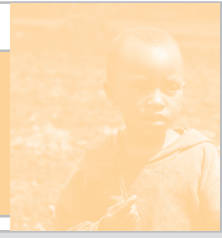


# The role of nutritional intervention in children with nephroblastoma



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**Objective.** To assess the effect of nutritional support on the nutritional status of hospitalised children with nephroblastoma.

**Design.** A retrospective, descriptive study.

**Setting.** A tertiary academic hospital in Durban, KwaZulu-Natal.

**Outcome measure.** Changes in weight with oral nutritional supplementation or nasogastric tube feeding.

**Results.** Complete data were available for 37 patients with a median age of 47.5 months and a median hospital stay of 7 months. Seventeen patients (45%) were malnourished on admission. All 37 patients received oral nutritional supplements in the form of additional snacks and oral nutritional drinks, and they had a significant median weight gain of 1.46 kg (−1.95 to 7.20 kg) during the period of study, which significantly exceeded the expected median weight gain of 342 g ( $p < 0.01$ , Wilcoxon signed ranks test). Seventeen patients (45%) received nasogastric (NG) feeds at some stage of their treatment. Patients were selected for tube feeding based on the clinicians' assessment of their clinical features and anthropometry and ability to tolerate oral feeding. Despite their more severe clinical diathesis, they gained as much weight as those not receiving nasogastric feeding. ( $p = 0.20$ ; Mann-Whitney *U*-test).

Twenty-two patients (58%) received Filgastrim. Overall, patients on Filgastrim gained less weight than those not receiving Filgastrim ( $p = 0.04$ ; Mann-Whitney *U*-test). Twenty-five patients (66%) received radiotherapy. Radiotherapy did not independently influence the change in weight ( $p = 0.15$ , Mann-Whitney *U*-test).

**Conclusion.** With aggressive nutritional support, patients being treated for nephroblastoma gained more weight over the treatment period than accounted for by normal expected growth. Chemotoxicity was shown to have a negative effect on weight gain. Such patients, and those with pre-existing malnutrition, should in future be targeted to receive nasogastric feeds.

Despite this being a retrospective descriptive study, with clear limitations and incomplete data, it suggests that early and continuous aggressive nutritional assessments and support are beneficial.

Malnutrition may be defined as a disorder resulting from reduced nutrient intake or impaired metabolism. There is currently no 'gold standard' or single measure of malnutrition.<sup>1</sup> The association between cancer-associated malnutrition and poor outcome has long been established in adult studies.<sup>2</sup> There is considerable evidence that nutritional depletion causes alterations in both cellular and humoral immune function and inflammatory responses, making cancer patients more susceptible to poor wound healing, increased infectious complications, prolonged post-operative ileus, and prolonged hospital stay.<sup>3</sup> The adverse nutritional effects of cancer can be severe, compounded by the effects of the treatment regimens and the psychological impact of the diagnosis.<sup>4</sup>

Cancer-induced cachexia is invariably associated with growth of the tumour, and leads to a malnourished state associated with anorexia and decreased food intake. In addition, the competition for nutrients between the tumour and the host leads to an 'accelerated' starvation state, which promotes severe metabolic disturbances in the host, including hypermetabolism. This leads to a decreased efficiency in the utilisation of energy, with loss of lean tissue mass.<sup>5</sup> Therefore, the objective of nutritional support in children with malignant diseases is to limit loss of weight and spare muscle mass, thereby allowing effective treatment with tolerable toxicity, fewer complications and improved survival.<sup>6</sup>

Weight loss of >10% over a 6-month period is considered clinically significant for adverse outcomes including complications and death.<sup>7</sup>

The objective of this study was to assess the effect of nutritional intervention on the nutritional status of hospitalised children with nephroblastoma.

## Patients and methods

This was a retrospective, descriptive study of a cohort of 56 children with nephroblastoma, admitted to hospital between 2002 and 2005. Nineteen patients could not be included in the statistical analysis because they were lost to follow-up, had died, or had insufficient retrievable data to allow inclusion.

Following diagnosis, all patients were treated with neo-adjuvant chemotherapy prior to radical nephrectomy. Subsequent treatment involved chemotherapy and, when necessary, radiotherapy to the whole abdomen and/or lungs. Each patient's tumour was staged, using National Wilms' Tumour Study Group guidelines.<sup>8</sup>

Stage I: Tumour limited to kidney and completely resected.

Stage II: Tumour extends beyond kidney but is completely excised.

Stage III: Residual non-haematogenous tumour confined to the abdomen.

Stage IV: Haematogenous metastases.

Stage V: Bilateral tumours.

Admission, peri-operative and discharge weights were recorded. The tumour weight was recorded post-excision. Admission weight was calculated by subtracting the excised tumour weight from body weight at admission. Change in weight was calculated for each patient over the treatment period as weight at discharge minus admission weight. Pre-operative weight was calculated by weight prior to surgery minus tumour weight.

For children who were able to stand, body weight and height were measured using a Seca electronic weight and height measurement scale. Infants or small children unable to stand were weighed using a Seca electronic baby scale. Weight was recorded to the nearest 100 g. Both scales are calibrated on a yearly basis by the manufacturer. If patients were unable to stand (infants and the sickly), length was recorded with a tape measure. Height and length were recorded to the nearest 1 cm. Nursing staff weighed and measured patients and recorded these figures in the patients' medical charts.

Arm anthropometry, i.e. mid-arm upper circumference and tricep skinfold thickness, and weight-for-height data were incomplete in this study and therefore excluded. Expected weight gain was calculated for each patient over the treatment period from published tables<sup>9</sup> to determine whether the change in weight was 'normal' growth.

In this retrospective study, anthropometry was analysed using Centers for Disease Control (CDC) growth charts to ensure consistency over a wide age range. Patients were classified as malnourished if weight-for-age fell on or below the third percentile.<sup>10</sup> World Health Organization (WHO) growth charts are inappropriate for children >5 years of age.

Nutritional supplementation in the form of snacks and nutritional drinks was given to all 37 patients, irrespective of nutritional status. The snacks were those available from the hospital snack list and were ordered by the clinical dietitian. They included peanut butter sandwiches, muffins, cheese and biscuits, jelly and custard, yoghurt, maas, etc. A different snack was ordered each day to prevent taste fatigue and provide variety. The nutritional drinks prescribed included Frebini (Fresenius Kabi SA) 200 ml (300 kcal, 7.5 g protein) and Paediasure (Abbott) 200 ml (200 kcal and 5.6 g protein), according to taste preference. Each patient received daily 1 nutritional drink and a snack in addition to their normal diet. The median energy and protein provided from the snacks was 204 kcal and 6.5 g, respectively. The median energy and protein provided from the nutritional drink was 250 kcal and 7.1 g, respectively. The paediatric diet provided 1127 kcal and 51 g of protein. Patients received a daily median total energy and protein intake of 1 581 kcal and 64.6 g respectively. Because of the retrospective nature of the study, actual intake was not available.

The majority of patients were weighed weekly; however, owing to incomplete weekly weights taken for all patients, admission, peri-operative and discharge weights were analysed. If a patient dropped a percentile group (space) as categorised in the growth charts e.g. 10th to 3rd percentile, or 50th to 25th percentile, and/or was unable to take a full diet for 3 or more days or had compelling clinical features, as determined by the clinician in charge, including intractable nausea, vomiting, or abdominal discomfort, feeding via nasogastric tube was commenced. At the discretion of the dietitian, nasogastric feeds (NG) were given overnight for 18 hours or continuously. When possible, overnight feeds were preferred, to allow normal social activity during the day.

The nasogastric feeds used included Paediasure Fibre (Abbott) (1 kcal/ml, 28 g protein/l, RTH (ready-to-hang)), Paediasure Plus (Abbott) (1.5 kcal/ml, 42 g protein/l, RTH) and Peptamen Junior (Nestle) (459 kcal/100 g, 13.7 g protein/100 g powder). Enteral feeds provided a median energy intake of 1 080 kcal and 27 g protein.

Filgastrim (Roche) (Neupogen) was given when the white blood count (WBC) fell below  $2 \times 10^9/l$ . Filgastrim use was used as a surrogate marker for bone marrow suppression due to chemotherapy.

This study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu-Natal. Data were entered into an SPSS v11.0 database,

and patients with incomplete data were excluded. Descriptive statistics were generated and non-parametric tests were utilised to assess the relationship between variables.

## Results

Complete data were available for 37 patients. There were 24 males and 13 females, with a median age of 47.5 months (9 - 148 months). Seventeen patients (45%) were malnourished on admission. The median age at discharge was 54.5 months (16 - 155 months), and the median hospital stay was 7 months. Table I depicts the tumour staging of patients. Analysis of weight gain in relation to pathological tumour staging was not possible owing to the small sample size in each group.

Table I. Tumour staging of study patients					
Tumour stage	I	II	III	IV	V
No. of patients	3	9	11	10	4

All 37 patients received nutritional supplements, and there was a significant median weight gain of 1.46 kg (-1.95 to 7.20 kg) during the period of the study (Fig. 1). This significantly exceeded the expected median weight gain of 342 g ( $p < 0.01$ , Wilcoxon signed ranks test). Not all malnourished patients received NG feeds. Those who did were selected on the criteria mentioned. Some non-malnourished patients also received NG feeds.

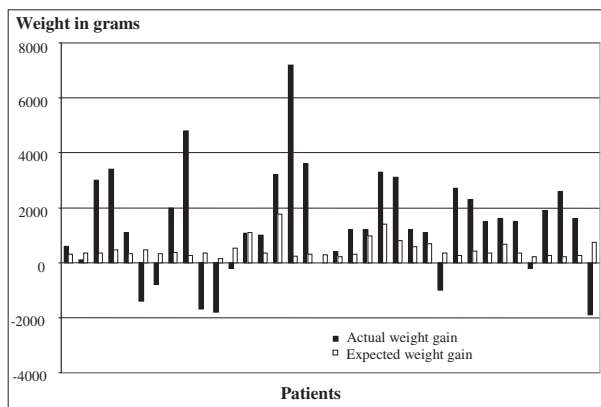


Fig. 1. Bar graph depicting the changes in actual and expected weight for each patient. Values below the abscissa imply weight loss during the treatment period.

Seventeen patients (45%) received nasogastric feeds. These patients were selected on the basis of progressive weight loss or anorexia. Despite their more severe clinical diathesis, they gained as much weight as those not receiving nasogastric feeding ( $p = 0.20$ ; Mann-Whitney  $U$ -test).

Twenty-two patients (58%) received Filgastrim, of whom 8 (36%) were malnourished. Of these malnourished patients, 5 received nasogastric tube

feeds. Overall, patients on Filgastrim gained less weight than those not receiving Filgastrim ( $p = 0.04$ ; Mann-Whitney  $U$ -test). Owing to the retrospective nature of the study, it was not possible to exclude intercurrent septicaemia as a cause of poorer weight gain in patients receiving Filgastrim.

Twenty-five patients (66%) received radiotherapy, of whom 12 (48%) received nasogastric feeds and 9 (36%) were malnourished. Six of the malnourished patients received nasogastric feeds. Radiotherapy did not independently influence the change in weight ( $p = 0.15$ , Mann-Whitney  $U$ -test).

## Discussion

Nutritional status is an alterable prognostic factor in children with malignant disease. A marginal pre-morbid diet, anorexia and the parasitic effect of the tumour conspire to render a significant cohort of patients malnourished at presentation. Surgery, chemotherapy-related nausea and vomiting, as well as acute radiotherapy toxicity following whole abdominal radiotherapy, tend to decrease food intake and allow further deterioration in nutritional reserves.<sup>11</sup> The challenge for the dietetic team is to reverse this negative trend in an attempt to improve the survival rate of these children.

In addition to malignancy and medical intervention, other possible factors that might have affected nutritional status of the children in this study include: HIV status, variation in meal size and calorie content of the diet provided by the hospital, and prescribed versus actual intake. These data were not recorded, and therefore these variables could not be assessed in this study.

The socio-economic circumstances of each patient were assessed by a social worker on admission. Where socio-economic circumstances allowed, patients were counselled and discharged home between treatments. Postoperative protocols lasted 4 - 6 months, depending on disease stage.

## Nutrition assessment

There are difficulties in the objective assessment of nutritional status of children with solid tumours as the tumour itself, very often massive in patients in the Third World, contributes to the measured weight of the patient.<sup>12</sup> Oedema and hemi-hypertrophy may similarly confound arm anthropometry, which is thought to be a more accurate assessment of nutritional status.<sup>13</sup> In an attempt to overcome these difficulties, admission weight of the patient was taken as the difference between the measured weight on admission and the tumour mass. As most tumours were considerably reduced by the neo-adjuvant chemotherapy, this tends to over-estimate the patients' nutritional status on admission.

During the treatment period, the median expected increase in mass was 342 g. Actual gain in mass was 1.46 kg, suggesting that nutritional status was enhanced by the nutritional interventions used during the study period. No control group could be justified ethically, so each child acted as his/her own control.

## Nasogastric tube feeds

Nutritional support is ideally provided via the enteral route, whenever possible, for a number of reasons. These include maintaining normal physiological, digestive and absorptive actions with a higher substrate utilisation than total parenteral nutrition (TPN); a more efficient plasma insulin response; it is safer and more cost-effective than TPN; maintaining gastrointestinal integrity and having a positive effect on the immunity of the small intestine; fewer complications; and easier to administer.<sup>3,14</sup> The best way to provide short-term enteral feeding is via a nasogastric tube.<sup>3</sup>

In patients who satisfied the criteria for NG feeding, weight gain was similar to those given only nutritional supplements in the form of snacks and nutritional drinks. This remains a positive outcome as, even with a worsened clinical diathesis, these patients managed to gain weight and improve their nutritional state.

## Chemotoxicity

Chemotherapy is a systemic therapy where the target of action is not limited to malignant tissue but also affects normal cells.<sup>4</sup> Chemotherapy toxicity adversely affects nutritional intake, digestion and absorption through one or several mechanisms.<sup>7</sup> Chemotherapeutic response rates are lower in patients with weight loss, and progressive malnutrition is associated with increasing therapy toxicity.<sup>7</sup> Malnutrition is also likely to influence the pharmacokinetics of chemotherapeutic drugs and host responses to therapy-related infections, e.g. chicken pox.<sup>7</sup> Even a weight loss of <5% of body weight at baseline may worsen prognosis and response during chemotherapy.<sup>4,7</sup>

All patients received neo-adjuvant chemotherapy to determine tumour response to the specific chemotherapy protocol and to reduce tumour size before surgery. This provided a window of opportunity during which nutritional status could be modified.

In this study, weight gain was less in those patients receiving Filgastrim, inferring that chemotoxicity has a negative effect on weight gain. Patients on Filgastrim receiving NG feeds gained more weight than those on Filgastrim and not receiving NG feeds.

## Radiotherapy

Whereas chemotherapy is a systemic therapy, radiation therapy affects only the tumour and surrounding area.<sup>11</sup>

Acute radiation reactions are inevitable but of limited duration, with anorexia, nausea and vomiting often occurring when the abdomen is irradiated.<sup>11</sup>

The nutritional effects of irradiation depend on the type of irradiation, the single and end dose, duration of radiotherapy, region and volume irradiated, and the combination with other modalities, especially chemotherapy.<sup>11</sup> In our patients, 15 Gy whole abdominal irradiation over 10 days was the standard regimen.

Twelve (48%) patients receiving radiotherapy required NG feeding due to these symptoms.

## Conclusion

Nutritional support can maintain or improve nutritional status in children with nephroblastoma during primary treatment. Despite having a poorer clinical status, patients selected to receive nasogastric feeds gained similar weight to those receiving only oral nutritional supplements. Chemotoxicity was shown to negatively affect weight gain. Such patients should be targeted to receive nasogastric feeds.

Despite this being a retrospective descriptive study, with clear limitations and incomplete data, it suggests that early aggressive nutritional support and frequent nutritional assessments are beneficial.

*'The greatest obstacle to discovery is not ignorance – it is the illusion of knowledge'* (Daniel J Boorstin). In this context, the greatest obstacle to new approaches in addressing the interaction of nutrition and chemotherapy is to think we have the right answers.<sup>7</sup>

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