Editorial

Religious fasting and the vascular health

Keywords:
- Caloric restriction
- Endothelial progenitor cells
- Atherosclerosis
- Primary prevention
- Lifestyle changes

1. Preamble

Prof. Rakesh Yadav, Editor-in-Chief of the Indian Heart Journal, during his interview with Prof. Jagat Narula complimented the legendary alum. Three major discussion points stood out. First, how did the Indian medicine influence the modern western medicine, and cardiology in particular? Prof. Narula claimed that even the name HEART was derived from Hridaya that conveyed a complete physiological meaning, comprising 3 verbs– HRU for harati (to receive from or to abduct), DA for dadati (to give or to donate), and YA for either yagati (control through self-generated rhythmicity) or Yama (maintaining balance for contraction and relaxation, to circulate).1 Second discussion point focused on the relevance of tradition of Upavasa, practiced in India for thousands of years. Prof. Narula highlighted a potentially strong association of fasting with exaggerated release of endothelial progenitor cells and consequently superior vascular health. The circulating levels of endothelial progenitor cells are manifold greater in women of reproductive age offering them a protection against endothelial injury and rendering them to be more resilient against heart disease. Supported by his 4 colleagues, he discusses global religious practices and the basis of improved vascular health resulting from fasting. During the third discussion point, Prof. Yadav lauded Dr. Narula’s editorial contributions to the field of cardiovascular medicine, and asked about the inspiration for his editorial prowess which the Indian Heart Journal would publish in a subsequent issue.

2. Upavasa and vascular endothelium

The global burden of atherosclerotic cardiovascular disease continues to grow, and is the most important cause of mortality worldwide.2 The deteriorating lifestyle behavior, including eating

Fig. 1. Fasting, hematopoietic stem cells (HSC) and vascular health. HSC contribute to clonal diversity and physiological cell renewal in various organ systems such as GI and respiratory tracts, endometrium and vascular endothelium. HSC population decreases with ageing (left) and is associated with increasing cellular loss and decreasing cell replenishment; somatic mutations are also associated with blood malignancies and vascular inflammation. Intermittent and/or prolonged fasting has been demonstrated experimentally to influence Insulin-Like Growth Factor-1 (IGF-1) signaling (right) and at least partially restore HSC integrity leading to superior vascular health, amongst other stem cell and non-stem cell-based beneficial consequences.

Abbreviations: HSC, hematopoietic stem cells; EPC, endothelial progenitor cells; IGF, insulin-like growth factor; PKA, protein kinase A; NAD, nicotinamide adenine dinucleotide.
patterns and lack of indulgence in physical exercise have contributed immensely to the growing burden of disease. The increasing prevalence of obesity is associated with increased incidence of metabolic disease, diabetes, hypertension, and fatty liver, all of which contribute to atherosclerotic cardiovascular disease. The need to reduce this global atherosclerotic burden is imperative. Caloric restriction has been demonstrated to be associated with improvement in physical endurance, blood pressure, heart-rate variability, and glucose metabolism.1–6 This review will focus on the potential role of stem cells in mediating the benefits of decreased caloric intake in prevention of atherosclerotic disease.

Since prehistoric times, more than 12,000 years ago, abstinence from food or drinking or both have been a part of human living. In pre-agricultural era during Paleolithic times, our prehistoric ancestors were forced to undertake intermittent fasting for various periods of time while searching for food, between hunting and gathering. These factors have compelled the human body to incorporate fasting as a physiological (rather than a pathological) process, and to adapt and thrive during both fasting and eating. About 10,000 years ago, during agricultural revolution in Neolithic era, when humans started to domesticate animals such as goats and sheep, and set farming and growing crops, undeniable fasting disappeared from diurnal human life. At this time, humans learned to store food, and arguably initiated a culture of scheduled meals through the day. Ayurveda (science of life, Sanskrit) has its roots in the Auj-veda (science of longevity)–an appendage to the Athar-vaveda, was compiled around 5000 BC, by the priests and the scholars of Ayurveda, including Dhanwantri, Charaka, Sushruta, and Vagbhata. Deliberate fasting was first introduced; in ancient India with an aim to strengthen the spirit and ensure health wellness; Ayurveda claims Linghamam param aushadh, or that fasting is the best medicine.

When Alexander invaded India in 326 BC, he brought the vai-dyas (Ayurvedic practitioners) with him to Greece, who in turn further influenced the evolution of Greek Medicine.19 There is no evidence that Hippocrates had proposed thy food to be thy medicine and thy medicine to be thy food,19 even though he has been credited for it. Ancient Greek philosopher, Pythagoras promoted fasting (abstinence from all food for a certain period) as a way to enhance physical strength, energy level and concentration in his students.11–13 Over the last decade, various types of fasting have gained popularity as a dietary modification for weight loss and as a part of the non-pharmacological strategy for primary prevention of cardiovascular disease.14

Intermittent fasting where food intake is restricted to a certain time period, has long been present in many cultures around the world and has been a part of all major religious beliefs and practices. Most prominent religions such as Christianity, Islam, Hinduism, Judaism, Buddhism, Jainism and Taoism promote different types of fasting for spiritual purposes as also for known health benefits and longevity. Numerous health benefits of fasting have been supported by experimental15 and clinical studies.16–18 Decreased inflammation, neuroendocrine activation, reduced mitochondrial oxidative stress,15 and activation of autophagy in endothelial cells that accompany intermittent fasting prevent cell death15 and promote proliferation, regeneration, and activation of endothelial progenitor cells.18 Fasting has beneficial effects on cardiovascular health through modification of common risk factors such as better blood pressure control, increased insulin sensitivity and better control of blood glucose level. The direct beneficial effects of prolonged fasting on the vasculature could be exerted through activation of endothelial progenitor cells (EPC) and promotion of endothelial cell regeneration. Caloric restriction has been demonstrated to impart cardiovascular benefits to fruit flies,19 rodents20–24 and humans.25–29

It is important to review different religious practices of fasting and their relationship with direct health benefits through promotion of EPC activity and vascular regeneration.

2.1. Different types of religious fasting and cardiovascular effects

Different types and durations of nutrient restrictions has been a part of cultural and religious practices all around the world.30–33 Fasting in Hinduism is commonly practiced, more so during religious festivals as an offering of self-sacrifice to pleasing the Gods. Ayurveda advocated fasting to cleanse the body of toxic materials and eliminating disease. Gandhi practiced fasting as an instrument of advocacy, to resolve moral dilemmas or during periods of self-reflection, and on many occasions fasting unto death during the pursuit for freedom of India from the British. He wrote “Food should be taken as one takes medicine in measured doses, at measured times and as required. A ‘full’ meal is a crime against God and humanity. Hence the need for total fasts at intervals and partial fasts forever. What is enough [food] is a matter of conjecture, therefore, of our own metal picture. What we often think is spare or meager is likely more than enough. More people are weak through over-feeding or wrong feeding rather than underfeeding.”31,32 Communal fasts in Hinduism are typically associated with religious events such as Ram Navami, Shivaratri and Janmashatmi, some Hindus fast on the eleventh day of the lunar fortnight called Ekadashi, and others fast on an elected day of the week often dedicated to a particular deity. The rigor of fasting intervals and type of food consumption vary. Fasts could comprise complete abstinence from food and water or simply consumption of vegetarian food. The Phalahar category includes food grown naturally such as vegetables, fruits, roots and tubers, flowers or leaves, and excludes anna, such as wheat, barley, rice and lentils.33

Buddhism integrates fasting as a part of Danjiki, an ascetic traditional ritual that involves fasting (abstinence from solid food, drinking water, with limited carrot juice and miso soup for electrolyte replenishment), meditation and strenuous physical training. Danjiki can be short-termed (2–3 days) and longer lasting (a week or longer). Limited studies/case reports have shown that Danjiki was associated with decrease in body weight by 5 kg, lower level of LDL cholesterol and triglycerides levels but no effect on fasting glucose level and blood pressure.36

In Christianity, particularly Roman Catholicism and Eastern Orthodoxy, there are various types of fasting throughout the year particularly during Advent, a penitential period before Christmas and a 40-day fasting during Lent, a spring period of penitence before Easter. In 1962–65 the Second Vatican Council allowed greater individual choice with mandatory fasting only on Ash Wednesday and Good Friday during Lent. Fasting frequently involves removing animal protein, refined sugars and sweets from the diet. Coptic Christians fast for 210 days in a year (www.culturalawareness.com). In the Indian state of Kerala many Catholics fast by avoiding meat including eggs for 25 days before Christmas. Protestant churches generally leave the decision to fast to individual followers.

In the Islamic lunar calendar, Muslims observe Ramadan during the ninth month, known as the month of the Quran. Fasting is one of the five pillars of Islam and it commemorates the revelation of the Quran to the Prophet Muhammad. During the month of Ramadan, Muslims abstain from any food and beverage (including water) during the daytime, between sunrise and sunset. Intermittent fast is integral part of worship and celebration of the Almighty and physical way to cleanse the body and soul. Exceptions from Islamic recommendations are those who are ill, elderly, children, pregnant or breastfeeding women or those traveling. Ramadan fasting most closely mimics form of intermittent fasting that has now gained
Changes in hematopoiesis, particularly after the age of 70 years, differentiate, and these changes contribute to biological aging. Function

2.2. Fasting promotes stem cell and endothelial progenitor cell function

Caloric restriction, therefore, has been advocated by most religions in periods of penitence such as Yom Kippur (the day of Atonement). Devout Jews avoid onions, garlic, root vegetables, fruits, fermented seeds, eggs, fish, and meat; they follow other ascetic practices including meditation and variable vows of silence. Zoroastrianism prohibits fasting because of its belief that frugality does not aid the faithful in combating evil. However, they are supposed to avoid meat during the eleventh month of the Parsi year. Sikhs celebrate major festivals of their native Indian state of Punjab such as Holla Mohalla, Holi, Baisakhi, and Sankranti. They also celebrate the day of foundation of the Sikh community and also honor their religious masters - Guru Teg Bahadur and Guru Arjan, for the martyrdom, and birthdays of Guru Nanak and Guru Gobind. During these festivals vegetarian meals are served in the community kitchen. Judaism has several dietary laws and customs and they observe fast days several times in a calendar year particularly during mourning or periods of penance such as Yom Kippur (the day of Atonement). Caloric restriction, therefore, has been advocated by most religions globally for over centuries.

2.2. Fasting promotes stem cell and endothelial progenitor cell function

With aging, stem cells lose the ability both to proliferate and differentiate, and these changes contribute to biological aging. Changes in hematopoiesis, particularly after the age of 70 years, are associated with immune dysfunction, reduced capacity for regeneration, cytopenia, and increased risk of blood cancers. At the cellular level there is a gradual but lifelong accumulation of molecular changes including oxidative and replicative stress, attrition of telomeres, somatic mutations and epigenetic changes. With ageing, there is a collapse of clonal diversity which is abrupt after 70 years, with loss of physiological cellular cellularity and the multipotent progenitors (CD48+/CD150+). In the heterogeneous hematopoietic stem cells, several HSC subtypes are identified as lymphoid (Ly-HSC), balanced (Bala-HSC), and myeloid (My-HSC) according to their distinct mature blood cell output. In both mice and humans, these HSC subtypes modulate hematopoietic lineage potential and play an important role in lineage-homeostasis during aging. The role of multiple prolonged fasting cycles, lasting 2 days or more, on age-dependent and chemotherapy-induced immunosuppression were investigated in HSC self-renewal, and hematopoietic reconstitution outcomes through Ly- , My-, and Bala-HSC subtypes; there was also a reversal of the age-dependent decline in the lymphoid-to-myeloid ratio. The number of total and BrdU mesenchymal progenitor stem cells increased 5- and 45-fold in the fasting (49.9 ± 17.95 and 69.8 ± 34.0) mice compared with control (95.5 ± 16.7 and 1.5 ± 0.6) mice. It has been proposed that a class of NAD+ dependent deacetylase enzymes, sirtuins (SIRT 1–7) mediate epigenetic and metabolic influences, including beneficial effects of caloric restriction on progenitor cells. Circulating endothelial progenitor cell contributed to ongoing endothelial repair. Fasting-induced HSC could contribute to renewal of endothelial cells throughout the vasculature and contributes to vascular health.

2.3. Conclusions

Targeted studies are needed to determine how intermittent fasting in humans improves vascular health. Is it a simple replenishment of risk factor (hypercholesterolemia, smoking, hypertension, hyperglycemia)-mediated exfoliation of endothelial cells? And that could be the easiest explanation for immediate effect of fasting. Or, is it a complete endothelial progenitor cell-mediated adult vasculogenesis as a main pathway of vascular regeneration including partial reemergence of traditional angiogenesis program? Irrespective of the mechanism involved therein abundance of endothelial progenitor cell release consequent to various fasting regimens is sufficient evidence for scientific basis of fasting or intermittent fasting rather than sidetracking it to be an unsubstantiated religious fad.

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