of the study were as follows: 1) to determine the nutritional status of children with medulloblastoma at diagnosis; 2) to document patterns of weight change resulting from first-line treatment; and 3) to document patterns of weight change resulting from nutritional intervention.

**MATERIALS AND METHODS**

**Data Collection**

A retrospective chart review of all children who were newly diagnosed with medulloblastoma and supratentorial PNET over a 10-year period (1991–2001) at the Hospital for Sick Children (Toronto, Ontario, Canada) was performed. Ethics approval was granted by the Institutional Research Ethics Board. Demographic information, including age and gender, was collected and recorded from each patient record, as was information on height and weight at diagnosis, treatment modalities and dietetic interventions implemented, complications associated with gastrostomy tubes, and hospital stays before and after gastrostomy tube insertion. Patient weights were measured at diagnosis; before and after surgery; before and after radiotherapy; before and 3 months into chemotherapy; before, 1 month after, and 3 months after dietetic intervention; and at the end of treatment.

Patients were grouped according to treatment modality and dietetic intervention type. Treatment modalities included surgery, radiotherapy, and chemotherapy. Dietetic intervention types included oral diet counseling, enteral nutrition, and parenteral nutrition.

The number of patients who had both a ventriculoperitoneal shunt and a gastrostomy tube was recorded. Gastrostomy tube complications were categorized as minor or major. Minor complications were defined as localized site infections that were treated at home or in hospital. Major complications included cases of peritonitis, abscess formation, and ventricular shunt infection that could be directly attributed to gastrostomy. In those children with a gastrostomy tube, the number of days hospitalized was compared pre- and postgastrostomy tube insertion to determine if there was a significant difference.

**Data Analysis**

Ideal body weight (IBW) at diagnosis was determined using Tanner–Whitehouse Growth Charts\textsuperscript{9} and was defined as the weight percentile that corresponded to a child’s height percentile. Percentage of IBW was calculated as \((\text{actual weight}/\text{ideal weight}) \times 100\%\). Patients were categorized as being at risk for malnutrition if they weighed less than 90\% of their IBW. Changes in weight were expressed as percentages: percentage weight change was calculated as \((\text{actual weight} - \text{initial weight})/\text{initial weight}) \times 100\%. Significant weight loss or gain was defined as a change of 5\% or more. Patients with a weight change of less than 5\% were defined as having stable weight. Changes in weight were determined at time points associated with specific stages of treatment or dietetic intervention (before and after surgery; before and after radiotherapy; before and 3 months after the initiation of chemotherapy; before, 1 and 3 months after dietetic intervention and at the end of treatment).

**Statistical Analysis**

Statistical analysis was performed using the Analyse-It software package (Analyse-It Software, Leeds, United Kingdom). Descriptive statistics were calculated with 95\% confidence intervals (CIs). To test for statistical levels of significance in differences between groups of measurements, the analysis-of-variance method was used (repeat measures for related samples). Spearman rank correlations were used to test for associations between variables.

**RESULTS**

**Patient Characteristics**

One hundred twelve patients were newly diagnosed with medulloblastoma and supratentorial PNET at the Hospital for Sick Children between 1991 and 2001. One hundred three cases were evaluable. Patient char-
characteristics and treatment modalities are summarized in Table 1.

All patients underwent tumor resection. Eighty patients received postoperative radiotherapy (XRT), including 63 who received XRT and chemotherapy. XRT included craniospinal radiation (dose, 23.4–45 grays [Gy]) as well as tumor boost (to a total dose of 42–54 Gy). Sixty-nine percent of these 80 patients were treated with conventionally fractionated, standard-dose (34–36 Gy) craniospinal irradiation (CSI); the remaining patients were treated with reduced-dose CSI (23.4–30 Gy; 20%) or high-dose CSI (39.6–45 Gy; 11%). Chemotherapy protocols are listed in Table 1.

### Nutritional Status

The median percentage of IBW at diagnosis was 94%. Thirty-one percent of patients presented as being at risk for malnutrition. The distribution of nutritional status at diagnosis is shown in Figure 1.

### Treatment

The distributions of treatment modalities and changes in weight after treatment are shown in Figure 2. The median weight change after surgery was $-0.35\%$ (95% CI, $-0.82\%$ to $+0.63\%$; $P = \text{not significant}$). The median weight change after radiotherapy was $-0.78\%$ (95% CI, $-2.09\%$ to $+0.63\%$; $P = \text{not significant}$). The median weight change from the start of chemotherapy to 3 months into chemotherapy was $-4.35\%$ (95% CI, $-5.80\%$ to $-2.93\%$), indicating a statistically significant loss of weight ($P < 0.001$). Forty-six percent of patients receiving chemotherapy lost a clinically significant amount of weight ($> 5\%$ of their body weight).

#### Nutritional Intervention

The distribution of nutritional intervention types is described in Table 2. Fifty-one percent of patients were seen by a dietician. Patients treated with chemotherapy were more likely than those who did not receive chemotherapy to be referred for dietetic intervention (66.7% vs. 4%; $P < 0.001$). The median weight change from beginning to end of cancer treatment among patients seen by a dietician was $+6.38\%$ (95% CI, $+3.05\%$ to $+13.74\%$). Patients who did not see a dietician had a median weight change of $+0.48\%$ (95% CI, $-1.82\%$ to $+6.97\%$). However, the difference in weight change between the two groups was not significant. Patients who were seen by a dietician had an average of 1.58 nutritional interventions per individual.

Thirty patients received oral diet counseling. Oral diet counseling stressed the importance of consuming

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**TABLE 1**

**Patient Characteristics**

<table>
<thead>
<tr>
<th>No. of PNET cases identified (1992–2002)</th>
<th>112</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of evaluable casesa</td>
<td>103</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>93</td>
</tr>
<tr>
<td>PNET</td>
<td>10</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>64</td>
</tr>
<tr>
<td>Female</td>
<td>39</td>
</tr>
<tr>
<td>Age at diagnosis (yrs)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>6.1</td>
</tr>
<tr>
<td>Range</td>
<td>0.1–15.4</td>
</tr>
<tr>
<td>Treatment (%)</td>
<td></td>
</tr>
<tr>
<td>Surgery + RT + chemotherapy</td>
<td>61.2</td>
</tr>
<tr>
<td>Surgery + RT</td>
<td>16.5</td>
</tr>
<tr>
<td>Surgery + chemotherapy</td>
<td>14.5</td>
</tr>
<tr>
<td>Surgery onlyb</td>
<td>7.8</td>
</tr>
<tr>
<td>Chemotherapy protocol (%)</td>
<td></td>
</tr>
<tr>
<td>ICE</td>
<td>48.1</td>
</tr>
<tr>
<td>CCG 9961 (Packer et al., 19995)</td>
<td>15.2</td>
</tr>
<tr>
<td>Baby POG 8633/9233 (Duffner et al., 199310)</td>
<td>13.9</td>
</tr>
<tr>
<td>POG 9631c</td>
<td>11.4</td>
</tr>
<tr>
<td>Other</td>
<td>11.4</td>
</tr>
</tbody>
</table>

PNET: primitive neuroectodermal tumor; RT: radiotherapy; ICE: ifosfamide, carboplatin, etoposide; CCG: Children’s Cancer Group; POG: Pediatric Oncology Group.

a Evaluable cases were those for which health records were available and complete.
b Three patients died shortly after surgery, and five patients were transferred to other centers.
c Protocol consisted of oral etoposide during radiotherapy and three postradiotherapy courses of etoposide and cisplatin followed by eight courses of vincristine and cyclophosphamide.

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**FIGURE 1.** Percentage of ideal body weight at diagnosis.

**FIGURE 2.** Weight changes after treatment, according to treatment group.
calorie-rich foods during times when intake was easiest and/or the importance of using nutrition supplements such as meal replacement formulations. These 30 patients had a median weight change of $-2.44\%$ (95% CI, $-4.02\%$ to $0.88\%$) at 1 month after intervention, indicating a significant loss of weight ($P = 0.032$). The median weight change at 3 months was $-1.38\%$ (95% CI, $-3.30\%$ to $2.56\%$; $P$ not significant). Fifteen of these patients (50%) required additional nutritional support, either enteral or parenteral.

Parenteral nutrition was implemented for 19 patients a combined total of 23 times. The use of parenteral nutrition resulted in a median weight change of $2.67\%$ (95% CI, $1.22\%$ to $9.20\%$) at 1 month and a change of $5.23\%$ (95% CI, $-4.88\%$ to $+14.61\%$) at 3 months. While the weight gain was significant at 1 month ($P = 0.031$), it was not significant at 3 months. Eleven patients (58%) received a nasogastric or gastrostomy tube after the administration of parenteral nutrition.

Twenty-one children received a combined total of 26 gastrostomy tubes and 5 nasogastric tubes. Two children who initially received nasogastric tubes later received gastrostomy tubes. One child received two gastrostomy tubes over the course of his treatment. Enteral nutritional support resulted in a median weight change of $+4.78\%$ (95% CI, $-0.80\%$ to $+7.19\%$) at 1 month and a change of $+11.73\%$ (95% CI, $+8.30\%$ to $+14.75\%$) at 3 months. The outcome was significant at both 1 and 3 months after gastrostomy/nasogastric tube insertion ($P = 0.0055$ and $P < 0.001$, respectively). Two patients (7%) received parenteral nutrition after the initiation of enteral feeds, including 1 patient who required home parenteral nutrition in addition to gastrostomy tube feedings.

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Dietetic Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
</tr>
<tr>
<td>Any dietetic assessment$^a$</td>
<td>53/103 (51.5)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>52/78 (66.7)</td>
</tr>
<tr>
<td>No chemotherapy</td>
<td>1/25 (4)</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>43/80 (53.7)</td>
</tr>
<tr>
<td>No radiotherapy</td>
<td>10/23 (43.5)</td>
</tr>
<tr>
<td>Total no. of interventions</td>
<td>84$^b$</td>
</tr>
<tr>
<td>High-energy diet</td>
<td>30/84 (36)</td>
</tr>
<tr>
<td>Enteral nutrition</td>
<td>31/84 (37)</td>
</tr>
<tr>
<td>Gastrostomy tube</td>
<td>26/84 (31)</td>
</tr>
<tr>
<td>Nasogastric tube</td>
<td>5/84 (6)</td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>23/84 (27)</td>
</tr>
</tbody>
</table>

$^a$ All patients in this group underwent surgery.

$^b$ Combined total among 53 patients.

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Gastrostomy Complications

Twenty-six gastrostomy tube insertions were documented in 25 children, 11 (44%) of whom also had a ventriculoperitoneal shunt. A combined total of 25 complication episodes were recorded in 16 individuals. Localized infections that were treated at home accounted for 10 episodes distributed among 6 individuals (1–4 episodes per individual). A combined total of 13 exit-site infections that were treated in hospital occurred in 9 individuals (0–5 episodes per individual). Two patients suffered a major complication, including an episode of peritonitis and an abdominal wall abscess. The episode of peritonitis occurred 1 week after gastrostomy tube insertion and was followed by a ventriculoperitoneal shunt infection that made revision of both the shunt and the gastrostomy tube necessary. The patient with the abdominal wall abscess required prolonged hospitalization so that treatment with intravenous antibiotics could be administered. For patients receiving gastrostomy tubes, the median hospital stay before insertion was 9.15 days per month (95% CI, 5.78–12.44 days per month). After insertion, the median hospital stay was 8.23 days per month (95% CI, 2.98–11.75 days per month). The difference between these two values was not significant.

Figure 3 summarizes the patterns of weight change, by nutritional intervention type, at 1 and 3 months after implementation of the intervention.
DISCUSSION
The current retrospective review suggests that malnutrition in children with medulloblastoma is a significant issue. The majority of children treated with craniospinal irradiation and chemotherapy experience major nutritional problems, and the consequences of malnutrition in the short and long term remain unclear. Malnourished children experience inadequate growth, have the potential for delayed cerebral development, and are more susceptible to infection. Previous studies of patients with malignancies have reported that malnutrition also can affect survival. There is little information documented in the literature on disease and treatment related nutritional morbidity and its effects in children with brain tumors. In a retrospective study, Tyc et al. reported that children with central nervous system (CNS) malignancies require nutritional support for longer periods of time compared with the general pediatric oncology population. Within this population, children with CNS malignancies also appear to account for a large proportion of patients who receive gastrostomy tubes. The findings of the current study confirm that children with medulloblastoma/PNET are at risk for malnutrition.

The etiology of malnutrition in pediatric oncology is multifactorial and includes causes related to both altered caloric utilization and altered caloric intake. The modality of treatment may account for the decline in nutritional status. The intensity and type of primary therapy (surgery, radiotherapy, and/or chemotherapy) may be associated with the severity of secondary protein-energy malnutrition.

While the majority (69%) of children with medulloblastoma and supratentorial PNET appeared to be satisfactorily nourished, 31% were at risk for malnutrition based on evaluation of IBW. Children with medulloblastoma often present with a history of recurring emesis and nausea, which eventually can cause significant weight loss. Due to the limited amount of available data, we were unable to evaluate dietary intake, body composition, and/or weight changes before diagnosis. Therefore, the proportion of patients at risk for malnutrition may be underestimated. Albumin levels were not used to evaluate nutritional status; the clinical usefulness of measuring these levels is limited, due to the multitude of variables, such as disease and hydration status, that can alter the measurement.

The results of the current study suggest that weight loss during treatment occurs primarily because of chemotherapy. This finding is consistent with the existing literature, in which patients receiving intensive chemotherapy have been identified as being at risk for malnutrition. Prolonged emesis, mucositis, diarrhea, suboptimal dietary intake, and decreased appetite all are side effects of chemotherapy that contribute to weight loss. The relative stability of patient weight during the perioperative period and during radiotherapy may be related to the frequent use of steroids prescribed to reduce the risk of increased cranial pressure or radiation-induced side effects. Because the current study was a retrospective one, our ability to evaluate the use of steroids in the study population was limited. Steroids often are discontinued after radiotherapy, and many children experience significant weight loss after the initiation of postradiotherapy chemotherapy. This weight loss also can be aggravated by postradiation somnolence, which is characterized by extreme tiredness and loss of appetite.

Most chemotherapy protocols for medulloblastoma/PNET are administered over a period of time on the order of 1 year. These protocols generally involve repeated cycles of intensive chemotherapy every 4–6 weeks. Due to the recognition of prognostic factors affecting survival, separate protocols for average-risk and high-risk patients have been developed. The policy of the Hospital for Sick Children during the greater part of the study period was to consider the use of craniospinal radiation only for average-risk patients age > 3 years and the use of radiotherapy + chemotherapy for patients with high-risk features. Currently, all patients receive postradiation chemotherapy. High-risk protocols are more intensive and may have more nutritional consequences compared with less intensive protocols, which are administered to average-risk patients. However, the small number of patients with average-risk features who were treated with chemotherapy in the current series precludes any comparison of the nutritional consequences of high-risk versus average-risk protocols.

To effectively reverse and prevent weight loss, adequate amounts of calories and protein must be provided in a manner that is accepted and tolerated by the child and his or her family. Oral diet counseling, enteral nutritional support, and parenteral nutrition all are modes of nutritional intervention that are used in the pediatric oncology population. All three modes of nutritional intervention were used in the current study population. Diet counseling is considered the simplest and least invasive form of dietary intervention. The current study suggests that diet counseling was not an effective mode of nutritional intervention for this population. The literature supports our finding: although high energy diets may be useful in preventing weight loss in children who are nourished and who have less-advanced disease, they
have not been effective in preventing malnutrition in children undergoing intensive therapy.\textsuperscript{14}

Parenteral nutrition proved to be an effective means of weight gain only at 1 month after its initiation. Although it is indicated at specific times during treatment, parenteral nutrition may increase the risk of potentially serious metabolic and infectious complications and may be unnecessary when the gastrointestinal tract is functional.\textsuperscript{19} It typically is administered in an inpatient setting, and its cost implications are significant. Therefore, parenteral nutrition should be used only when enteral nutrition is not indicated.

Unlike parenteral nutrition, enteral nutrition is compatible with the use of a functional gastrointestinal tract and allows a more physiologic use of nutrient substrates.\textsuperscript{20} The current study showed enteral nutrition to be the only effective method of providing nutrition to facilitate weight gain throughout cancer treatment. Studies on the effect of enteral nutrition in the pediatric oncology population support our findings.\textsuperscript{13,21}

Enteral nutrition can be delivered through either a nasogastric tube or a gastrostomy tube. Due to the small number of nasogastric tube insertions, we were unable to evaluate patient tolerance of these tubes and associated complications, such as sinusitis and epistaxis. Previous studies indicate that nasogastric feeding during intensive treatment results in an improved nutritional status with minimal complications.\textsuperscript{21–23} Although nasogastric feeding is an effective mode of nutritional support, its potential psychologic unacceptability, along with the necessity of long-term nutritional support, may limit its usefulness in patients with medulloblastoma/PNET.

Twenty-six patients underwent insertion of a gastrostomy tube. The use of gastrostomy tubes in children undergoing intensive chemotherapy may seem questionable, particularly for children harboring ventriculoperitoneal shunts. Localized infections of the exit site accounted for the majority of complications associated with gastrostomy tubes, and patients with these infections sometimes were treated as inpatients and other times as outpatients. An abdominal wall abscess occurred in one patient, who did not comply with the indications for hygienic care of the gastrostomy site. Because the current study was a retrospective chart review, our ability to distinguish inflammation from true infection was limited. Therefore, reports of minor complications may have been overestimated. In the current study population, the median hospital stay per month slightly decreased in duration after gastrostomy tube insertion. Although this decrease was not significant, it suggests a potential benefit of improved nutritional status with respect to the incidence of complications during intensive chemotherapy. The cost implications of the different interventions were not evaluated in the current study. However, in a study of 25 pediatric patients who underwent gastrostomy tube placement and received enteral nutritional support, Aquino et al.\textsuperscript{25} estimated that the monthly costs of gastrostomy tube nutritional support were 9% of those associated with the use of total parenteral nutrition.\textsuperscript{25} The use of gastrostomy tubes in patients with ventriculoperitoneal shunts raises concerns about the potential for CNS or peritoneal infection and shunt malfunctioning, particularly when intensive chemotherapy is delivered. Among the 11 individuals who had both a gastrostomy tube and a ventriculoperitoneal shunt, there was 1 case of a shunt infection that could be attributed to gastrostomy tube insertion. Our results support the finding that complications are common but typically are not serious.\textsuperscript{13,21,25,26}

In addition to providing nutritional requirements, a gastrostomy tube can perform other functions. Clinical experience has demonstrated that gastrostomy tubes are an effective way to deliver medications and to provide hydration to children experiencing excessive emesis. The quality of life of both the child and the caregiver also appears to improve, as eating is a frequent source of conflict between child and caregiver. Providing nutrition through a gastrostomy tube alleviates the frustration associated with forced feeding of the child via the mouth.

Maintenance of normal patient nutrition throughout cancer treatment decreases potential complications, allows normal growth, improves quality of life, and may facilitate the administration of treatment. Pharmacologic interventions with anabolic steroids or megestrol acetate have been proposed, primarily for adult and geriatric patients undergoing chemotherapy.\textsuperscript{27,28} Information regarding the use of these agents in children is limited, and evidence that it may be beneficial is lacking.\textsuperscript{28}

The current study supports the systematic screening of all children with medulloblastoma and supratentorial PNET by a registered dietician. As a population, these children require early and aggressive nutritional intervention and dietetic input. Weight loss should no longer be an acceptable side effect of cancer therapy in this group of patients, as an effective method of preventing and reversing malnutrition exists.

REFERENCES