# Summary and conculsions

Breast cancer is the most common cancer of women, and its incidence is rising especially in developing countries, an estimated 1.7 million women will be diagnosed with breast cancer in 2020, a 26% increase from current levels, mostly in the developing world. Apoptosis is a form of programmed cell death that plays a critical role in the maintenance of tissue homeostasis. The dysregulation of apoptosis is a hallmark of cancer, with both the loss of pro-apoptotic signals and the gain of anti-apoptotic mechanisms contributing to tumorigenesis.

Among pharmacological agents, many cancer chemotherapeutic drugs are known to activate apoptotic mechanisms of tumor cell death; this may be a mechanism for current cancer treatment. Moreover, apoptosis has been proposed as a novel target for cancer chemoprevention.

Multiple stimuli such as ionizing radiations, DNA lesions, nitric oxide, hypoxia, chemotherapeutic agents, or oncogenic stimuli can activate p53. In response to activation it could induce different effects. p53 is a transcription factor involved in the control of cell cycle phase transition, in DNA repair, and in induction of senescence, apoptosis.

Survivin, is a small 16.5 kDa protein belonging to the inhibitor-of-apoptosis (IAP) family. Interest in survivin stems from its pattern of expression: it is upregulated in almost all tumour types while being minimally expressed in terminally differentiated tissues. Moreover, it plays a key role in both apoptosis and control of cell-cycle progression.

DNA fragmentation is the hallmark of apoptosis, Correlations between the occurrence of cell-free DNA in blood of tumor patients and malignancy of their disease were reported. DNA integrity and DNA integrity index may vary between healthy individuals and cancer.

Cytc is a multi-functional enzyme that is involved in life and death decisions of the cell. The intrinsic pathway of apoptosis is mediated by various stimuli that cause the release of Cytc from mitochondria into the cytoplasm, triggering caspase activation.

Some *in vitro* studies have reported that vitamins A, C, and E, as well as carotenoids, can enhance the effectiveness of chemotherapy.

**Aim of the work:**

The present study aimed to evaluate the possible effects of vitamin A and E supplementation during chemotherapy on apoptosis in breast cancer patients.

**Subjects and methods:**

This study included forty-five breast cancer subjects; they were divided into two groups: control group (Group Ia & Ib), 20 patients in this group received 6 cylces of chemotherapy, and the vitamins-treated group (Group IIa & IIb), 25 patients in this group received a daily vitamins A and E supplementation along with the chemotherapeutic course. From each patient in both groups, a blood sample was collected before starting the chemotherapy, and another sample was collected two weeks after the last cycle of chemotherapy.

**The following markers were assesed for in sera of all patients in the two studied groups:**

- Concentration of p53.
- Level of Survivin.
- Determination of free circulating DNA.
- Level of cytochrome c.

**The results of this study revealed that:**

- p53 protein showed a significant increase in its level in the control group and vitamins-treated groups after chemotherapy (Group Ib & IIb) as compared to its level in the corresponding groups before chemotherapy (Group Ia & Ib).
- The level of serum survivin concentration didn't show any significant diffrence when comparing Group Ib with Group Ia. While, it showed a significant decrease when comparing Group IIb with both groups IIa & Ib.
- After chemotherapy, the apoptotic bands of cDNA in the vitamins-treated group were more intense and predominant rather than that in the control group.

- The level of serum cytochrome C concentration didn't show any significant difference when comparing Group Ib with Group Ia, and when comparing Group IIb with IIa. However, its level showed a significant increase when comparing Group IIb with Ib.

**From all these results obtained in this work, we can conclude that:**

(1) Apoptosis may not be the most dominant form of cell death for solid tumors, it might be due to the fact that chemotherapy is not specifically designed to induce apoptosis, but it may result in apoptosis as a secondary effect, caused by induced cellular damage.

(2) Enhancement of the apoptotic potential of convential breast cancer therapies may thus increase the overall tumor cell death.

(3) The combination of vitamins with chemotherapy showed a strong synergistic activation of apoptosis.

(4) Vitamin A and E supplementation exerts its apoptotic effect in cancer cells by various mechanisms, through down-regulation of some inhibitors of apoptosis proteins, such as surivin, rather than up-regulation of tumor suppressor proteins, such as p53. It is also found that they act through activation of intrinsic "mitochondrial" pathway, which results in cytochrome c release, and subsequent acitivation of caspases cascade.

**From all results found in this study, we can recommend the followings:**

(A) Recommendation for research:

(1) Further studies with larger number of patients and different doses of vitamins and more biochemical parameters are recommended to obtain more definite results.

(2) Studying the action of various promising drug candidates and also comparing their efficacy and therapeutic index in combination with chemotherapy/radiotherapy, would be another worth while pursuit.

(3) Survivin-directed therapies could be incorporated into a broad spectrum of oncological practice either as single agents or, more likely, in combination with existing chemotherapeutics, particularly those that exert their effects through apoptosis.

(B) Recommendation for public health:

(1) It is a good recommendation to provide vitamin supplements, which act as an attractive public health strategy for the prevention of cancer.

(2) A diet including different forms of vetegtables and fruits which contain large amounts of vitamin is highly recommended to act as stragety to decrease the incidence of breast cancer.

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