CYP27B1 GENETIC VARIANTS' INFLUENCE IN NEPHROTOXICITY DUE TO PLATINUM-BASED CHEMOTHERAPY IN NON-SMALL CELL LUNG CANCER

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Background and importance

Platinum-based doublet-chemotherapy is the standard treatment for non-small cell lung cancer (NSCLC) for EGFR wild type patients, which presents high percentages of severe adverse events, such nephrotoxicity (20-30%).

Nephrotoxicity is characterized for high morbidity and mortality. cisplatin is one of the major causes of nephrotoxicity.

Several studies have shown that vitamin-D activation through CYP27B1 and CYP2R1 enzymes is protective against chronic kidney disease among others pathological pathways. However, few studies focused on the role of vitamin-D pathway genetic polymorphisms in nephrotoxicity.

Aim and objectives

The aim of this study was evaluated the influence of CYP27B1 and CYP2R1 gene polymorphisms on nephrotoxicity due to platinum-based chemotherapy in non-small cell lung cancer.

Material and methods

Prospective cohort' study. 165 patients diagnosed with NSCLC between 2003-2019, followed-up until December 2020.

CYP27B1 (rs4646536, rs3782130, rs703842, rs10877012) and *CYP2R1* (rs10741657) polymorphisms were analyzed by real-time PCR using TaqMan® probes.

Nephrotoxicity was evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.0.

Results

Patients median age at NSCLC diagnosis was 62[53-67] years; 73.3% (121/165) men; 69.09% (114/165) stage IIIB-V; 59.39% (98/165) adenocarcinoma; 58.18% (96/165) family history of cancer; 24.24% (40/165) Previous lung disease; EGFR status: 10.91% (18/165) Mutated. Chemotherapy agents: 18.29% (30/164) Gemcitabine; 21.34% (35/164) Paclitaxel; 24.39% (40/164); 35.98% (59/164). Nephrotoxicity: 17.58% (29/165).

Patients carrying the CYP27B1-rs4646536 (p=0.0312; OR:0.32; CI95%:0.10-0.84; AG vs AA); CYP27B1-rs3782130 (p=0.0247; OR:0.22; CI95%:0.05-0.85; CC vs G); CYP27B1-rs703842 (p=0.0121; OR:0.15; CI95%:0.03-0.67; CT vs CC) and CYP27B1-rs10877012 (p=0.0239; OR:4.50; CI95%:1.17-17.2; TT vs G), were associated with nephrotoxicity.

However, for CYP2R1-rs10741657 we did not find a statistically significant association.

Conclusion and relevance

Our results suggest that rs4646536, rs3782130, rs703842, and rs10877012 influence nephrotoxicity in platinum-based chemotherapy. CYP27B1 is the only enzyme capable of activating vitamin-D.

Therefore, genetic study of these polymorphisms could be used as a toxicity prediction biomarker in NSCLC patients going under based platinum chemotherapy.

References

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