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Review Article

The Effect of Fasting on Metabolism and Chemotherapy Related Treatment: A Review

[1]*R Ganesan, [1]Sanjai V, [2]Bsava Reddy, [3]Sanjay R. kamble and [2]Ranjith A. Reddy

[1]Department of Swasthavritta and Yoga (Preventive & Social Medicine), Smt. Vimladevi Ayurvedic Medical College & Hospital, Wandhari, Chandrapur, India
[2]Department of Pharmacognosy, Aditya College of Pharmacy, Bhalki, India, Karnataka, India
[3]Department of Pharmacy Practice, Aditya Bangalore Institute of Pharmacy Education and Research, Yelahanka, Bangalore, India

Article Info

Correspondence:
Department of Swasthavritta and Yoga (Preventive & Social Medicine), Smt. Vimladevi Ayurvedic Medical College & Hospital, Wandhari, Chandrapur, India
*grnation.pharma@gmail.com

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Abstract

Although fasting can be an effective strategy for managing obesity, it should be practiced thoughtfully, with individualized plans that prioritize long-term health and well-being. Research on pairing fasting with chemotherapy is still developing, so any such approach must be carried out under the strict supervision of the patient's oncology team. To safely include fasting in a cancer treatment regimen, it's vital to choose suitable patients, provide ongoing monitoring, and tailor the plan to each individual's needs. Since fasting's impact on blood sugar control can differ from person to person, careful tracking of glucose levels is especially important for people with diabetes or other health conditions. When used properly, fasting may support the effects of diabetes medications in controlling blood sugar. Additionally, the timing and length of fasting sessions can affect how cancer cells respond, with shorter intermittent fasting possibly helping to trigger cancer cell death more selectively, while extended fasting might offer extra advantages. Overall, expert guidance, personal assessment, and vigilant monitoring are key to safely incorporating fasting, reducing risks, and enhancing its potential benefits.

Keyword: fasting, chemotherapy, obesity, glycemic, diabetes, antidiabetic medications, apoptosis

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Introduction

People today live much longer than they did a century ago, largely thanks to major advancements in preventive medicine, clinical treatments, and public health measures [1]. Fasting offers various physical benefits, such as improved overall wellness, lower cholesterol levels, removal of toxins, reduced strain on the digestive system and other organs, better circulation, and enhanced heart and brain performance. Several studies also suggest that fasting may boost mental well-being by building self-esteem, confidence, willpower, and self-discipline. For many years, scientists have understood that depriving cancer cells of nutrients can be beneficial. Without the fuel they need, cancer cells become more sensitive to chemotherapy and targeted drugs, while healthy cells tend to enter a protective dormant state, making them less susceptible to harmful side effects of treatments like androgen deprivation therapy and chemotherapy.

Good nutrition plays an essential role in fighting cancer. Both excessive weight and poor nutrition are linked to worse outcomes for most types of cancer [2–4]. Interest in fasting is growing among researchers and the wider public alike. Evidence shows that fasting can contribute to better general health and may help slow down aging [5–7], while also being linked to protection against illnesses such as cancer, high blood pressure, and diabetes [8–10].

Animal studies have found that fasting can help mice tolerate oxidative stress better and potentially extend their lifespan [11]. For example, research by Bagherniya et al. showed that fasting mice with neuroblastoma for 48 hours before receiving etoposide could reduce the harmful side effects of chemotherapy [12]. Statistically, about 40% of both men and women will face a cancer diagnosis at some point in their lives. In the U.S., factors such as smoking, obesity, lack of exercise, drinking alcohol, and poor diet are believed to cause around 18% of new cancer cases and 16% of cancer-related deaths each year [13].

Fasting, which involves deliberately abstaining from food—and sometimes drinks—for a specific period, dates back to ancient times. As far back as the fifth century B.C., Hippocrates recommended fasting to treat certain health conditions [14]. Today, people fast for religious, health-related, or ceremonial reasons. In oncology, fasting is being explored as a way to lessen the side effects and toxicities of treatment, manage body composition, and improve heart and metabolic health in cancer patients [15, 16]. Although only a few small-scale studies have been done so far, current research suggests that fasting is generally safe for people undergoing cancer therapy [17–20].

Combining fasting with exercise appears to create additional benefits, improving factors like body composition, cholesterol, and insulin sensitivity in people without cancer [21]. However, much of this research has focused on sports and short-term effects [22]. Fasting may also help counteract cancer cachexia, which is the severe loss of body fat and muscle mass that weakens the immune system, reduces the body's ability to tolerate treatment, and is linked to poorer outcomes [23]. Emerging evidence indicates that intermittent fasting might help prevent and treat cancer by making anticancer treatments more effective and tolerable, and by boosting patients' quality of life through various biological pathways [24–27].

Research so far shows that fasting can benefit overall health by lowering oxidative stress and inflammation, slowing aging, supporting cellular repair, and promoting better heart and brain function. However, human studies examining fasting's impact on cancer are still limited, often involving only small groups of younger people for brief periods.

Method

A systematic search was performed through PubMed and Google Scholar using the terms *fasting*, *cancer treatment*, and *time-restricted feeding*. Studies were included if they investigated fasting during cancer therapy or focused on short-term fasting interventions, typically lasting between 24 and 72 hours. The sections that follow discuss various fasting methods and summarize early findings from ongoing clinical research.

Lipid Metabolism: Research has demonstrated that alternate-day fasting over periods of 8 to 12 weeks can lead to reductions in LDL cholesterol levels by 20–25% and triacylglycerol levels by 15–30%, often accompanied by an increase in LDL particle size [52]. Similarly, alternate-day fasting trials lasting 3 to 12 weeks have consistently shown decreases in total cholesterol (by 10%–21%) and triglycerides (by 14%–42%) across individuals of normal weight as well as those who are overweight or obese. Studies of whole-day fasting over longer durations—12 to 24 weeks—also show favorable impacts on lipid profiles, with total cholesterol declining by 5%–20% and triglycerides by 17%–50% [53]. Collectively, these findings indicate that intermittent fasting (IF) can positively influence blood lipid levels. According to Sheryl Salis [28], many participants overcame initial challenges with prolonged fasting once they noticed improvements in weight management and sleep quality. In addition, they adopted important behavioral changes such as increased physical activity, heightened energy levels, more consistent exercise routines, portion control, and greater awareness of healthy eating. Numerous investigations confirm that fasting can contribute to weight loss. A review of 27 studies found that IF produced weight loss ranging from 0.8% to 13% of initial body weight, independent of total calorie intake. In trials lasting 2 to 12 weeks, participants' average body mass index dropped by about 4.3% to a median of 33.2 kg/m², with hunger levels remaining stable or declining and no severe adverse effects reported [29]. Despite the promise shown by IF, obesity continues to be a challenging condition to address in primary care, as patients have often already attempted calorie restriction. Current evidence on IF is mixed, making it difficult to directly compare with other dietary interventions. While intermittent fasting is emerging as a potential approach for managing obesity in primary care settings, more data are needed on its long-term sustainability and health implications [29].

During fasting, amino acids such as lysine, leucine, isoleucine, and taurine display biphasic patterns, reaching their lowest concentrations about six hours into fasting and partially recovering by 12 hours. Overall, essential amino acid levels tend to drop more significantly than nonessential amino acids [54]. Another study indicated that during fasting, when urea concentrations are low, ammonia levels also decrease markedly, while total nitrogen remains relatively stable [55].

Chemotherapy:

Chemotherapy remains one of the main treatment modalities for cancer but is often limited by its toxic side effects, particularly in advanced stages [30,31]. Emerging findings suggest that regular fasting may protect healthy cells and tissues during chemotherapy while increasing the vulnerability of cancer cells to treatment [31,32]. This protective effect is thought to result from reduced insulin and IGF-1 levels, which in turn leads to the inactivation of IGF-R1 [33,34]. One study aimed to assess whether the duration of fasting influences common chemotherapy-related side effects such as fatigue, hair loss, nausea, vomiting, constipation, and diarrhea. The researchers compared fasting for 24 hours before chemotherapy with fasting for 48 hours beforehand and fasting for 48 hours prior plus 24 hours post-treatment (a total of 72 hours). They observed significant differences in nausea and vomiting: the incidence of nausea dropped from 100% for the 24-hour fast to 86% for the 48-hour fast and to 43% for the 72-hour fast ($p = 0.019$); vomiting dropped from 83% at 24 hours to 43% at 48 hours and to 0% at 72 hours ($p = 0.003$). However, these findings might partly reflect the effect of having an empty stomach. Notably, this study depended on self-reported data and did not use randomization [35].

A small case series reported adverse events linked to fasting in ten patients with various cancer types (breast, esophageal, prostate, lung, uterine, and ovarian). Using a non-validated questionnaire based on the National Cancer Institute's Common Terminology Criteria for Adverse Events, researchers explored whether fasting was practical, safe, and effective in reducing chemotherapy-related side effects. Although participants used different fasting regimens, all reported experiencing fewer treatment-related toxicities when fasting. Symptoms such as nausea, vomiting, diarrhea, stomach cramps, and mucositis were absent when fasting but appeared on five out of six occasions when they did not fast. While this may partly reflect the empty gut, fasting also seemed to ease fatigue and weakness [36].

Two clinical studies further explored short-term fasting during cancer treatment [37,38]. Dorff et al. [37] aimed to identify the optimal fasting window for a larger future study. Patients with urothelial, non-small cell lung, uterine, breast, or ovarian cancer undergoing neoadjuvant or adjuvant platinum-based chemotherapy were assigned to fast for either 24 hours before treatment, 48 hours before, or 72 hours total (48 hours before and 24 hours after chemotherapy). There was no control group. Following the fasting protocol, two patients achieved a complete response (no detectable cancer), six had partial radiographic responses (over 30% tumor reduction), three had stable disease, and eight could not be evaluated using the RECIST criteria (Response Evaluation Criteria in Solid Tumors) [39]. Upon completing the entire course of treatment, five patients showed a complete pathological response, including four from the 72-hour group and one from the 48-hour group [37].

Zorn et al. [40] conducted a controlled cross-over study comparing fasting and a ketogenic diet in 51 women with gynecologic cancers. Participants were split into four groups and followed either a modified short-term fasting regimen—restricting energy intake to 400 kcal daily for three days before and one day after chemotherapy—or other dietary interventions. Blood samples confirmed compliance. Like Bauersfeld et al. [41], Zorn et al. found a notable drop-out rate, and randomization was done by selective allocation rather than purely random methods.

Glycemic Control

Both calorie restriction (CR) and intermittent fasting (IF) have shown promising results in improving glucose regulation and insulin sensitivity in humans [42–44]. Studies suggest that IF and alternate-day fasting may be equally effective as CR for weight loss and cardiovascular benefits. Research in animal models indicates that CR and IF enhance insulin action by altering lipid droplet protein profiles and lowering levels of intracellular diacylglycerol. They also help reduce visceral fat and improve adipokine balance, which contributes to cardiovascular protection [43–44]. However, their precise effects on human intermediary metabolism remain unclear.

Antidiabetic Medications

Drugs known as insulin secretagogues, such as sulfonylureas (SU), can significantly increase the risk of hypoglycemia when used alone or with other medications [45]. Among these, glibenclamide has been shown to carry a particularly high risk of causing low blood sugar episodes [46]. For patients who plan to fast for extended periods (more than 12 hours), skipping SU doses on the fasting day and the night before may be advisable. Medications like metformin, pioglitazone, alpha-glucosidase inhibitors, and incretin-based therapies (DPP-4 inhibitors and GLP-1 analogues) are generally safe to continue, as they carry minimal hypoglycemia risk. Sodium-glucose cotransporter-2 inhibitors pose only a slight risk for hypoglycemia; however, prolonged fasting without enough fluid intake may increase the risk of dehydration and low blood pressure when using these drugs.

Apoptosis

Fasting can lead to notable shrinkage of the jejunal mucosa by reducing cell growth and promoting programmed cell death (apoptosis). This process also boosts iNOS production in intestinal epithelial cells (IEC), raising nitrite concentrations in the jejunum. The activation of iNOS in IEC during fasting may stimulate apoptosis through pathways involving IFN-γ and reactive oxygen species (ROS). Additionally, nNOS might play a regulatory role in this fasting-induced apoptotic mechanism [47].

Side Effects of Fasting

A study by De Groot et al. [48] found that the side effects reported were unrelated to the fasting protocol itself. In a larger follow-up trial conducted in 2020 [49], the main adverse event noted was a dislike for certain foods, which made adherence to the regimen challenging. According to Dorff et al. [50], fatigue was the most commonly reported issue during fasting, followed by headaches, dizziness, episodes of low blood sugar, unintended weight loss, low sodium levels, and low blood pressure. By contrast, Riedinger et al. [51] reported no adverse effects in their study participants.

Potential Risks and Limitations

Extended fasting can result in nutrient deficiencies, which is a particular concern for cancer patients who are already at higher risk for malnutrition due to their illness or treatment side effects. Inadequate intake of protein, vitamins, or minerals can weaken overall health, immune response, and the patient's ability to handle aggressive treatments. Additionally, fasting may worsen muscle loss and contribute to cancer cachexia—a severe wasting condition that reduces physical strength and resilience. This could negatively affect recovery and treatment outcomes.

Fasting may also trigger metabolic problems such as low blood sugar, electrolyte imbalances, or dehydration. These risks are heightened in cancer patients, especially those with other health issues or those receiving intensive therapies. Such complications require careful medical oversight to prevent serious consequences. Moreover, fasting can be psychologically taxing, adding to the emotional and mental burden that many cancer patients already carry. Strict fasting schedules may be difficult to follow and could lower quality of life for some patients.

Discussion

Research on the potential negative effects of fasting in both animal models and human cancer patients is still relatively limited. For example, studies have shown that protein deprivation in rats can worsen Adriamycin-induced heart damage. Meanwhile, some medications like Metformin—commonly used for type 2 diabetes—appear to mimic some metabolic benefits of calorie restriction and have even been linked to reduced breast cancer risk and recurrence.

While fasting holds promise as a tool for weight loss and metabolic health, it should be implemented carefully and tailored to each individual's condition, with a focus on long-term well-being and sustainability. A holistic lifestyle plan that combines fasting with a balanced diet, regular exercise, and behavioral support may be the most effective approach for sustainable weight control and better metabolic outcomes. Evidence on pairing fasting with chemotherapy continues to evolve, so any such strategy must be undertaken under the close supervision of an oncology team. Careful screening, monitoring, and personalized planning are essential to safely and effectively incorporate fasting into a cancer care plan.

Individual responses to fasting can vary greatly, particularly regarding blood sugar control. Therefore, monitoring glucose levels is crucial for people with diabetes or other medical conditions. When properly managed, fasting may complement diabetes medications to help regulate blood sugar. Finally, the timing and duration of fasting can influence how effectively it triggers apoptosis in cancer cells. Shorter, intermittent fasts may better target cancer cell death, while longer fasting periods may offer additional therapeutic benefits.

Conclusions

Fasting has demonstrated potential to enhance apoptosis, reduce cancer cell invasiveness, and boost the effectiveness of chemotherapy treatments. However, further studies are needed to better understand how different ethnic groups may respond to fasting, how various medications interact with fasting protocols, and what the short- and long-term impacts of alternating fasting and regular eating might be for this population. To safely and effectively integrate fasting into healthcare or cancer treatment plans, it is essential to provide appropriate guidance, carry out individualized assessments, and maintain careful, ongoing monitoring. This approach helps minimize risks while maximizing the possible health benefits of fasting.

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