

Original Article

Inhibitory Effects of a Nutrient Mixture on Human Testicular Cancer Cell Line NT 2/DT Matrigel Invasion and MMP Activity

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Abstract

Current treatment of testicular cancer is associated with secondary malignancy, infertility, and cytotoxicity. Based on reported antimetastatic potential, we investigated the effect of a nutrient mixture (NM) containing lysine, proline, arginine, ascorbic acid, and green tea extract on human testis cancer cell line NT 2/DT by measuring cell proliferation/cytotoxicity, modulation of MMP-2 and MMP-9 secretion, and cancer cell invasive potential. Human testis cancer cells NT 2/DT (ATCC) were grown in DME medium. At near confluence, the cells were treated with NM dissolved in media and tested at 0, 10, 50, and 100 $\mu\text{g}/\text{mL}$ in triplicate at each dose. Cells were also treated with PMA 200 ng/mL to study enhanced secretion of MMP-9. Cell proliferation/cytotoxicity was evaluated by MTT assay, MMP activity by gelatinase zymography, and invasion through Matrigel. The nutrient mixture showed no significant effect on testis cancer cell growth. Zymography demonstrated secretion of MMP-2 by untreated human testis cancer cells and MMP-9 with PMA induction. NM inhibited secretion of both MMPs in a dose-dependent fashion with virtual total inhibition of MMP-9 at 100 $\mu\text{g}/\text{mL}$. Invasion of human testis cancer cells through Matrigel was reduced by 84% at 50 $\mu\text{g}/\text{mL}$ and at 100 $\mu\text{g}/\text{mL}$ ($p = 0.004$). NM significantly inhibited MMP secretion and matrix invasion in testicular cancer cells without toxic effect, indicating potential as an anticancer agent.

Key Words: Testicular cancer; MMPs; Matrigel invasion; nutrients; green tea extract; ascorbic acid; lysine.

Introduction

The American Cancer Society estimates 8,010 new cases and 390 deaths from testicular cancer in the United States in 2005 (1). Approximately 95% of patients diagnosed with stage I nonseminoma experience complete remission (2). Although commonly used cisplatin-based combination chemotherapy (cisplatin, etoposide, and bleomycin) claims a suc-

cess in approx 80% of patients with metastatic testicular cancer (3), it is associated with numerous side effects and a substantial loss of quality of life.

Standard treatment of stage I seminoma involves removal of the testicle through a radical inguinal orchiectomy followed by radiation therapy. CT scan showing metastasis to the lymph nodes will generally be treated by a retroperitoneal lymph node dissection. A retrospective study on 124 randomly selected patients in complete remission treated at Hanover University Medical School for testicular cancer found that 20% of the patient population was unable to father children 2 yr following cure as well

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