

Nutrigenomic Effect of Micronutrient Vitamin c in The Management of Cancer

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ABSTRACT

Nutrigenomic is science, study the relationship between human genome, human nutrition and health. Nutritional genomics is the relation between food and inherited genes. Nutritional research typically focuses on preventive measures trying to identify what nutrients or food will rise / lower risk of disease and damage to human body. Studies show that micronutrient (vitamins and minerals) has ability to change genetic expression by acting on gene. Micronutrient like vitamin A, vitamin C, vitamin D and mineral like selenium has ability to generate dietary signal. This dietary signal has role in maintain health and produce disease. With the help of this micronutrient we can prevent or control diet related disease like hypertension, diabetes mellitus and cancer. Cancer is most fatal disease and leading cause of death worldwide. Cancer is mutation of gene that cause uncontrolled cell growth. Micronutrient has ability to act on gene and change genetic expression. That helps change gene expression in mutant cancer cell and cause cell death. Among all the micronutrients Vitamin c has effective role in much type of cancer like colon, breast, tongue and laryngeal cancer. It causes death of cancerous cell through apoptosis, necrosis and necroptosis by acting on gene. It activate caspase independent pathway, PKC (protein kinase c) and increase intracellular ROS (reactive oxygen species) which cause death of cancerous cell. Vitamin c has cytotoxic and cytostatic effect on cancerous cell. Too high dose of vitamin c may cause cytotoxic effect on normal cell. Is has carcinostatic effect and also has ability to cell cycle arrest. Cell cycle arrest prevent cell division. That help to prevention of cancer growth. Vitamin c may has preventive role in different type of cancer. It may help to prevention of cancer growth.

Keyword: Nutrigenomic, Micronutrient, Vitamin C, Cancer Nutrigenomics

I RESEARCH PROBLEM AND MOTIVATION FOR WORK

Is nutrigenomic effect of vitamin c having any role in cancer prevention?

and producing diseases in body by action on gene. Along with the energy production, diet like micronutrient control genome and transcription. ⁽¹⁾ Diet like micronutrient act as a signal, that detected by cellular sensor system. This type of signal to gene called as dietary signal to genes. Dietary signal can change or control the gene expression, protein expression, metabolic product. With the help of this gene expression and protein expression we can prevent or control diet related disease like diabetes mellitus, hypertension and cancer.

II BACKGROUND AND RELATED WORK

Nutrition or diet which we take daily that mainly acts on gene. This diet is important signal for maintaining health

Table 1

vitamin c: site of action, mechanisms of action and result of action in different type of cancer

Type of cancer	Site of action	Mechanism of action	Result of action
Tongue cancer	1. HSC-4 cell 2. DOK cell	1. Cytostatic effect 2. Suppress DNA synthesis 3. Suppress cellular proliferation	1. Apoptosis 2. Inhibit cell growth and multiplication
Colon cancer	1. KRAS cell 2. CRC cell 3. LS1034 cell 4. WiDr cell 5. C2BBe 1 cell	1. Apoptosis 2. Necrosis 3. DNA damage 4. Cytotoxic and anti-proliferative effect	1. Apoptotic cell death 2. Necrotic cell death
Breast cancer	1. MB231 cell 2. MCF7 cell 3. HS578T cell 4. SKBR 3 cell	1. Apoptosis 2. Caspase independent pathway 3. Cell cycle arrest	1. Apoptotic cell death
Laryngeal cancer	1. Hep-2 cell	1. Activate PKC 2. Increase cytoplasmic calcium level 3. Increase ROS	1. Apoptotic cell death 2. Necrotic cell death 3. Necroptotic cell death

Cancer is mutation of genes. Mutation of genes, control cell growth and cell mitosis. Due to mutation of this gene cell grows uncontrolled and become tumour. In this genetic mutation some micronutrient like vitamin C, vitamin A, vitamin D, vitamin E and selenium may act on genes and help for prevention or control of some kind of cancer.

Generally vitamin C is administrating to counteract the growth of malignant tumour. It's affectivity seen in many type of cancer like oral cancer, lungs cancer, laryngeal squamous cell carcinoma, breast cancer, colon cancer and tongue cancer. Plasma concentration of vitamin c significantly reduces in cancer patient. This indicates that relation between vitamin c and cancer. Vitamin c act on cellular genes and produce different type of action in cancerous cell.

In laryngeal squamous cell carcinoma vitamin c act on Hep 2 cell. Vitamin c not cause apoptosis in Hep 2 cell but induce necrotic cell death ⁽³⁾. In laryngeal cancer Vitamin c activate PKC (protein kinase c). PKC is family of protein kinase enzyme that play important role in signal transmission which leads to apoptosis or necrosis of cell.

In breast cancer Vitamin c act on MCF7, MB231, HS578T and SKBR-3 breast cancer cell line. It causes death through apoptosis in HS578T cell line, without causing harm to normal breast cell ⁽⁶⁾. It induces cell death through a caspase-independent pathway in human breast cancer cell ⁽⁶⁾. At the high concentration, vitamin c exhibit cytotoxic activity in breast cancer cell line MCF7 and MDAMB231 ⁽¹⁰⁾. Cell cycle arrest is an inhibitor on cancer growth. Vitamin c induce cell cycle arrest in human breast cancer ⁽⁶⁾. Vitamin c induce G₀ or G₁ phase elongation and G₂ or M phase slowdown.

Vitamin c selectively kill KRAS mutant colon cancer cell. It has effect on three CRC (colorectal carcinoma) cell line, CL40, SW1417 and CW 2. It has cytotoxic effect and anti-proliferative effect on all three CRC cell line. This effect depends on cell line and vitamin c concentration ⁽⁸⁾. It induce apoptosis cell death in LS1034 (cecum adenocarcinoma cell line) cell and necrosis cell death in WiDr (colon carcinoma cell line) cell ⁽⁸⁾. In LS1034 cell line vitamin c shows DNA damage, anti-proliferative effect and cytotoxic effects ⁽⁸⁾. Vitamin c increases expression of p53 gene in WiDr cell. Vitamin c induce cell death in C2BBE1 (colorectal cancer cell line) cell by action on p53 gene. P53 family play central role in apoptosis by acting as stress sensor of the cell ⁽²⁾. P53 also trigger activation of pro-apoptotic gene ⁽²⁾ like BAX.

In tongue cancer Vitamin c act on DOK and HSC-4 cell. Vitamin c show cytostatic effect in HSC-4 cell and DOK cell ⁽¹²⁾. Cytostatic effect is inhibition of cell growth and multiplication. That result in decrease cell number. Cytostatic effect more seen in HSC-4 cell than DOK cell

⁽¹²⁾. High dose of vitamin c suppress cellular proliferation, suppress DNA synthesis and induce apoptosis.

Aim of this review is study and present the action of vitamin c and mechanism of action of vitamin c in different type of cancer.

III APPROACH AND UNIQUENESS

- (a) **Cell cancer cycle, and vitamin c :** Cell cycle is event of cell division and growth. Normally it is necessary for growth and repair of body. Uncontrolled cell proliferation (cell division) is cancer. It is cause due to the mutation of cellular genes, minute mutation even leads to cancer. Cancer start in single cell due to mutation in their gene. The mutation occur in single cell, that grow and divide rapidly and become tumour from single cell. This single mutant cell causes cancer. If this single destroy at developing stage that may help in prevention of cancer. Vitamin c has ability to target cell that displaying metabolically abnormal. Vitamin c selectively target cancerous cell without causing any harm to normal cell. This ability only present in vitamin c and because of this we can administrate it in healthy person of any age. Vitamin c can administrate through daily regular diet. Many studies shows that vitamin c can act on gene of cancer cell. It enter in cancerous cell through SDVCT (sodium dependent vitamin c transpoter) and GLUT (glucose transpoter) transporter. In cancer cell vitamin c act on p53 gene, Bcl-2 gene and Bax gene. That causes apoptosis cell death, necrotic cell death. It also activate ROS and caspase independent pathway and this all cause death of cancer cell. Vitamin c act on p53 gene which play central role in apoptosis. By targeting single cancer cell or mutant cellular gene it may help in prevention of cancer. In healthy person vitamin c act as antioxidant. It help to prevent cell damage in normal cells. Pharmacological concentration has effective role in cancer. Dietary vitamin may have role in cancer.
- (b) **Vitamin c after development of cancer:** Action of vitamin c in cancerous cell is dose dependent and time dependent. High dose of vitamin c is effective in tongue cancer, breast cancer and laryngeal cancer. In cancer patient vitamin c may administrate through diet and through supplement also. Body can absorb 30-180 mg of vitamin c per day. Above the 180 mg per day we can administrate through supplement. It is not toxic up to 2000 mg per day. 2000 mg per day can act as high dose for cancerous cell. In cancerous cell it causes cell cycle arrest ⁽⁶⁾. By entering in cell cycle of cancer cell it cause G₀ or G₁ phase elongation and G₂ or M phase slowdown. Elongation of G₁ phase increase

duration of growth in cancer cell. That also increase duration of RNA synthesis and protein synthesis required for DNA synthesis. By slowdown G2 or M phase vitamin c increase duration of nuclear division and cytoplasmic division. Nuclear division and cytoplasmic division is cell division. By actin this way vitamin c increase time duration of cell division that may help to control tumour growth. High dose of vitamin has selective cytotoxic effect on tumour cell.

Increase in cytoplasmic concentration of calcium activate calcium calmodulin kinas (CaMk) 2 in human neuroblastoma⁽⁷⁾. In human neuroblastoma CaMK 2 trigger necroptosis. In laryngeal cancer vitamin c increase cytosolic calcium level in Hep2 cell line. This increase cytosolic calcium level may activate CaMK 2 in laryngeal cancer. That may trigger necroptosis.

Cancer cell is generally are not destroyed by immune system up till it become tumour. But regular vitamin c rich diet may destroy the cancer by various mechanism. Vitamin c supply through Diet may play effect role in prevention of cancer in healthy person. It help in reduce growth of cancer tumour after supply through diet.

IV RESULT AND CONTRIBUTION

Vitamin c causes death in cancer cell, through necrosis, apoptosis, necrosis and necroptosis. It may prevent cancer in person taking daily vitamin c rich diet. Vitamin c help in prevention of cancer growth. High dose of vitamin c promotes necrosis cell death in cancerous cell. In cancer patient dietary vitamin c intake reduce cancer specific mortality. Daily requirement of vitamin c is 30-180 mg. it can easily complete through diet.

REFRENCES

- [1]. Reddy V S et al (2018), Nutrigenomics: opportunities and challenges for public health nutrition, *Indian journal of medical research*: 148 (5)
- [2]. An SH et al (2011), Vitamin C increase the apoptosis via upregulation p53 during cisplatin treatment in human colon cancer cell, *BMB reports*: 44 (3)
- [3]. Beak MW et al (2016), Ascorbic acid induces necrosis in human laryngeal squamous cell carcinoma via ROS, PKC, and calcium signalling, *Journal of cellular physiology*: 232 (2)
- [4]. Guerriero E. et al (2014), vitamin c effect on mitoxantrone induce cytotoxicity in human breast cancer cell line, *PLoS one*: 9 (12)
- [5]. Harris HR et al (2014), vitamin c and survival among women with breast cancer: A meta-analysis, *European journal of cancer*: 50 (7)
- [6]. Hong SW. et al (2007), Ascorbate (vitamin c) induce cell death through the apoptosis inducing factor in human breast cancer cell, *oncology report*: 18 (4)
- [7]. Nomura M et al (2014), Accumulation of Cytosolic Calcium Induce Necroptotic Cell Death in Human Neuroblastoma, *cancer res*: 74 (4)
- [8]. Pires AS et al (2016), Ascorbic acid and colon cancer : an oxidative stimulus to cell death depending on cell profile, *European journal of cell biology*: 95 (6-7)
- [9]. Chen QI et al (2005), pharmacological ascorbic acid concentration selectively kill cancer cells: action as a pro-drug to deliver hydrogen peroxide to tissue, *Proceeding of National Acadmy of Sciences*: 102 (38)
- [10]. Kurbacher CM et al (1996), Ascorbic acid (vitamin c) improves the antineoplastic activity of doxorubicin, cisplatin, and paclitaxel in human breast carcinoma cell in vitro, *cancer letter*: 103 (2)
- [11]. Aguilera O. et al (2016), vitamin c uncouples the Warburg metabolic switch in KSAR colon cancer, *oncotarget*: 7
- [12]. Ohwada R et al (2017), High-dose ascorbic acid induce carcinostatic effect through hydrogen peroxide and superoxide anion radical generation- induce cell death and growth arrest in human tongue carcinoma cells, *free radical research*: 51 (7-8)
- [13]. Irimie A. et al (2019), Role of key Micronutrient from Nutrigenomic and Nutrigenomic Perspective in Cancer Prevention, *medicina*: 55 (6)
- [14]. Korsmeyer S.J. (1999), Bcl-2 family and regulation of programmed cell death, *cancer res*: 59(7)
- [15]. Mullen et al (2003), Nutrigenomics: goals and strategies, *nature review cancer*: 4
- [16]. Irimie A I et al (2019), Role of Key Micronutrient from Nutrigenetic and Nutrigenomic Perspectives in Cancer Prevention, *medicina*: 55(6)
- [17]. Ryter S. et al (2007), Mechanism of cell death in oxidative stress, *antioxid redox signal*: 9(1)

- [18]. Sharma M. et al (2009), Oxidant-antioxidant status in indian patient with carcinoma of posterior one-third of tongue, *cancer biomark*: 5 (6)
- [19]. Chen Qi et al (2015), An unpaved journey of vitamin c in cancer treatment, *Canadian Journal of Physiology and pharmacology*: 9 (12)
- [20]. Hall J. E. et al (1956), Genetic control of Protein synthesis, cell function, and cell reproduction, *Gytone and Hall Textbook of Medical physiology*, W B Saunders. PP 38