

Synergistic effect of aged garlic extract and naltrexone on improving immune responses to experimentally induced fibrosarcoma tumor in BALB/c mice

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ABSTRACT

Background Garlic, a medicinal plant, and Naltrexone (NTX), an opioid receptor antagonist, both have immunomodulatory and antitumor effects. Current study was designed to evaluate synergistic antitumor effects of aged garlic extract (AGE) and NTX. **Materials and Methods** WEHI-164 fibrosarcoma cells were implanted subcutaneously on day 0 into right flank of 80 BALB/c mice at age of 8 weeks. Mice were randomly categorized in four separate groups: The first group received AGE (100 mg/kg, i.p.), the second group received NTX (0.5 mg/kg, i.p.), the third group received both of them, and the fourth group received phosphate buffered saline as control group. Treatments were administered three times per week. Tumor growth was measured and morbidity was recorded. Subpopulations of CD4⁺/CD8⁺ T cells were determined using flowcytometry. WEHI-164 cell specific cytotoxicity of splenocytes and in vitro production of interferon-gamma (IFN-g) and interleukin-4 (IL-4) cytokines were measured. All statistical analyses were conducted with SPSS 16 software and $P < 0.05$ was considered to be statistically significant. **Results** The mice who received AGE+NTX had significantly longer survival time compared with the mice treated with AGE or NTX alone. An enhanced inhibitory effect on tumor growth was seen in combination therapy group. The CD4⁺/CD8⁺ ratio and in vitro IFN-g production of splenocytes were significantly increased in AGE+NTX and NTX groups. WEHI-164 specific cytotoxicity of splenocytes was also significantly increased at 25:1 E:T ratio in AGE+NTX treated mice. Coadministration of AGE with NTX resulted in improvement of immune responses against experimentally implanted fibrosarcoma tumors in BALB/c mice. **Conclusions** AGE showed synergistic effects with NTX on inhibition of tumor growth and increment of survival times.

KEYWORDS

Aged garlic extract . fibrosarcoma . naltrexone . synergism . tumor therapy

REFERENCES