Genotoxic Effects Induced by Fotemustine and Vinorelbine in Human Lymphocytes

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The aim of this study was to investigate the *in vitro* genotoxic effects of the anticancer drugs fotemustine and vinorelbine on human lymphocytes and to determine individual and sex-related responses to these drugs. Fotemustine is a DNA-alkylating drug while vinorelbine is a semi-synthetic *Vinca* alkaloid. The study was carried out with twenty independent healthy donors for each drug. We have tested the ability of these drugs to induce chromosome aberrations (CAs) and sister chromatid exchanges (SCEs) as well as effect on the mitotic index (MI) in cultured human lymphocytes. Fotemustine was shown to induce CAs and SCEs at all concentrations tested (2, 4 and 8 μg/ml) in a dose-dependent manner. Additionally it also decreased the mitotic index in a similar dose-dependent manner. Vinorelbine had no effect on structural CAs, but it significantly increased the numerical CAs at all doses tested (0.5, 1 and 2 μg/ml). Vinorelbine also induced SCE events and increased the MI values.

Two-way analyses of variance were used to compare the individual and gender-related susceptibilities to fotemustine and vinorelbine with respect to the CA, SCE and MI values. The results indicated that individuals in fotemustine treatment groups showed different genotoxic responses with respect to CA and SCE induction and additional findings indicated a gender-specific response in this group. Individuals in the vinorelbine test group also exhibited statistically significant numerical CA, SCE and MI responses to vinorelbine. A statistically significant gender-related SCE response to this drug was also evident. This study indicates that these drugs have potentially harmful effects on human health.

Key words: Fotemustine, Vinorelbine (Navelbine), Genotoxicity