Exp Oncol 2013
35, 1,72

LETTER TO THE EDITOR

Experimental ONCOLOGY

VITAMIN C: ATTENUATING EFFECT ON GROWTH AND PROLIFERATION IN SYSTEMIC MALIGNANCIES

S. Kapoor
Mechanicsville, VA 23111, USA

The recent article by J. Cha et al. provided for highly interesting reading [1].Vitamin C may attenuate tumor growth in a number of other systemic malignancies.

Vitamin C has a negative impact on tumor growth in breast cancers. Similarly it mitigates tumor metastasis. It mediates this effect in part by attenuating IL-6 levels [2]. Similar effect is seen on VEGF levels. Interestingly, intravenous ascorbic acid has been shown to significantly improve the quality of life in breast cancer survivors during chemotherapy [3]. For instance, symptoms such as depression and nausea are markedly decreased. Enhanced anti-proliferative effects are seen when vitamin C is administered in conjunction with agents such as retinoic acid [4]. In one recent study, the reported synergistic ratio of retinoic acid and vitamin C was 1.72. Vitamin C also augments the anti-neoplastic activity of chemotherapeutic agents such as cisplatin [5]. Similarly it increases the sentivity of breast cancer cells to agents such as doxorubicin.

Similar effects are seen in gastric malignancies. Vitamin C tends to augment intra-tumoral apoptosis. It mediates this effect by down-regulating 14–3–3σ via a mitochondrial dependent pathway [6]. Part of these pro-apoptotic effects are also mediated via p38-MAP kinase-dependent up-regulation of transferrin receptor [7]. It also increases the Bax/ Bcl-xL ratio. These effects are dose dependent. Administration of vitamin C also augments superoxide dismutase activity. Vitamin C also enhances MHC class I expression by the cancerous cells [8]. At the same time Fas (CD95) expression is markedly augmented. As a result the sensitivity of cancer cells to anti-Fas antibodies is significantly accentuated.

Similarly, decreased RBC vitamin C levels have been noted in patients with prostate carcinomas. In fact, recent studies indicate that vitamin C markedly attenuates tumor growth in hormone refractory prostatic malignancies [9]. It also has a negative impact on tumor metastasis. Part of these effects are mediated via VEGF inhibition. At the same time vitamin C has an inhibitory effect on MMP-9 [10].

The above examples clearly highlight the significant anti-neoplastic effects of vitamin C.

Received: January 25, 2013
Correspondence: E-mail: shailendrakapoor@yahoo.com

REFERENCES

1. Cha J, Roomi MW, Ivanov V, ***et al.*** Ascorbate depletion increases growth and metastasis of melanoma cells in vitamin C deficient mice. Exp Oncol 2011; **33**: 226–230.

2. Cha J, Roomi MW, Ivanov V, ***et al***. Ascorbate supplementation inhibits growth and metastasis of B16FO melanoma and 4T1 breast cancer cells in vitamin C-deficient mice. Int J Oncol 2013; **42**: 55–64.

3. Vollbracht C, Schneider B, Leendert V, ***et al.*** Intravenous vitamin C administration improves quality of life in breast cancer patients during chemo-/radiotherapy and aftercare: results of a retrospective, multicentre, epidemiological cohort study in Germany. In Vivo 2011; **25**: 983–90.

4. Kim KN, Pie JE, Park JH, ***et al***. Retinoic acid and ascorbic acid act synergistically in inhibiting human breast cancer cell proliferation. J Nutr Biochem 2006; **17**: 454–62.

5. Kurbacher CM, Wagner U, Kolster B, ***et al***. Ascorbic acid (vitamin C) improves the antineoplastic activity of doxorubicin, cisplatin, and paclitaxel in human breast carcinoma cells *in vitro*. Cancer Lett 1996; **103**: 183–9.

6. Ha YM, Park MK, Kim HJ, ***et al.*** High concentrations of ascorbic acid induces apoptosis of human gastric cancer cell by p38-MAP kinase-dependent up-regulation of transferrin receptor. Cancer Lett 2009; **277**: 48–54.

7. Nagappan A, Park KI, Park HS, ***et al***. Vitamin C induces apoptosis in AGS cells by down-regulation of 14–3-3sigma via a mitochondrial dependent pathway. Food Chem 2012; **135**: 1920–8.

8. Yu Y, Bae S, Kim H, ***et al***. The anti-tumor activity of vitamin C via the increase of Fas (CD95) and MHC I expression on human stomach cancer cell line, SNU1. Immune Netw 2011; **11**: 210–5.

9. Surapaneni KM, Ramana V. Erythrocyte ascorbic acid and plasma vitamin E status in patients with carcinoma of prostate. Ind J Physiol Pharmacol 2007; **51**: 199–202.

10. Pollard HB, Levine MA, Eidelman O, Pollard M. Pharmacological ascorbic acid suppresses syngeneic tumor growth and metastases in hormone-refractory prostate cancer. In Vivo 2010; **24**: 249–55.