INVESTIGATING GENOTOXIC EFFECT OF GADOBUTROL BY IN VITRO CHROMOSOME ABERRATIONS TEST

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ABSTRACT
Magnetic Resonance Imaging (MRI) is a technique that uses powerful magnets and radio waves to create detailed images of organs and tissues in the body to diagnose diseases or follow the response to treatment and does not contain ionizing radiation harmful to health. Although MRI has advantages such as high resolution and soft tissue differentiation, contrast agents are administered to patients in cases where contrast cannot be achieved completely. Among the contrast agents, the most widely used group is gadolinium-based contrast agents (GBCAs). Since gadolinium (Gd^{3+}) alone has high toxicity, GBCAs are used as a chelate complex. Gadobutrol is a widely used GBCA being a non-ionic, paramagnetic complex consisting of Gd^{3+} chelated with the macrocyclic compound dihydroxy-hydroxymethylpropyl-tetraazacyclododecane-triacetic acid (butrol). Considering this common use of gadobutrol, it causes great concern for human health. Thus, this study aimed to evaluate the genotoxic effects of gadobutrol by in vitro chromosome aberrations test. For this purpose, 7,000, 14,000, 28,000, 56,000, and 112,000 µg/mL of gadobutrol was administered to lymphocytes obtained from three healthy donors for 24 and 48 hours. Distilled water as negative control and Mitomycin-C as a positive control was also used. Gadobutrol induced a significant increase in abnormal cell frequency at the highest concentration 112,000 µg/mL in both 24 and 48-hour applications and at the two highest concentrations 56,000 and 112,000 µg/mL in 24-hour applications in CA/Cell frequency. Gadobutrol induced mostly chromatid break and sister chromatid union as structural aberrations and polyploidy and endoreduplication as numerical aberrations. The results revealed that especially higher concentrations of gadobutrol were found to have genotoxic potential on human lymphocytes. Hence, further in vitro and in vivo genotoxicity test systems are recommended to be carried out for a better understanding of the genotoxic potential of GBCAs.
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Keywords: Magnetic resonance imaging, gadolinium-based contrast agent, gadobutrol, genotoxicity, chromosome aberration