

Fishing Clues for the Efficacy of Chemotherapy: Role of Fasting

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Basic unit of human is cell. These cells divide normally but due to some disturbance in this division, leads to an abnormal growth of cells which is called as Tumor. If this tumor spreads through out the body it is called as malignancy or Cancer. Cancer, also known as a malignant tumor, is a cluster of diseases involving abnormal cell growth with the potential to spread or invade to other parts of the body^[2]. Metastasis involves the spread of cancer cells from the primary tumor to surrounding tissues and to distant organs via Angiogenesis. Angiogenesis is a physiological process through which new blood vessels form from pre-existing vessels^[3, 4].

Fasting is the one of oldest therapies in medicine. Many physicians throughout history and many of the oldest healing system have recommended fasting as a fundamental method of healing and prevention. Hippocrates believed that fasting enable to body heal it.

And fasting is the part of most spiritual tradition in the world and It is one of the religious practice among Christianity, Islam, Hinduism and many more^[5].

Few recent studies found that fasting can improve quality of life of the patients undergoing chemotherapy for breast and ovarian cancer. This study used a 60 hour fasting starting 36 hours before the start of chemotherapy. The results shown that participants fasting during chemotherapy reported

ABSTRACT

This Article is on how Fasting is effective in chemotherapy and how it prevents cancer. Fasting in disease intercept and treatment has recently become a popular topic; and fasting is the part of most spiritual tradition in the world. Cell is the basic unit to the human body. Actually these cell division takes normally but due to some disturbance or mutation in cell it lead to cancer or tumor. chemotherapy is used to treat the cancer but it having the side effect. In this article we are describing about how cancer is prevented by fasting by different mechanism like Cellular fasting mechanism, Systemic changes by fasting, Mechanism of killing cancer cells in solid tumors by fasting and Autophagy Mechanism.

KEYWORDS: Fasting, Cancer prevention, Chemotherapy, IGF-1, oxidative phosphorylation, Cancer cell death

INTRODUCTION

Cancer remains leading cause of death globally and It is the second leading cause of death in the USA and It is the major leading disease in the world. It is expected to continue to increase because of the growth of the aging population and prevalence of risk factors such as smoking, obesity, and poor dietary habits^[1]. National institute of cancer prevention and Research states that in India around 2.25million people are living with cancer and 7, 84, 821 cancer deaths annually.

higher tolerance to chemotherapy, few chemotherapy related side effects are decreased and higher energy levels were observed in fasted patients when compared with those who did not fast^[6].

Can Fasting cure the cancer:-

The cure is extremely difficult for the advanced metastatic tumors if it once spread to the other organs. Major factors that trigger cancer was the dietary and lifestyle related factors, Cancers being more likely dependent on dietary habits than the other factors. There are few cancers more likely dependent on the dietary habits^[7-15]. High curiosity and interest to prevent cancer by certain calorie limited diets or by fasting is raising up. Later several experiments were conducted to know, Anticancer agent tolerability and efficacy can be increased by calorie restriction^[16-18].

There was a study made by Changhan Lee et al., to know whether the fasting can increase the effectiveness of the high dose chemotherapy? So this curiosity made to do experiments on the mice. In process of experiment they injected murine breast cancer cells (4T1), melanoma cells (B16) and two neuro blastoma cell lines (NXS2 and Neuro-2a) in the immune competent mice. Unfortunately it found to be true, fasting potentiated the effects of chemotherapy and prolonged the survival of mice^[16]. And there is also a case study indicating that reduced side effects of the chemotherapy is seen in the cancer patients who have

voluntarily fasted for 4 or more days along with the continuation of chemotherapy^[19].

1. Cellular fasting mechanism:

Fasting changes the activity of many metabolic pathways. The changes in levels of metabolites translate and circulating hormones into a downfall in metabolic activity and cell division. Normal cells sensitized to chemotherapy and other cancer therapies by these starvation conditions^[16-17].

2. Systemic changes by fasting :

Fasting can reduce the levels of glucose, growth hormone, insulin, adrenaline, glucocorticoids. During initial post – absorptive phase, which typically lasts 6 – 24 hours, insulin levels start to decline, and glucagon levels rise, initiate the breakdown of glycogen stores of liver and consequent release of glucose for energy^[18]. Low level of insulin and glucagon also stimulate the breakdown of triglycerides into fatty acids and glycerol. While fasting, fatty acids are utilized by the tissues for energy, while the brain relies on glucose and ketone bodies^[12]. Ketone bodies helps to perform gluconeogenesis to maintain glucose levels and also it's very crucial and mostly it is utilized by brain.

Adrenaline & glucocorticoids also needed for direct metabolic adaptations to fasting, which helps to maintain the blood glucose levels. Fasting reduces the hormone leptin, and increases the levels of adiponectin, which increases fatty acid breakdown. Although, fasting at least increase lipolysis and gluconeogenesis and decline peripheral glucose uptake^[19].

Although fasting can at least temporarily increase GH levels (to increase gluconeogenesis and lipolysis and to decrease peripheral glucose uptake), Fasting ultimately reduces IGF1 levels. In addition, under fasting conditions, IGF1 biological activity is restrained in part by an increase in the levels of insulin-like growth factor binding protein 1 (IGFBP1), which binds to circulating IGF1 and prevents its interaction with the corresponding cell surface receptor²².

Finally the hallmarks of the mammalian systemic response to fasting are low levels of glucose and insulin, high levels of glucagon and ketone bodies, low levels of IGF1 and leptin and high levels of adiponectin^[18,19].

3. Mechanism of killing cancer cells in solid tumors by fasting :

Fasting declines the nutrients and factors like (glucose, IGF1 and insulin) levels which promote growth to tumor. Fasting causes an anti – Warburg effect by reducing the glucose uptake, by this cancer cells forced to perform oxidative Phosphorylation; by this increased production of the oxygen reactive species in cells of cancer, result is DNA damage and cell death, specifically in response to the chemotherapy.

4. Autophagy Mechanism :

Fasting reduces CD 73 levels in some cancer cells, adenosine production gets blunt in extracellular environment and prevents the transfer of macrophages towards an immunosuppressive M2 phenotype. At last, fasting down regulates the Heamoxxygenase 1 (HO1) expression in breast cancer cells, it gets more susceptible to CD8+ cytotoxic T cells. Primarily, fasting shows opposite and even very different effects in cancer cell types or even in same cancer cell type^[18,19].

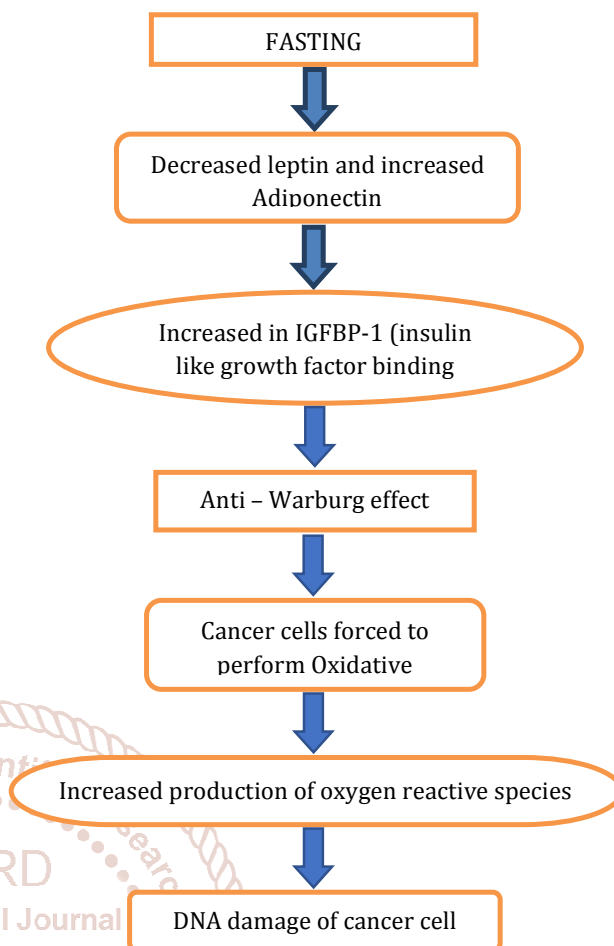


Fig-1: Summary- How fasting effects the cancer cell damage.

Types of fasting:-

- **Calorie Restriction** :20-40% reduction in calorie intake over along period of time (1200 calories for women vs 1400 calories for men per day)
- **Intermittent Fasting** :complete avoidance of calorie intake for 16-18 hours daily or alternation a fasting day with a normal energy intake day
- **Fasting**: complete avoidance of calorie intake for anywhere from 1 day to several weeks
- **Intermittent Calorie Restriction**:50-70% reduction in calorie intake for short periods of time (600-1000 calories per day)

- Calorie intake less than 20% of the Total day's caloric intake is beneficial.
- Maintaining 12hrs starvation is more beneficial, that is entirely skipping Breakfast and make the lunch be the first meal of the day^[20].

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Conclusion:

Fasting decreases the growth factors (IGF-1), insulin, glucose. Thus leads to Anti – Warburg effect. So, Cancer cells forced to perform Oxidative Phosphorylation and an Increased production of oxygen reactive species, leads to the

DNA damage of cancer cell (specifically in response with chemotherapy).

In fasting, as tumor cells are more exposed to chemotherapy compared to that of normal cells. Chemotherapy efficacy increases on tumour cells with less Adverse drug Reactions.

On the other hand, Cancer can be prevent by fasting, as there is decrease in growth factors which contribute for the formation of tumour cells.

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