

Aggressive Approach to Childhood Cancer Worth Risks, Review Finds

May 14 2010, By Carl Sherman

Neuroblastoma is among the most common of childhood cancers and fortunately, some children will get better spontaneously. Yet for children with high-risk disease the outlook is poor: more than half will relapse despite chemotherapy.

In light of the seriousness of the disease, some children undergo intense treatment beyond standard chemotherapy. First, clinicians administer chemotherapy at doses high enough to destroy bone marrow. Next, they transplant stem cells harvested from the child before treatment began to restore his or her ability to create [blood cells](#).

A new review suggests that this “myeloablative therapy” is worth the effort: children who receive this treatment stay disease-free and live longer than do those who have conventional chemotherapy. Certain adverse effects, however, appear to be more common with the more aggressive approach.

“Based on the currently available evidence, myeloablative therapy seems to be a good treatment option for children with high-risk neuroblastoma,” said Bilgehan Yalçın, M.D., lead review author.

Nita Seibel, M.D., of the National Cancer Institute, agreed that on balance, benefits appear to outweigh risks. Seibel, head of pediatric solid tumor therapeutics in the Clinical Investigations Branch of the Cancer Therapy Evaluation Program of the NCI, has no affiliation with the new review.

This review appears in the latest issue of The Cochrane Library, a publication of the Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews draw evidence-based conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

“We found many studies which reported on the results of high-dose chemotherapy for neuroblastoma, but only three were real randomized controlled trials,” said Yalçın, a professor of pediatrics and a pediatric oncologist at Hacettepe University Faculty of Medicine in Ankara, Turkey.

The review pooled and analyzed data from these three studies, which included 739 young patients whose neuroblastoma was judged high risk: they were older than one year, their disease had spread and their tumors had certain genetic and biological characteristics, indicating a poor prognosis.

The reviewers found that children who had high-dose chemotherapy with hematopoietic stem cell rescue - the transplant of their own blood-producing cells - remained well and without recurrent disease for longer than did those who received conventional chemotherapy. They also lived significantly longer.

In one of the three studies, for example, 47 percent of the patients who received myeloablative therapy were alive and free of disease three years later, compared with 31 percent of those who had standard therapy.

While the three studies reported differences in recurrence and survival rates among subgroups of patients, as defined by such factors as (1) age, (2) response to initial chemotherapy, (3) laboratory indications of disease activity, and (4) prior, concurrent or subsequent treatment, the reviewers could find no consistent patterns, they said.

Data on adverse effects were “very limited,” the authors wrote. Two studies contained information on treatment-related death and secondary malignant disease. These events were rare, and no more likely in children who received myeloablative therapy than those who had conventional chemotherapy.

The single study with detailed information on other severe adverse effects found that treatment made no difference in the risk of sepsis and serious infection. However, children who had high-dose chemotherapy were significantly more likely to certain side effects affecting their kidney, lungs and liver.

Renal effects usually are not painful, but can lead to kidney failure. Interstitial pneumonitis is a potentially serious lung inflammation and veno-occlusive disease is an obstruction of blood vessels in the liver that is extremely uncomfortable and that could become dangerous if it progresses to the point that the abdomen fills with fluid.

“Each of these [adverse] effects can be life-threatening, but medical teams have gotten much better at treating them and identifying them as early as possible,” said NCI’s Seibel. “And in high-risk neuroblastoma, the risk of dying from the cancer is much greater than and worth the risk of the side effects.”

None of the studies described the influence of treatment on quality of life, the authors observed.

They also noted that the three studies employed different criteria in defining “high-risk” children and used different combinations of drugs, both for high-dose and conventional [chemotherapy](#). Prior treatments that patients had received, such as radiation and surgery, also varied.

Consequently, they wrote that while the data supported the idea of

myeloablative treatment, it was impossible to draw conclusions about specific programs.

Seibel said that treatment of these tumors is an active area of research. “The NCI is sponsoring numerous studies in all risk categories of neuroblastoma,” some involving variants of myeloablative therapy alone or in combination with other treatments.

In addition, she said, “There are several new agents that have been identified for [neuroblastoma](#) in which the NCI is sponsoring trials.”

More information: Yalçin B, et al. High-dose chemotherapy and autologous haematopoietic stem cell rescue for children with high-risk neuroblastoma (Review). Cochrane Database of Systematic Reviews. Issue 5, 2010.

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