Study on the effects of the combination of curcumin with paclitaxel on the chemo-resistance and miR-148a and its target genes expression in the prostate cancer cell line PC3

Abstract

Background: In men, prostate cancer (PC) is the second most common cause of cancer-related death. However, paclitaxel resistance is a major challenge in advanced PC. Curcumin, a natural antioxidant, has been demonstrated to have cytotoxic effects on cancer stem cells (CSCs).

Aim: The goal of this study is to explore if curcumin can help lower chemoresistance to paclitaxel through the regulation of miR-148a-mediated apoptosis in prostate CSCs.

Material and Methods: The 3-(4,5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide (MTT) assay and 4',6-diamidino-2-phenylindole (DAPi) labeling were used to determine cell survival. Immunohistochemistry was used to detect the expression of P-glycoprotein protein (P-gp) and CD44 proteins. Finally, real-time PCR was used to evaluate the regulatory effects of curcumin and paclitaxel on miR-148a and its target genes.

Results: Curcumin and paclitaxel co-treatment significantly reduced the IC_{50} value in $CD44^+$cells compared to paclitaxel alone. Additionally, combining these drugs considerably increased apoptosis in $CD44^+$cells. We also discovered that when curcumin and paclitaxel were combined, the expression of CD44 and P-gp was significantly reduced compared to paclitaxel alone. Curcumin and paclitaxel co-treatment also increased miR-148a levels and regulated the levels of its target genes MSK1 and IRS1.

Conclusion: Curcumin may restore paclitaxel sensitivity by raising miR-148a expression and inhibiting its target genes.

Key words: Prostate Cancer; hsa-miR-148a; MSK1; IRS1; Curcumin; Paclitaxel; Drug Resistance