**Introduction**

Irinotecan, one of the pivotal agents in the first-line treatment of metastatic colorectal cancer, is a prodrug activated to 7-ethyl-10-hydroxycamptothecin or SN-38 by carboxylesterase. After exertion of its cytotoxic effects, SN-38 is inactivated via glucuronidation. This step is mediated by UDP-glucuronosyltransferase (UGT) 1A enzymes, with UGT1A1 playing a major role in the detoxification of SN-38. Although the drug is now used widely, especially for colorectal and lung cancers, patients and oncologists have grave concerns about the dose limiting toxicity of irinotecan, resulting in leukopenia and/or diarrhea. We aimed to assess the prevalence of irinotecan induced neutropenia and diarrhea during past one year in all referral hematology-oncology center in Iran. We also reviewed the related data of irinotecan toxicity and its relation to UGT 1A1 enzyme polymorphisms.

**Methods and Materials**

We prospectively collected all data over the prevalence of irinotecan induced neutropenia and diarrhea for last one year in all cancer patients who received irinotecan by standard doses in our hospital. We also performed a literature search according to frequencies of irinotecan toxicities and UGT 1A1 enzyme polymorphisms. Materials were obtained by searching ELSEVIER, web of knowledge, PubMed, Scopus, clinical trials, and Cochrane database of systematic reviews in different clinical studies which enrolled patients with different ethnicities and implemented diverse regimens containing irinotecan.

**Results**

Analysis of distribution of the genotype frequencies of UGT1A1 *6 (G/G, A/G, A/A) in different ethnicities in the Iranian population of 300 unrelated healthy individuals, including Persian, Azari, Lure, Kurdish, Arab, Baluch and Caspian revealed that the genotype frequencies of A/G and A/A were 13% and 0.33 %, respectively. The frequency of the heterozygous (A/G) variant of UGT1A1 * 6 was significantly high in the Bluch ethnic group (20%) and subsequently in the Persian (15.69%) ethnic group (p < 0.00001). The results indicate that the frequency of the homozygous (A/A) variant of UGT1A1 *6 was significantly observed in Central Iran, while no frequency was indicated in North, South, East and West Iran, indicating an insignificant contribution of this allele in most parts of Iran. The frequency of the heterozygous (A/G) variant of the UGT1A1 *6 allele was highest in Central Iran. Toxicity result 300 evaluated case of cancer patients received irinotecan in our institute, showed that less than 9% have been affected by irinotecan–induced diarrhea and more than 20% experienced neutropenia in regular dose of 100 mg/m2. The prevalence of diarrhea associated by irinotecan administration is lower in Iranian patients than worldwide reports.

**Discussion**

The UGT1A1*28 polymorphism is due to a change in the number of TA (Thymidine- Adenine) repeats in the TATA box of the UGT1A1 promoter from the wild-type 6 repeats to the variant 7 repeats. UGT1A1*28 was found to be associated with decreased activity and SN-38 glucuronidation in humans. Besides being associated with reduced SN-38 glucuronidation in humans, the presence of UGT1A1*28 is assumed to be a risk factor for the occurrence of toxicity. Indeed, there are fairly strong evidences that individuals with UGT1A1*28/28 genotype tend to have a higher prevalence of irinotecan-induced neutropenia. However, the association between UGT1A1*28 polymorphism and severe diarrhea is far less clear. Surly, ethnicity is a matter of interest for irinotecan associated adverse effects.

**References**