

IN VITRO RADIOSENSITIVITY TEST AS ONE OF THE PROGNOSTIC SCORE PARAMETERS FOR THE DESIGN OF THERAPEUTIC STRATEGIES IN THE CUTANEOUS RADIATION SYNDROME

¹ Di Giorgio, M; ² Portas, M; ¹ Dubner, D; ² Navarro, M

¹Autoridad Regulatoria Nuclear; Av. Del Libertador 8250, CP: C1429BNP, mdigiorg@cae.arn.gov.ar; ²Hospital de Quemados del Gobierno de la Ciudad de Buenos Aires, Av. Pedro Goyena 369, , quemados_informatica@buenosaires.gov.ar -Buenos Aires, Argentina

Abstract: The cutaneous radiation syndrome (CRS) constitute the most frequent accidental radiological event. It is caused by complex interactions between antiproliferative and proinflammatory process, following a clinically well-defined time pattern. A research project for diagnostic and therapeutic approach of CRS is in progress: 67 persons, which developed acute and/or late CRS, were included in this protocol. There exist individual variations that could condition the response to ionizing radiation (IR). Deficiencies in DNA repair mechanisms would be involved on hypersensitivity to deterministic effects of IR. The characterization of DNA repair capacity in lymphocytes through cytokinesis blocked micronucleus and alkaline single-cell microgel electrophoresis (comet) assays was conducted to evaluate in vitro individual radiosensitivity in patients included in this research protocol that showed acute and/or late cutaneous reactions with grades 3 and 4 of the EORTC and RTOG [1]. Blood samples were in vitro irradiated with 2 Gy. DNA repair capacity was evaluated through comet assay for initial damage and after specific times of repair. Captured images were analyzed by CASP image analysis software, quantified by the Olive tail moment and fitted by a mono-exponential model to describe the kinetic profile. Previous studies [10] have identified three subpopulations, characterized by the mean values of their repair mean half-time: healthy controls (2.6 ± 0.3 minutes), average-reactor cancer patients (4.7 ± 2.9 minutes) and over-reactor cancer patients (24.9 ± 10.4 minutes). In this paper, 10 representative cases have been assessed retrospectively. The therapeutic response was evaluated through clinical follow-up, serial photographic record and complementary tests (telethermography and high frequency ultrasonography). Therapeutic response and its correlation with radiosensitivity test results have also been studied.

Overall, 4 cases showed favorable local recovery and almost complete to complete remission of signs and symptoms after 5 to 12 months of the beginning of the treatment. In these patients, both MN frequencies and comet assay showed values compatible with normal/average radiosensitivity. However, three cases showing average radiosensitivity presented complications attributed to radiation exposure (treatment or diagnosis) or to comorbidity factors. Finally, 3 cases presented a partial response with pain and acute repetitive crisis. In vitro radiosensitivity test results indicated that these patients (over-reactors) presented a greater risk than average patients of developing radiation toxicity. These results would ensure in vitro radiosensitivity test to constitute one of the prognostic score parameters, jointly with applied radiation dose, radiation quality, localization (including thickness and vascularization of the dermis) in case of CRS for the design of therapeutic strategies.

References:

1. Toxicity Criteria of the Radiation Treatment of Cancer (EORTC) and Radiation Therapy Oncology Group (RTOG).
2. Di Giorgio M., Busto M. et al. "DNA repair capacity as predictive radiation sensitivity test. Inferences for clinical practice and radiation protection", Radiation Research Society-Proceedings of the 47 Annual meeting of the American Society for Therapeutic Radiology and Oncology, Denver, Colorado, USA (2005).