MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjms.2023.467.473

Physiological Effects of Health Promotion Fasting: An Interventional Study

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ABSTRACT

The principle of Naturopathy emphasizes the inherent healing capacity of the body, with fasting being a vital modality that enables the body to heal and purify itself without external interference. Fasting has exhibited remarkable effects in various conditions such as autoimmune diseases, inflammatory disorders, psychiatric ailments, metabolic imbalances, hormonal irregularities and genetic disorders. High-Protein Fasting (HPF) has been recognized as a means to maintain overall health and physical fitness. This study aimed to investigate the physiological changes occurring in healthy individuals during fasting. The objectives of this study were twofold: (1) To analyze the physiological effects of HPF and (2) To assess the presence of any adverse effects. A single-arm interventional pilot study was conducted in an outpatient setting during December 2018, involving 9 healthy male and female volunteers aged between 20 and 35 years. Purposive sampling was employed based on predefined inclusion and exclusion criteria, following ethical considerations. The intervention spanned a duration of 5 days, during which pre- and post-assessments were conducted to measure vital signs, anthropometric parameters and blood parameters. The results revealed significant reductions in systolic blood pressure, anthropometric measurements (including arm, chest, waist, hip, thigh circumference and skin fold thickness at various sites), blood sugar levels and granulocyte percentage. Conversely, significant increases were observed in urea, creatinine, alkaline phosphate, total protein, cholesterol, high-density lipoprotein (HDL), uric acid, mean corpuscular hemoglobin concentration (MCHC), mid-range cell percentage (MID%) and platelet distribution width (PDW). Additionally, improvements in sleep quality were reported, although a negative change was observed in the psychological index following the intervention. In conclusion, HPF demonstrated significant changes in vital signs, anthropometric measurements and blood parameters. This approach proves highly beneficial and effective in maintaining physical fitness. It is recommended to incorporate HPF into one's routine occasionally to reap its advantages.

OPEN ACCESS

Key Words
Water fasting, short fast, lemon honey water fasting, calorie restriction

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Received: 20 June 2023
Accepted: 14 July 2023
Published: 15 July 2023

Citation: Shivangi Pandey, Satyalakshmi Komarraju, Yuvaraj Paul, D. Sathyanath and Shrikanth Muralidharan, 2023. Physiological Effects of Health Promotion Fasting: An Interventional Study. Res. J. Med. Sci., 17: 467-473, doi: 10.59218/makrjms.2023.467.473

INTRODUCTION

Naturopathy, a system of holistic healing aligned with the constructive principles of nature, advocates for treatments utilizing natural elements. Central to naturopathic principles is the belief in the body's inherent healing capacity, with fasting emerging as a significant modality for empowering the body to self-heal and purify, unimpeded by external obstacles. Fasting has been practiced since ancient times, taking various forms such as religious fasting, political fasting and therapeutic fasting, tailored to individual beliefs, comfort and compatibility. Health Promotion Fasting (HPF) specifically refers to fasting applied to healthy individuals. Naturopathy posits that diseases manifest in the body due to the accumulation of unhealthy substances and disruptions in the body's absorption system. Time-restricted feeding (TRF) involves restricting food intake to a specific time window of 4-12 hrs each day. The effects of TRF primarily rely on peripheral tissue circadian clocks. Intermittent fasting (IF) is characterized by alternating periods of little or no energy intake, which can last a day or more. Two commonly used IF patterns are alternate-day fasting (ADF) and the "5:2" diet. Unlike other fasting regimens, IF can interact with non-coding RNAs (ncRNAs) to regulate hepatic glucose and lipid metabolism. Furthermore, IF regimens have been shown to promote self-renewal of hepatic stellate cells (HSCs) and axonal regeneration. Fasting-mimicking diet (FMD) involves reducing caloric intake for only 5 days each month. FMD has been associated with the regeneration and differentiation of multiple tissues and cells, including beta cells, intestinal stem cells (ISCs), oligodendrocyte precursor cells (OPCs) and neurons. Both TRF and IF can affect appetite regulation and promote fat mobilization. Similarly, IF has been found to enhance beta cell and ISC regeneration and boost the host's immune response against tumors. Although the core molecular machinery and signaling regulation may differ, studies in animals and humans have demonstrated that all three fasting regimens-TRF, IF and FMD can impact autophagy, gut microbiota and mitochondrial function. Extensive research supports the effectiveness of fasting in a range of conditions, including rheumatic diseases, chronic pain syndromes, chronic degenerative disorders, chronic inflammatory diseases, hypertension and metabolic syndrome[1]. Fasting elicits neuroendocrine activation, triggers a hermetic stress response, boosts the production of neurotrophic factors, reduces oxidative stress in mitochondria, decreases signals associated with aging, promotes autophagy and overall confers health-promoting effects[1]. Studies on Naturopathy fasting therapy (NFT) demonstrate decreased lipid profiles and improved blood parameters[2]. For instance, a 4-day lemon honey juice fasting regimen led to significant reductions in weight, body mass index (BMI), fat mass (FM), free FM (FFM), total serum triglycerides (TSTGs), fat percentage and total serum cholesterol compared to baseline[3]. Additionally, fasting has been associated with changes in various parameters, such as reduced blood pressure[4], heart rate variability and respiratory rate[5]. However, the effects on systolic blood pressure (SBP) are more consistent, while changes in diastolic blood pressure (DBP) vary or exhibit minimal alterations[5]. Despite the wealth of studies investigating fasting, there is a dearth of research on the adverse effects of fasting. Existing literature primarily focuses on Ramadan fasting, intermittent fasting and calorie restriction, often conducted on individuals with pre-existing conditions as therapeutic interventions. Consequently, the present study aims to fill this knowledge gap by examining the physiological changes in healthy individuals following HPF. By elucidating the physiological effects of HPF, this study contributes to our understanding of fasting as a health-promoting practice. The findings will not only expand our knowledge of fasting's impact on healthy individuals but also inform recommendations for incorporating HPF as a beneficial modality for overall well-being.

MATERIALS AND METHODS

A single-arm interventional pilot study was conducted in an outpatient department (OPD) of a hospital in December, following the approval of the ethics committee (Ref. No: 7-2/NIN/IEC/2018-19/). A group of individuals aged between 20 and 35 years were selected using purposive sampling based on predefined inclusion and exclusion criteria. Prior to participation, participants provided informed consent after receiving detailed information regarding privacy and all aspects of the study. Questionnaires assessing psychological index and sleep quality were administered to the participants. Additionally, a daily diary was provided to ensure adherence to the study protocol, monitor any encountered difficulties and document observed changes during the fasting period.

Eligibility criteria

Inclusion criteria: Participants of the study will be healthy volunteers both male and female of 25-45 years of age those who will to participate in the study.

Exclusion: Pregnant women or breast-feeding women, subject with diabetes, those who have eating disorder, subject under medication or has taken antibiotics in past 1 month, BMI<18.5.

Intervention: The intervention lasted for a total of 5 days, which consisted of a 1 day preparatory phase and a 1 day period for breaking the fast. The daily calorie intake was restricted to approximately 1000 kcal day^{-1}. To support this, stimulants such as

Table 1: Diet chart for day 1 (preparatory phase)

Morning (10:00 am)	2 Idli (200 g)
Afternoon (2:00 pm)	Foxtail millet khichadi (200 g)
Evening (6-7 pm)	Papaya (300 g) or bottle gourd soup (250 mL)

Water intake should be there whenever they need and want.

Table 2: Diet chart for day 2,3,4 (intervention)

8:00 am	1 tender coconut water (240 mL)
10:00 am	1 glass lemon honey water (250 mL) [1/2 lemon, 2 tablespoon honey]
1:00 pm	1 glass lemon honey water (250 mL) [1/2 lemon, 2 tablespoon honey]
4:00 am	1 glass lemon honey water (250 mL) [1/2 lemon, 2 tablespoon honey]
7:00 pm	1 tender coconut water (240 mL)

Water intake should be there whenever they need and want, minimum of 2.5 L in the whole day

Table 3: Diet chart for day 5 (breaking the fast)

Morning (10:00 am)	Papaya (300 g) or bottle gourd soup (250 mL)
Afternoon (2:00 pm)	Foxtail millet khichadi (200 g)
Evening (6-7 pm)	2 idli (200 g)

caffeine, alcohol and nicotine were eliminated. The participants engaged in mild to moderate physical activity and underwent emotional preparation. During the fasting period, participants were allowed to consume a maximum of 250-500 kcal day^{-1}. This included options like lemon honey water and tender coconut water, if desired. It was also mandatory for participants to consume at least 2.5 L of calorie-free liquids and primarily water (Table 1-3).

Data collection and analysis: Blood and urine samples were collected for assessment on the morning before the intervention began and on the 5th day. A total of 5 mL of blood sample and an early morning urine sample were collected. The samples were sent to the laboratory for analysis, where the following parameters were checked: Liver function test (LFT), kidney function test (KFT), lipid profile, complete blood count (CBC), fasting blood sugar (FBS), postprandial blood sugar (PPBS) and urine analysis. Additionally, various other measurements and assessments were performed. Blood pressure (using the Diamond regular BP Apparatus, India), respiratory rate and axillary temperature (measured with a manual thermometer) were recorded. Radial pulse was also measured. Anthropometric measurements, such as circumference using a measuring tape and skinfold thickness using a skinfold caliper, were taken. Height was measured using a height measuring scale and weight was measured using a digital weighing machine. Furthermore, psychological indexes and sleep quality questionnaires were assessed manually. For statistical analysis, both pre and post-intervention data were stored and analyzed using Excel and SPSS software. The analysis was conducted on an exploratory basis.

RESULTS

This study includes data from 9 participants, with 56% males and 44% females. The participants were aged between 20-35 years, with a mean age of

Table 4: Details of the intervention

No. of participants	9
Age	27.3±3.71
Sex	44% female and 56% male

27.3±3.7081. All participants were highly educated and received a 5 day intervention symmetrically. The details of the intervention can be found in Table 4. Statistical analysis was performed using the "paired sample t-test" to determine the significance of the results. The results are presented in their respective tables. Vitals are presented in Table 5, anthropometric measurements in Table 6 and laboratory test results in Table 7. The findings of the study showed a significant reduction in systolic blood pressure (SBP), as well as in various anthropometric measurements such as arm circumference, chest circumference, waist circumference, hip circumference, thigh circumference and skinfold thickness in the iliac, subscapular, chest and axilla regions. Significant reductions were also observed in fasting blood sugar levels and the percentage of granulocytes (GRAN%). On the other hand, significant increases were observed in urea, creatinine, alkaline phosphatase, total protein, cholesterol, high-density lipoprotein (HDL), postprandial blood sugar levels (PPBS), uric acid, mean corpuscular hemoglobin concentration (MCHC), percentage of middle-sized cells (MID%) and platelet distribution width (PDW). The mean values of white blood cells (WBC) and platelets also showed an increase. These findings are presented in the form of data tables and graphs. Sleep quality was also improved and psychological index shows negative change after the intervention.

DISCUSSIONS

The present study investigates the physiological changes and their clinical significance. Significant changes were observed in various parameters including SBP, Anthropometric Measurements, Haemoglobin, LFT, RFT, Lipid Profile, Blood Sugar and other blood parameters, which contribute to maintaining good health. While some studies have reported a decrease in both SBP and DBP[4]. This study specifically highlights significant changes in SBP and reduction in other vital signs. Notably, a 4-day lemon honey juice fasting regimen resulted in a significant reduction in weight, body mass index (BMI), fat mass (FM), free FM (FFM), total serum triglycerides (TSTGs), fat percentage and total serum cholesterol compared to the baseline. Similarly, a study on naturopathic fasting therapy (NFT) demonstrated a decrease in total serum cholesterol and triglycerides, while haematological indices such as Haemoglobin, PCV, RBC Count and MCHC increased significantly after NFT[5]. In line with these findings, the present study also observed significant changes in liver and renal parameters following the intervention, consistent with

Table 5: Paired sample t-test

Parameters	Before	After	Difference (%)	T-value	p-value
Systolic blood pressure	109.6±6.7	101.1±10.1	-0.15119	1.849	0.05*
Pressure	68.9±5.7	72.2±8.8	0.183954	-0.990	0.18
Pulse	76.8±8	82.9±14.9	0.387129	-1.246	0.10
Respiratory rate	16.9±4.6	17.2±3 .6	0.445336	-0.216	0.40
Temperature	97.2±0.8	97.2±0.7	0.834025	0.248	0.40

Table 6: Anthropometric measurements

Parameters	Before	After	Difference (%)	T-value	p-value
BMI	22.4±1.3	21.3±1.4	0.961561	7.761	2.700
Arm circumference	11.1±0.8	10.8±0.8	0.923398	2.811	0.010*
Chest circumference	34.4±1.7	33.6±1.6	0.929452	3.653	0.003*
Waist circumference	31.5±3.1	30.3±3.8	0.94181	2.425	0.020*
Hip circumference	36.8±0.8	36.0±0.6	0.681456	3.776	0.002*
Thigh circumference	20.2±1.3	19.4±1.7	0.83431	2.312	0.020*
Iliac crest skin fold thickness	8.3±3	5.3±2.3	0.706633	3.939	0.002*
Subscapular skin					
Fold thickness	8.9±3.5	7.2±3.3	0.866764	2.673	0.010*
Chest skin fold thickness	6.8±3.5	5.8±3.3	0.963663	3	0.008*
Axilla skin fold thickness	7.6±4.2	6.7±4.5	0.975358	2.530	0.020*

Table 7: Laboratory test results

Parameters	Before	After	p-value
Urea	17.5±4.6	30.8±8.2	0.0002*
Creatine	1.0±0.2	1.5±0.2	0.0002*
SGPT	20.6±7.8	19.5±6.1	0.2
SGOT	23.2±6	20.9±4.5	0.1
Alkaline phospohate	60.0±16.5	73.9±19.2	0.001*
Total protein	7.8±0.5	8.09±0.2	0.04*
Albumin	4.2±0.2	4.42±0.2	0.3
Cholestrol	147.0±25.3	169.2±26.3	0.0004*
HDL	44.0±5.7	51.0±6.1	0.001*
LDL	99.7±25	120.9±25.3	8.2
Uric acid	4.2±1.2	7.5±2.5	0.0009*
Bilirubin direct	0.3±0.1	0.4±0.1	0.002*
Bilirubin total	1.0±1	1.9±2.5	0.1
FBS	76.5±10.8	67.0±16	0.04*
PPBS	94.6±4.3	115.9±27	0.03*
Hemoglobin	13.6±1.9	15.0±1.8	0.0003*
RBC	5.6±0.6	6.1±0.6	1.4
MCHC	31.1±1.2	28.8±1.6	0.001*
WBC	7.1±1.4	7.7±2.1	0.2
MID (%)	6.8±1.4	4.9±1.2	0.001*
GRAN (%)	61.9±8.7	67.3±8.9	0.03*
PDW	14.7±0.1	14.7±0.1	0.02*
Platelets	311.6±49.6	333.8±52.5	0.1

Water intake should be there whenever they need and want

the effects of short-term fasting reported by previous research[2,6]. Another study reported increased levels of uric acid and creatinine, as well as a decreased glomerular filtration rate, while the present study showed elevated levels of serum urea, S. creatinine and S. uric acid, which may be attributed to tissue nucleic acid breakdown and reduced uric acid clearance[7]. Haematological indices demonstrated a significant increase in RBC and Haemoglobin values after the intervention. Fasting was associated with a decrease in organ size and an increase in iron concentration in the tissues, resulting in a reduction of fasting total iron binding capacity (TIBC) values and an increase in plasma iron (PI). The mechanism responsible for fasting-induced hyperbilirubinemia remains undetermined, although a review article by Woreta suggests that fasting and stress can elevate bilirubin levels[8]. It is worth noting that one male participant had Gilbert syndrome, an inherited disorder that may explain the substantial increase in bilirubin levels, possibly due to consanguineous marriage between parents. Similarly, PPBS levels increased for all participants but one individual experienced a significant change due to sleep deprivation, which can affect metabolism, including insulin resistance, leading to elevated PPBS[9]. Prolonged fasting is known to induce significant hormonal changes in the body, although the exact triggers for this neuroendocrine activation are not fully understood. Several factors, such as decreased availability of brain glucose, consumption of leptin and insulin and the sensation of hunger, are believed to play important roles. Additionally, Foxa2, a transcription factor, has been found to act as a metabolic sensor in neurons of the lateral hypothalamus, integrating metabolic signals, adaptive behaviors and physiological responses[10]. Leptin levels serve as a potent signal for biological adaptation to starvation and have been associated with mood disorders[11]. Studies have demonstrated that fasting can deplete leptin levels[12,13]. Leptin is involved in modulating the brain's reward circuitry by enhancing the value of behaviors that are incompatible with feeding[14]. Furthermore, research has shown that fasting-induced neuroendocrine activation is linked to increased concentrations of norepinephrine, epinephrine, dopamine and cortisol in both urine and serum[15]. Similarly, a prospective study involving obese individuals revealed that fasting for more than 16 days resulted in substantial weight loss while reducing baseline and exercise-induced serum levels of norepinephrine, epinephrine and dopamine[16]. Moreover, prolonged fasting is associated with an increase in the concentration of the growth hormone glucagon and a decrease in thyrotropin and blood T3/T4 levels[17]. According to the daily diary maintained by the participants, on the second day, some experienced mild discomfort (healing crises) such as headaches, nausea, body pain, dizziness and increased frequency of water intake, resulting in more frequent urination. Most participants reported irregular bowel movements and some did not defecate during the intervention period. Appetite and cravings were heightened during this phase. By the third day, participants exhibited increased tongue coating, mouth odor, sweating, feelings of tiredness, anger, on/off mood swings and reduced cravings, indicating the onset of the ketosis stage. By the end of the fourth day, most participants had regained their natural hunger. Due to the participants' professional commitments as doctors, complete rest was challenging, leading to reduced water intake, which subsequently increased levels of urea, creatinine, epithelial cells and pus cells. After completing the 5 day intervention and returning to their normal diets, participants experienced a restoration of their natural hunger, regular bowel movements, increased satisfaction and improved sleep quality. Research has demonstrated that fasting-induced changes in neurotrophic factors and neurotransmitters may contribute to the enhancement of emotions during fasting[18-21]. Fasting has been found to stimulate neurogenesis and promote synaptic plasticity, leading to the regulation of pain sensations, improved cognitive function and enhanced anti-aging capabilities of the brain. These positive effects may be associated with alterations in neurotrophic factors and neurotransmitters[21]. During prolonged fasting, serotonin release and turnover tend to increase[18]. The heightened activity of the serotonergic system can lead to improved mood and reduced sensitivity to pain[22]. Studies conducted on rats have shown that fasting increases the availability of tryptophan and serotonin in the brain, which may explain the therapeutic effects of fasting in individuals with migraines[20]. Moreover, brain-derived neurotrophic factors (BDNFs) induced by intermittent fasting may be involved in the regulation of central serotonergic pathways. Notably, there is a reciprocal relationship between BDNF and serotonergic signaling, as BDNF enhances the production and release of serotonin[23]. Changes in the release of endogenous opioids as a result of fasting represent another potential mechanism for mood enhancement. The levels of plasma β-endorphins significantly increase during fasting periods of 5-10 days[19]. Certain neuropeptides may also be implicated in the enhancement of mood during fasting. BDNF may contribute to fasting-induced mood enhancement by facilitating serotonin production and release[18,20]. Other neuropeptides, such as orexin and neuropeptide Y, are involved in the regulation of eating behavior, appetite and mood. They are inhibited in response to feeding-related signals but released during fasting. Fasting has been found to increase the expression of neuropeptide Y genes in specific brain regions in rodent studies. Neuropeptide Y acts through its spinal receptors to reduce spinal neuronal activity and alleviate symptoms of inflammation and neuropathic pain[24]. Therefore, neuropeptide Y induced by fasting may have analgesic effects. Overall, fasting may activate specific cellular stress resistance mechanisms that serve as self-protective measures, counteracting any potential adverse effects of increased glucocorticoids and catecholamines. In contrast, chronic neuroendocrine activation associated with excessive feeding can contribute to neuronal degeneration and impair neurogenesis[25].

LIMITATIONS OF THE STUDY

- **Lack of participant monitoring:** Conducting the study in an outpatient department (OPD) setup could have made it challenging to closely monitor and observe the participants. This limitation may have led to incomplete or inaccurate data collection, potentially affecting the reliability and validity of the study's findings
- **Small sample size:** The study's sample size was relatively small, which could limit the generalizability of the results. With a small sample, there is a higher risk of obtaining statistically insignificant or unreliable findings. A larger sample size is generally preferred to increase the statistical power and enhance the study's reliability
- **Compliance of participants:** The difficulty in ensuring participants' adherence to the study protocol can be a significant limitation. Non-compliance or lack of motivation to adhere to the prescribed interventions or procedures may introduce bias or confounding factors that can impact the study's outcomes
- **Absence of control group:** The absence of a control group is another limitation. Without a control group, it becomes challenging to establish a basis for comparison and determine the true effect of the intervention being studied. The inclusion of a control group helps researchers differentiate between the effects of the treatment being investigated and other external factors or natural variations

CONCLUSION

HPF gives tremendous beneficial effect and one should practice it once in a while to detoxify owns body and get immense health benefits. During fasting rest is must and it is basically done under the supervision of expert in an IPD hospital. This study highlights how fasting can help to improve the major biochemical parameters around health. Further long term studies are required to support such evidence in the Indian set up.

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