

LETTER to the EDITOR

Chemotherapy Through a Combination of Fasting and Chronopharmacology

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Dear Editor

The present letter is a congruity study of 'Toxicity in Chemotherapy- When Less is more' divulging the idea of integrating fasting or calorie restriction (CR) co-instantaneously with chemotherapy treatment that trotted out fasting as felicitous combination to optimizing efficacy in chemotherapy patients (Laviano and Fanelli, 2012). Not long ago, chemotherapy conspicuously exemplifies the most puissant cancer treatment. However, instead of only razing cancerous cells, the therapy also caused inevitable detrimental effects upon normal cells thus constituting privation searches in the optimity of chemotherapy. Chemotherapy is a treatment that pursuance anti-cancer drugs in protracting the survival of patients diagnosed with omnifariouly metastasized cancer cells that commenced from primary tumor (Safdie et al., 2007).

Fasting being worldwide custom adaption in many religions, begets a better response to chemotherapy as these malignant cells become more susceptible in regard to mitochondrial dysfunctional (Warburg, 1930). This mitochondrial dysfunction is elucidated through the presence of smaller and lesser number mitochondria as well as fewer cristae formation than those manifested in normal cells (Maximo and Sobrinho-Simoes, 2000). Substantiated studies conducted from University of Southern California explicated the phenomena of normal cells to be entering a hibernation state during nutrient deprivation while cancer cells synthesize new proteins and generate other steps to persist mitotically alongside adapting a cascade of events that procreate free radicals. The free radicals in retaliation disintegrate the cancer cells' own DNAs that resulted in cellular suicide (University of Southern California, 2012).

Ascribable to mitochondrial dysfunctional, the cancer cells are further incapable of carrying out Krebs cycle corroborating clearly the high demand and dependency on glucose compared to normal cells while suggesting energy merely being harvest through Glycolysis even in the presence of oxygen (Warburg effect). The expression of multitude insulin receptors (IRs) on cancer cells substantialize hyperactivation of the IGF1R-IR pathway when glucose rich meals provoke insulin and insulin-like growth factor (IGF)-1 production that in return facilitates tomorigenesis and aggravates the outcome in cancer patients. Cancer epidemiological and anthropological studies again revealed glucose restriction diet that depicts fasting, may debilitate the response of cancerous cells towards chemotherapy (Klement and Kämmerer, 2011;

Petit and Kroemer, 1998; Zamzami et al., 1996).

Among that, fasting too enhances resistance in normal cells against oxidative stress actuated during chemotherapy at which time cancerous cells are reported busy preoccupying in channeling energy for proliferation purposes, in place of undergoing these natural protective changes. This finding of Dorff and Longo (2011) adumbrate that proto-oncogenes negatively regulate stress resistance and therefore oncogenes block cancer cells participation into protected mode. Seeing that chemotherapy conducts its job predominantly through the induction of oxidative stress, fasting became a supplemental conception in protecting normal cells against chemotherapy side effects without decreasing the efficacy against cancer cells.

General acceptance of a causal relationship between chemotherapy and calorie restriction has unequivocal assured short term fasting laboratory mice in displaying increased treatment responses compared to ad libitum-fed mice (Lee et al., 2012). Some patients with breast, prostate, ovarian, uterine, lung and esophageal cancers who perceived the results in mice had undertaken fasting prior to their respective chemotherapy regimens. Allowing this approach is an apparent subject to significant bias, however, the severity of side effects did seem to be less during fasting cycles (Dorff and Longo, 2011).

Another study that seems to synergistically exerting the efficacy of chemotherapy is the combination of the method called chronotherapy in cancer. Cancer chronotherapy is seeking attention as a novel method in implying anti-cancer drugs during optimal timing based on circadian rhythms. This revolve around the concept of medications being administrated during times where it will be most effective on cancer cells while minimizing the effect of side effects. The circadian dosing time influences the extent of toxicity of more than 230 anticancer drugs that have been demonstrated in animal models influencing the varies of survival rate for at least 50% depending on the time the lethal dose had been administrated. The consummation of this study revolves the association of cellular repair mechanisms with circadian regulation, expounding the advantageous of many key genes in xenobiotic metabolism and transport. Remarkably, the administration of a particular drug at a circadian time when it is best tolerated achieves the best anticancer activity thus suggesting the circadian clock in playing a vital role in cancer prevention and chemotherapy (Huang et al., 2011). Even Indian Ayurvedic system was employed these methods since immemorial time.

Ayurveda, also called Ayurvedic medicine, is a system of medicine that originated in India over 5000 years ago. The Ayurvedic practitioners will consult with astrologers for optimal timing for drugs administration. By uniting the ancient practices with the modern medical technology we are able to protect ourselves from various ailments. Therefore future cancer research should be focused on using all the tools of both ancient wisdom and modern science. Well-designed clinical and laboratory studies concatenating chemotherapy with fasting and chronopharmacology should be a new field in breaching the modern improvement of scientific medical regimens symphonizing in preventing cancer during early stage as to optimize cancer chemotherapy and improve prognosis.

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