Background: Patients undergoing chemotherapy for colon cancer are at significant risk for developing moderate-to-severe side effects as a result of their treatment regimens. These side effects can be debilitating to the patient and are often associated with a number of negative health and economic consequences. There is currently no accurate method to identify which patients are at risk for chemotherapy-induced side effects. If such a prediction tool were available, it would provide opportunities for directed prophylactic interventions.

This study adopted a novel approach to filling the unmet clinical need for an accurate risk prediction tool. It capitalized on the growing body of evidence that genetic factors (in particular, networks of interacting genes) play a role in determining the likelihood of a patient’s risk for developing side effects. Specifically, the study was designed to assess the feasibility of identifying SNPs that could accurately predict the risk for common chemotherapy-induced side effects: chemotherapy-induced nausea and vomiting (CINV), diarrhea, oral mucositis (OM), cognitive dysfunction (CD), peripheral neuropathy (PN), and fatigue.

Methods: Patients (n=57) with colon cancer who received at least 3 cycles of FOLFOX6 +/- bevacizumab were enrolled. After informed consent, saliva samples were collected, DNA was isolated, and SNPs were analyzed on Illumina Omni microarrays (2.5 x 106 SNPs). Side effects under consideration were observed using Patient Care Monitor©, a validated patient-reported symptom assessment tool. SNPs were identified that were associated with moderate-to-severe side effects and used to develop predictive networks.

Results: The side effects most often reported by patients were at risk for CINV, diarrhea, OM, CD, PN, and fatigue.

Conclusions: The study calls attention to the potential to modify choices in treatment regimens, aggressiveness of care, and appropriate use of prophylactic therapies, with consequent health and economic impacts.

Abstract

Background

Despite current supportive care options, the risk for side effects among patients receiving chemotherapy for colon cancer is significant. There is no effective way to predict side-effect risk. Consequently, providers and patients are limited to reacting to side effects as they occur. The ability to understand risk prospectively has the potential to modify choices in treatment regimens, aggressiveness of care, and appropriate use of prophylactic therapies, with consequent health and economic impacts.

The biological basis underlying the development of side effects is not fully understood, it is clear that genetics plays a significant role in determining individual patient risk. The incidence of moderate-to-severe side effects in the population of patients with colon cancer receiving FOLFOX6 +/- bevacizumab was 60% for CINV, diarrhea, OM, CD, PN, and fatigue (56%).

Conclusion

The frequencies of studied side effects exceeded the expected rates based on literature reports. Standard supportive care strategies were not able to effectively mitigate significant side-effect development. Accurate SNP-based BNs (Figure 2) were created that were highly predictive of each of the 6 side effects.

Methods

Fifty-seven subjects with histologically proven colon cancer who were treated for at least 3 cycles of FOLFOX6 +/- bevacizumab were enrolled. After informed consent, saliva samples were collected, DNA was isolated, and SNPs were analyzed on Illumina Omni microarrays (2.5 x 106 SNPs). Side effects under consideration were observed using Patient Care Monitor©, a validated patient-reported symptom assessment tool. SNPs were identified that were associated with moderate-to-severe side effects and used to develop predictive networks.

Results

- The incidence of moderate-to-severe side effects in the studied population was as follows: CINV (52%), diarrhea (16%), OM (26%), CD (21%), PN (26%), and fatigue (56%).
- Accurate SNP-based BNs (Figure 2) were created that were highly predictive of each of the 6 side effects (Table).

References