A Double-Blind comparison of Empirical Oral and Intravenous Antibiotic Therapy for Low-risk Febrile Patients with Neutropenia during Cancer Chemotherapy

Reviewers: Li Liu, MD
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Background
Fever and neutropenia (low white count) are major complications among cancer patients treated with intensive cytotoxic chemotherapy. Serious and potentially life-threatening medical complications, such as hypotension, pulmonary compromise, and altered mental status, may occur. Prompt and adequate treatment of these patients with empirical intravenous therapy with broad-spectrum antibiotics is the standard of care. However, not all patients have the same risk for life threatening systemic infections. Patients with fever and neutropenia of no more than 7 to 10 days and without any other underlying conditions may be considered as low-risk. Therefore, aggressive inpatient treatment with intravenous antibiotics may be unnecessary. Freifeld et al. undertook a multicenter, randomized, double-blinded, placebo-controlled study to determine whether oral empirical therapy is as effective as intravenous therapy in low-risk patients with granulocytopenia.

Methods
Patients (age ranged from 5 to 74) with cancer who had fever with neutropenia were eligible if their neutropenia was expected to resolve within 10 days after the onset of fever and if they did not have hemodynamic instability, abdominal pain, nausea and vomiting, diarrhea, neurologic or mental-status changes, intravascular-catheter infection, catheter-tunnel infection, or a new pulmonary infiltrate. Patients were randomly assigned to receive either the oral regimen consisting of 30 mg/kg of ciprofloxacin (Cipro) per day in three divided doses plus 40 mg/kg of amoxicillin-calvulanate (Augmentin) in three divided doses or the intravenous regimen consisting of 90 mg/kg of ceftazidime (Fortaz) in three divided doses. Each active regimen was paired with a placebo preparation.

Results
A total of 232 episodes of neutropenia (defined as < 500 neutrophils per cubic millimeter) were included with 116 episodes in each group. Treatment was successfully administered without modifications in approximately two thirds of patients in each group. There were no deaths. The efficacies of the oral and intravenous regimens were similar (71% vs. 59%, p=0.07). Fever of unexplained origin was successfully treated in 85% of the episodes in the oral-therapy group and 90% of the episodes in the intravenous-therapy group. For patients with documented infection, oral-therapy was successful in 41% of the episodes vs. 33% of those treated in the intravenous-therapy group (p=0.4). Adverse effects appeared to be comparable, except for diarrhea, which was more common in the oral-therapy group.

Discussion
In low-risk hospitalized patients with cancer who have fever and neutropenia, empirical oral-therapy with Cipro plus Augmentin was found to be as effective as intravenous-therapy with Fortaz. However, how to use these regimens appropriately in individual patients remains challenging. Further studies may be necessary before adopting this oral regimen for outpatient use.