Study Suggests It Is Safe to Ease Neutropenic Restrictions

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A recent study has suggested that restrictions on social contacts, pets, and diet did not affect rates of infectious complications among children undergoing intensive chemotherapeutic regimens (J Clin Oncol [published online ahead of print June 6, 2016]. pii: JCO667881). There is good evidence to support the pharmacologic measures of anti-infective agents and granulocyte growth factors to decrease the risk of infection in patients receiving chemotherapy. However, data are lacking regarding the effectiveness of the common recommendations of dietary restrictions, such as banning fresh fruits and vegetables, and implementing social contact restrictions. Given that these can affect QOL, the researchers set out to determine whether these restrictive measures were worthwhile.

“One of the main points is the fact that even if the theoretical rationale of a policy is plausible, the clinical effectiveness has to be proven, in particular, if the policy impairs the quality of life of our patients,” says Thomas Lehrnbecher, MD, corresponding author and professor of pediatrics in the department of hematology and oncology at the Johann Wolfgang Goethe University in Frankfurt, Germany.

Study Details and Results

The AML-BFM 2004 clinical trial, also known as the Therapy-Optimization Trial for the Treatment of Acute Myeloid Leukemias (AML) in Children and Adolescents, was a multicenter study performed between March 2004 and April 2010 in Germany, Austria, Switzerland, and the Czech Republic. It was a pediatric AML trial that stratified patients into risk groups and aimed to intensify therapy in high-risk patients while limiting toxicity. Recommendations regarding anti-infective measures were included in the protocol, but were not mandatory. Data regarding infectious complications were abstracted from the charts at the treating hospitals. To provide information regarding restrictive directives given to patients, a survey was sent to the treating hospitals in Germany asking about the policy concerning patient restrictions with regard to food, social interactions, and pets. The scoring system of the survey provided a number, and the higher the number, the more restrictive the recommendations were to patients.

A total of 629 children were treated on protocol in German centers. Of these, 339 had data available regarding infectious complications and also had been treated at an institution that answered the survey (37 different centers), thereby providing a full data set. Antifungal prophylaxis was given to the majority of patients, and approximately one-third received antibacterial prophylaxis. Of the 339 patients included in the study, 227 (67%) had at least 1 episode of fever of unknown origin (FUO), 174 (51%) had at least 1 episode of bacteremia, 77 (23%) had at least 1 episode of gastroenteritis, and 45 (13%) had at least 1 episode of pneumonia.

Restrictions on attending school were given to 90% of patients, and greater than 80% of patients were given restrictions regarding eating raw meat or fish. Restrictions concerning friends visiting at home or eating takeout food were recommended in approximately one-third of the patients. When adjusted for sex, age, weight group, AML risk group, and type of antibiotic prophylaxis, none of the restriction scores regarding food, pets, or social contacts was found to be significantly associated with the risk of FUO, bacteremia, pneumonia, or gastroenteritis.

KEY POINTS

- Evidence is lacking that the commonly placed restrictions on diet, social contacts, and pets decrease infection rates in patients undergoing intense chemotherapy.
- The current study supports the relaxation of neutropenic restrictions.
- More research is needed to study social contact and pet restrictions, but major centers have relaxed dietary restrictions and emphasize a common sense approach.

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The adjusted multivariable analysis also revealed that patients who were underweight had an increased risk of FUO compared with normal or overweight children. Bacteremia was found to be significantly associated with AML risk stratification: those in the high-risk group had a higher incidence and those who were given prophylactic nonabsorbable antibiotics had a lower risk. High-risk patients also had a higher risk of pneumonia. Furthermore, gastroenteritis was found to be significantly associated with age, with older children having a lower risk of developing the complication.

“This study addresses an important question regarding the impact of 3 environmental exposures on the infection risk in children with AML: diet, pets, and social interactions,” says Hana Hakim, MD, MS, medical director of infection prevention and control at St. Jude Children’s Research Hospital in Memphis, Tennessee. “These restrictions originated from the ‘protected environment’ concept initiated in the 1960s as a measure to reduce infection risk in cancer patients. However, existing evidence supporting these restrictions has been limited or lacking because of the difficulty in designing studies that provide high-level evidence, such as randomized multicenter clinical trials.”

Clinical Impact

The authors state that they believe that it is safe, in general, for these children to attend school or daycare. On the topic of pets, their institutional policy does not ban pets, but includes a common sense approach of advising hand washing after contact with pets, avoiding cage cleaning, and avoiding reptile pets.

“This study provides a step forward toward addressing the research gap,” says Dr. Hakim. “However, it used a survey design to the participating centers to evaluate restriction practices related to diet, pets, and social interactions. Adherence of patients to each of the centers’ policies has not been reported. Also, all of the responding centers were in Germany, which makes conclusions nongeneralizable to other nonsimilar settings. This is among other limitations pointed out by the authors,” Dr. Hakim adds.

The authors believe that changing the strict restrictions on diet, social contacts, and pet contacts may increase the QOL for pediatric patients with AML without increasing the risk of infection, and they call for future studies in children with different types of malignancies.

“In the context of another study, we have prospectively collected data on infectious complications in children with acute lymphoblastic leukemia, acute myeloblastic leukemia, and non-Hodgkin lymphoma over a period of 2 years,” says Dr. Lehrnbecher. “As we now changed the policies of restrictions regarding food, we will extend this analysis for another 2 years, which will demonstrate whether the change of our policy regarding food restrictions is associated with an increased risk of infection or not. In addition, we plan to evaluate quality of life.”

Dr. Hakim points out that other recent studies, including single-center randomized trials, have shown there is insufficient evidence that a neutropenic diet is helpful in preventing infections.

“At St. Jude Children’s Research Hospital, patient education has recently emphasized eating safely guidelines; for example, fresh vegetable salad is now an acceptable option when following these guidelines, but raw or undercooked seafood, meat, poultry, or eggs remain restricted,” she says. “In summary, this study adds to the recently growing body of literature, but more evidence and research is needed, especially related to the impact of pets and social interactions on infection risk.”

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