

MODELING OF DOSE-RESPONSE RELATIONSHIPS BETWEEN PB AND CD LEVELS IN TESTICULAR AND PROSTATE CANCER TISSUES AND TESTOSTERONE LEVELS

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Exposure to lead (Pb) and cadmium (Cd) poses risk to human health. It is known that these metals have toxic impact on male reproductive system, leading to physiological disorders and infertility. Limited data indicates the carcinogenic potential of Pb, while Cd has been recognized as carcinogen. Benchmark dose-effect modeling can be applied to data from human, animal and ecotoxicological studies with the aim to obtain Benchmark dose (BMD), starting point in human health risk assessment. The aim of this study was to use Benchmark modeling to determine the dose-effect relationship between Pb and Cd levels in tissues of testicular and prostate cancer patients and serum testosterone levels. The study was conducted at the Clinical Center of Serbia, and included 104 patients with prostate and testicular cancer. Cd and Pb levels (ng/g) were measured by atomic absorption spectrophotometry in isolated healthy surrounding and carcinoma-affected tissues. Testosterone levels (ng/mL) were measured using the chemiluminescence immunoassay (CLIA) method. Dose-effect modeling was performed using PROAST70.1 software with continuous data. The dose dependence was obtained between Cd levels in tumor tissue and testosterone levels (BMD: 0.0024 ng Cd/g, prostate cancer and 0.0038 ng Cd/g, testicular cancer). Dose dependence was obtained between Cd levels in healthy surrounding tissue and testosterone levels (BMD: 0.0092 ng Cd/g). No dose dependence was obtained when modeling Pb levels as a dose. The data from this study indicate a potential link between Cd and testosterone levels, i.e. potential association of Cd exposure with male reproductive health.

Acknowledgments

This research was supported by the Science Fund of the Republic of Serbia, PROMIS, Grant No 6066532, DecodExpo project.

MODELOVANJE ODNOSA DOZA-ODGOVOR IZMEĐU NIVOVA Pb I Cd U TKIVIMA KARCINOMA TESTISA I PROSTATE I NIVOVA TESTOSTERONA

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Izloženost olovu (Pb) i kadmijumu (Cd) predstavlja rizik po zdravlje ljudi. Poznato je da ovi metali deluju toksično na muški reproduktivni sistem dovodeći do poremećaja fizioloških funkcija i neplodnosti. Ograničen broj studija ukazuje na kancerogeni potencijal Pb, dok je Cd poznatihumani karcinogen. Benchmark modelovanje odnosa doza-efekat se teoretski može primeniti na podacima iz humanih, animalnih i ekotoksikoloških studija, sa ciljem dobijanja Benchmark doze (BMD) kao polazne tačke u proceni rizika po zdravlje ljudi. Cilj ovog rada bio je da se Benchmark modelovanjem utvrdi odnos doza-efekat između nivoa Pb i Cd u tkivima karcinoma testisa i prostate pacijenata i nivoa testosterona u serumu. Studija je sprovedena na Kliničkom centru Srbije i uključila je 104 pacijenta sa karcinomom prostate i testisa. Nivoi Cd i Pb (ng/g) su izmereni metodom atomske apsorpcione spektrofotometrije u izolovanim zdravim okolonim i karcinomom zahvaćenim tkivima. Nivoi testosterona (ng/mL) su mereni pomoću metode direktnog kompetitivnog hemiluminiscentnog imunoeseja (CLIA). Modelovanje odnosa doza-efekat je vršeno pomoću PROAST 70.1 softvera (RIVM, Holandija) uz upotrebu kontinuiranih podataka. Dozna zavisnost je dobijena između nivoa Cd u tumorskom tkivu i nivoa testosterona gde je BMD vrednost iznosila 0,0024 ng Cd/g (karcinom prostate) i 0,0038 ng Cd/g (karcinom testisa). Dozna zavisnost je dobijena i za modelovanje odnosa nivoa Cd u zdravom tkivu i testosterona, sa BMD vrednošću 0,0092 ng Cd/g. Pri modelovanju nivoa Pb nije dobijena dozna zavisnost. Podaci ove studije ukazuju na potencijalnu vezu između nivoa Cd u tkivu i nivoa testosterona, ukazujući na efekte izloženosti ovom metalu na muško reproduktivno zdravlje.

Zahvalnica

Ovo istraživanje je podržao Fond za nauku Republike Srbije, PROMIS, Projekat br. 6066532, „Dekodiranje uloge ekspozoma u endokrinom zdravlju“ – projekat DecodExpo.