A correlative blood assay to monitor patients at risk for chemotherapy-induced peripheral neuropathy

Angeleah Dadivas, OMS-II, Kinjal Parikh, MD, John Kennedy, BS, Amy Brady, OMS-I, Margaretha Wallon, PhD
Lankenau Institute for Medical Research, Wynnewood, Pennsylvania

Introduction

Chemotherapy-induced peripheral neuropathy (CIPN) is a disabling side effect of platinum-based chemotherapies like cis-, oxali- and carboplatin. These therapies cause bursts of reactive oxygen species (ROS), which can trigger structural changes in peripheral nerves including neuropathy, axonopathy and/or myelinopathy. There is no effective CIPN prevention strategy and medications to alleviate neuropathy often lack efficacy and/or have unacceptable side-effects.

Background

The “stocking and glove” distribution of neuropathy is primarily due to the vulnerability of long nerves in the peripheral nervous system. A meta-analysis of 31 CIPN studies involving 4,179 patients indicated CIPN in 48% of patients. Within the first month of completing chemotherapy, the prevalence of CIPN was 68.1%; after 6 months of completing chemotherapy, the prevalence of CIPN decreased to 30.0%. A separate study indicated colon cancer patients who received oxaliplatin-based adjuvant chemotherapy had numbness or tingling of hands and feet up to 6 years from starting treatment. Due to the high frequency of neuropathy, there is a need for a test that can help clinicians better guide therapy and prevent this detrimental outcome.

Objective

Glutathione, an antioxidant, plays an important role in red-ox homeostasis and the recycling of glutathione can be determined by the ChemoTox assay. The aim of this study was to determine if ChemoTox can provide clinicians with a blood assay to quantitate platinum-induced neuropathy.

Materials & Methods

The cohort of cancer patients are from the Lankenau Medical Center outside of Philadelphia, PA. The hospital sees ~1,100 cancer patients per year. Colorectal patients constitute 14.7% while 10.4% are lung cancer patients. Of the patients enrolled in this study, 84.4% are Caucasian, 14.0% are African-American and 1.6% are Asian.

Blood drawn from consented and chemotherapy naïve patients (N = 59) were tested for glutathione recycling capacity and normalized to total red cell numbers. Patients reported neuropathy using the Rotterdam Symptom Check List. Patient’s glutathione recycling capacities were correlated to self-reported neuropathy.

Results

42 of 59 patients stated they experienced neuropathy during chemotherapy. 21 high risk patients were identified as those who reported experiencing neuropathy as a “2,” or “quite a bit” on the Rotterdam Checklist. 19 of the 21 patients experienced increasing neuropathy within their first 5 treatments. Select correlates above are patient-reported neuropathy (0-3) in blue, and ChemoTox quantities (ng / ml plasma and 10⁶ RBC) in red.

Discussion

• 72.2% reported neuropathy during chemotherapy and 35.6% were recognized as high risk patients for progressive CIPN. These outcomes, despite the small cohort size, are representative of larger studies.

• Patients LH12-015, LH12-018 and LH12-039 display trends that initially show decreased glutathione recycling capacities and remain low over time. This correlation detects a patient population that can be addressed earlier as to the direction of treatment.

• Patients LH12-026, LH12-027 and LH12-036 illustrate a patient population that initially display adequate glutathione recycling capacity. However, the inability to maintain turnover during extended treatment cycles identifies the inverse correlation as a trend of concern.

• Low glutathione recycling also has a corollary to an increased risk for chemotherapy induced nausea and vomiting (CINV). Among the patients shown in results, 5/6 patients reported some level of nausea, and 4/6 reported moderate to severe delayed nausea.

Future Directions

• Taxane therapies, another culprit for causing CIPN via ROS, is a target population for future studies of ChemoTox efficacy.

• Platinum therapy as a treatment for breast cancer should be explored to see if systemic ROS provides a similar pattern to that of patients with lung and colon cancer.

References


• Lung cancer patients. Of the patients enrolled in this study, 84.4% are Caucasian, 14.0% are African-American and 1.6% are Asian.

Blood drawn from consented and chemotherapy naïve patients (N = 59) were tested for glutathione recycling capacity and normalized to total red cell numbers. Patients reported neuropathy using the Rotterdam Symptom Check List. Patient’s glutathione recycling capacities were correlated to self-reported neuropathy.

42 of 59 patients stated they experienced neuropathy during chemotherapy. 21 high risk patients were identified as those who reported experiencing neuropathy as a “2,” or “quite a bit” on the Rotterdam Checklist. 19 of the 21 patients experienced increasing neuropathy within their first 5 treatments. Select correlates above are patient-reported neuropathy (0-3) in blue, and ChemoTox quantities (ng / ml plasma and 10⁶ RBC) in red.

Discussion

• 72.2% reported neuropathy during chemotherapy and 35.6% were recognized as high risk patients for progressive CIPN. These outcomes, despite the small cohort size, are representative of larger studies.

• Patients LH12-015, LH12-018 and LH12-039 display trends that initially show decreased glutathione recycling capacities and remain low over time. This correlation detects a patient population that can be addressed earlier as to the direction of treatment.

• Patients LH12-026, LH12-027 and LH12-036 illustrate a patient population that initially display adequate glutathione recycling capacity. However, the inability to maintain turnover during extended treatment cycles identifies the inverse correlation as a trend of concern.

• Low glutathione recycling also has a corollary to an increased risk for chemotherapy induced nausea and vomiting (CINV). Among the patients shown in results, 5/6 patients reported some level of nausea, and 4/6 reported moderate to severe delayed nausea.

Future Directions

• Taxane therapies, another culprit for causing CIPN via ROS, is a target population for future studies of ChemoTox efficacy.

• Platinum therapy as a treatment for breast cancer should be explored to see if systemic ROS provides a similar pattern to that of patients with lung and colon cancer.

References


• Lung cancer patients. Of the patients enrolled in this study, 84.4% are Caucasian, 14.0% are African-American and 1.6% are Asian.

Blood drawn from consented and chemotherapy naïve patients (N = 59) were tested for glutathione recycling capacity and normalized to total red cell numbers. Patients reported neuropathy using the Rotterdam Symptom Check List. Patient’s glutathione recycling capacities were correlated to self-reported neuropathy.

42 of 59 patients stated they experienced neuropathy during chemotherapy. 21 high risk patients were identified as those who reported experiencing neuropathy as a “2,” or “quite a bit” on the Rotterdam Checklist. 19 of the 21 patients experienced increasing neuropathy within their first 5 treatments. Select correlates above are patient-reported neuropathy (0-3) in blue, and ChemoTox quantities (ng / ml plasma and 10⁶ RBC) in red.

Discussion

• 72.2% reported neuropathy during chemotherapy and 35.6% were recognized as high risk patients for progressive CIPN. These outcomes, despite the small cohort size, are representative of larger studies.

• Patients LH12-015, LH12-018 and LH12-039 display trends that initially show decreased glutathione recycling capacities and remain low over time. This correlation detects a patient population that can be addressed earlier as to the direction of treatment.

• Patients LH12-026, LH12-027 and LH12-036 illustrate a patient population that initially display adequate glutathione recycling capacity. However, the inability to maintain turnover during extended treatment cycles identifies the inverse correlation as a trend of concern.

• Low glutathione recycling also has a corollary to an increased risk for chemotherapy induced nausea and vomiting (CINV). Among the patients shown in results, 5/6 patients reported some level of nausea, and 4/6 reported moderate to severe delayed nausea.

Future Directions

• Taxane therapies, another culprit for causing CIPN via ROS, is a target population for future studies of ChemoTox efficacy.

• Platinum therapy as a treatment for breast cancer should be explored to see if systemic ROS provides a similar pattern to that of patients with lung and colon cancer.

References