Prostate Cancer and Prostatic Diseases (2000) 3, Suppl 1, S40
 1365–7852/00 $15.00
www.nature.com/pcan

Augmented cytotoxicity of estramustine in prostate cancer cell lines by N-acetyl-L-cysteine

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Hormone refractory prostate cancer remains lethal despite improvements in combination chemotherapy protocols. Anti-cancer drug resistance emerges as an important factor in treatment failure. Recently, nuclear factor κB (NFκB) has been shown to control expression of a number of genes that play a significant role in prostate cancer cell growth. NFκB expression follows therapy with anti-neoplastic agents and may be responsible for drug resistance. This study aims at defining the role of NFκB suppression in the resulting enhanced cytotoxicity of anti-neoplastic agent estramustine phosphate in prostate cancer cell lines.

Method

LNCaP, PC-3 and DU-145 cells were maintained as a monolayer in tissue culture flasks in culture medium consisting of RPM1 1640 supplemented with penicillin/streptomycin, L-glutamine (2 mM final concentration) and 10% fetal calf serum and incubated at 37°C in a 5% CO_2 humidified atmosphere. Incubation of cultures was performed in the presence of EMP (10 g/ml) with or without N-acetyl L-cysteine (NAC; 5 mM). Cytotoxicity in treatment groups was investigated at different time points (4, 8, 24 and 48 h) by lactic dehydrogenase release

Colorimetric test experiments were run in triplicate. Statistical analysis of data was performed by ANOVA.

Results

Growth of 3 cell lines was significantly inhibited by the addition of NAC; LDH cytotoxicity test displayed 28.7% more cell death in LNCaP cells by combination therapy, which increased to 64.4% with time. These rates were 35.2% and 40.1% for DU-145 cells and 30.1% and 92.9% for PC-3 cells.

Conclusion

A combination of chemotherapy with NAC, an NFκB suppressor, appears to be beneficial in terms of cytotoxicity in this experimental system. Clinical utility of these observations must be tested.