LOW DOSE CISPLATIN INDUCED GENE ALTERATIONS, CELL CYCLE ARREST AND APOPTOSIS IN HUMAN PROMYELOCYTIC LEUKEMIA CELLS

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Abstract: Cisplatin, Cis-diamminedichloroplatinum (II) (CDDP), is an organometallic potential anti-tumor drug for treatment of variety of cancer. However, at higher concentrations, cisplatin has adverse side effects on various organs including renal and nervous systems. The exact mechanism of anti-cancer property of cisplatin is largely unknown. In this research we studied the anti-cancer potential of cisplatin at lower concentrations (1µM, 2 µM or 3 µM) using human promyelocytic leukemia (HL60) cells as a test model. Our previous studies showed that lower concentrations of cisplatin significantly induced oxidative stress and DNA damage in HL60 cells. In this study, we further investigated cisplatin effects at the molecular level using RNA sequencing method. The sequencing results show that the genes responsible for the molecular and cellular functions of cancer cells including cellular growth and proliferation, cell death and survival, cellular function and maintenance, cellular development, and cell cycle regulatory genes were significantly altered. We further conducted cell cycle analysis for 24, 48, 72, and 96 hour exposure of the cisplatin drug using propidium iodide dye. The results indicated that at 1 µM and 24 hour treatment cells were arrested at the synthesis phase, and as the concentration and treatment time increase the cells started to accumulate at the sub G1 phase. Arresting cells at sub G1 phase indicated that the cells started to enter into the apoptotic phase. Also, we investigated the HL60 cells apoptotic status for the above mentioned cisplatin concentrations and treatment periods using propidium iodide and cellometer Vision. Interestingly, as cisplatin exposure and concentration increase cells significantly entered into the apoptotic and necrotic phases. Altogether, the sequencing results, cell cycle and apoptosis data show that the low doses of cisplatin (1, 2 or 3 µM) over 24 to 96 hour exposure show significant impact on the viability of HL60 cells.

Keywords: Cisplatin, HL60 cells, Sequencing, Cell cycle, and Apoptosis.

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