Clinical outcome and cisplatin excretion influenced by GSTM1, GSTT1 and GSTP1 ile105val polymorphisms in head and neck squamous cell carcinoma patients treated with cisplatin chemoradiation

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Statement of the Problem: Cisplatin (CDDP) associated with radiotherapy (RT) is used in treatment of patients with head and neck squamous cell carcinoma (HNSCC). The responses to treatment as well as its side effects vary among individuals, and this fact may be explained by the genetic variability in metabolism of CDDP. The aim of this study was to access if inherited ability to cellular CDDP detoxification, mediated by GSTs enzymes alters the therapeutic and side effects of CDDP and RT and urinary concentration of CDDP in HNSCC patients.

Methodology & Theoretical Orientation: We evaluated, prospectively, 90 consecutive HNSCC patients, who received CDDP plus RT as treatment. Genotypes of GSTM1, GSTT1 and GSTP1 Ile105Val polymorphisms were analyzed by multiplex polymerase chain reaction (PCR) and PCR followed by restriction enzyme digestion, respectively, in peripheral blood DNA. Treatment side effects as well as renal and hearing toxicities were ranked through questionnaire and laboratory tests. Urinary doses of CDDP were performed by high performance liquid chromatography (HPLC).

Findings: Patients with GSTT1 null genotype presented less vomiting (20.0% vs. 64.4%; P=0.002), ototoxicity (41.7% vs. 79.3%; P=0.03), nephrotoxicity (69.94±21.40 vs. 62.87±20.72 EDTA-51Cr mL/min/1.73m²; P=0.03) and eliminates more CDDP (429.58±116.24 vs. 253.42±95.20 □g CDDP/mg creatinine; P=0.04) than those with the gene. Patients with GSTP1 Ile105Val homozygous variant genotype had shorter progression-free survival and those with GSTP1 Ile105Val homozygous wild genotype had shorter overall survival.

Conclusion & Significance: Our data indicate that SCCHN patients with inherited distinct abilities for CDDP metabolism, associated with GSTT1 and GSTP1 Ile105Val polymorphisms, exhibit distinct toxicities to treatment and urinary CDDP excretion. We believe that this data may constitute preliminary basis of future personalized.

Biography

Eder de Carvalho Pincinato has completed his Doctor degree from University of Campinas, Brazil. He is a Pharmacist, Assistant Professor of Hematology and Coordinator of Pharmacy course at Mackenzie Presbyterian University.

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