

Effects of Wet and Dry Intermittent Fasting on Weight and Cardiovascular Risk Indicators



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ABSTRACT: Intermittent fasting (IF) has two broad types: wet (with water) and dry (without water) fasting. Studies suggest that both are effective for reducing weight and for promoting overall metabolic well-being; however, their relative efficacy is not yet established. The study was a 9-day cross-over clinical trial with the purpose to compare the effectiveness of wet and dry fasting. Adult overweight women (n = 18) from Dhaka, Bangladesh were recruited as subjects of this study. It included 3 days of wet IF and 3 days of dry IF (14 h fasting and 50% calorie restriction), with a 3-day washout period (ad libitum intake) in between. Both types of IF resulted in significant weight loss. The loss was significantly higher after 3 days of dry IF (-0.23 ± 0.02 kg; $P < 0.05$). Waist circumference and BMI were significantly reduced in both interventions ($P < 0.05$) and diastolic pressure changed significantly after dry fasting ($P < 0.05$). None of the biochemical parameters (total cholesterol, triglycerides, HDL-C, LDL-C, atherogenic coefficient, and fasting plasma glucose) changed significantly within or between interventions. The intervention compliance percentage was high for both, with no significant difference. The study findings suggest that both wet and dry IF were effective for weight loss but dry IF was more effective. The biochemical parameters did not change significantly in short term and so longer trials are needed. [Trial registration number: UMIN000041481]

KEYWORDS: Intermittent fasting; Wet fasting; Dry fasting; cardiovascular diseases; Weight loss

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Introduction

Influencing the energy balance by dietary interventions is the most commonly used strategy to tackle the growing problem of obesity and its associated comorbidities. Most current guidelines recommend continuous energy restriction (CER), which can achieve initial but often poorly sustained weight loss (Howard *et al.*, 2006; Harvie *et al.*, 2013). Recently, intermittent fasting (IF), a modified form of energy restriction and the age-old fasting practice, has emerged as an alternative strategy. Some studies state that IF may be more beneficial over CER because of more ease of compliance, greater fat-mass loss, greater reductions in fasting insulin, and so on (Alhamdan *et al.*, 2016; Gabel *et al.*, 2019). However, the evidence is yet not sufficient enough to recommend the use of IF for the long term (Harvie and Howell, 2016).

IF is a type of diet that cycles between brief periods of fasting and periods of restricted eating. It is mainly of two types: wet fasting (with water) and dry fasting (without water). There are various protocols for it but typically includes 14 to 16 h of food abstinence and 25-60% caloric restriction during non-fasting hours. IF promotes changes in the metabolic pathways and cellular processes such as stress resistance, lipolysis, and autophagy (De Cabo and Mattson, 2019). It also promotes stem cell regeneration as well as long-lasting effects (Longo, De Cabo and Mattson, 2019). A plethora of clinical trials

suggests that 3 to 12 weeks of wet fasting can result in 3% to 7% of body weight reduction and improvements in lipid profiles, blood pressure, and many other metabolic risk indicators (Horne *et al.*, 2013; Antoni *et al.*, 2017; John F Trepanowski *et al.*, 2017; Trepanowski *et al.*, 2018).

In contrast, the number of studies investigating the effect of dry fasting is minimal and mostly observational (Kul *et al.*, 2014; Cherif *et al.*, 2016; Fernando *et al.*, 2019). Although there are possibilities of dehydration and such due to dry fasting, a recent study suggests that it has no notable complication; in fact, it results in 50-100% more weight reduction than wet fasting (Papagiannopoulos *et al.*, 2013). It may even alleviate the symptoms of oedema, obesity, and inflammatory and ischemic diseases by reducing the time for glycogen burning before lipolysis (Papagiannopoulos-Vatopaidinos, Papagiannopoulou and Sideris, 2020). However, further evidence is needed before recommending it to the people, especially in the hotter climate.

This study compared the effects of wet fasting and dry fasting on weight and cardiovascular disease risk indicators in overweight women in a 9-day cross-over clinical trial. Additionally, it compared the subjects' compliance with the prescribed protocols (14 h fasting and 50% calorie restriction) during the fasting days. The hypothesis was that dry fasting

would result in more significant weight loss and more pronounced improvements in risk indicators for cardiovascular diseases.

Materials and Methods

Study design

The study was a randomized 9-day cross over trial, with two interventions:

1. Wet fasting: For three consecutive days, the subjects abstained from any food for 14 hours (from 4:00 a.m. to 06:00 p.m.) and consumed up to 50% of daily energy requirement (ER) in the feeding window. Participants were allowed to drink calorie-free beverages along with water during the fasting.
2. Dry fasting: For three consecutive days, the subjects abstained from all forms of food and drink for 14 hours (from 4:00 a.m. to 06:00 p.m.) and consumed up to 50% of ER in the feeding window.

The subjects were randomly assigned to either intervention (1:1) followed by three days of washout period (*ad libitum* intake). It was fixed to be 3 days as it was found in a study that cholesterol level returned to the baseline after 48 hours of

the fasting day (Horne *et al.*, 2013). After the washout period, the interventions were altered for each subject.

Sample Size

Sample size was calculated by assuming a 10% change in LDL-cholesterol concentrations, with a power of 80% and α risk of 5%, as found in the previous literature (Varady and Bhutani, 2009; Varady *et al.*, 2013). Our calculation suggested recruiting $n = 16$ in the study. Considering the drop-out risk of 5%, we included $n = 18$ in the final analysis. Only adult overweight females were considered for our study.

Subjects

Participants were recruited from Dhaka, the capital city of Bangladesh. The whole trial spanned within January 2020. A total of 25 women expressed interest, but only 20 were eligible to participate after the preliminary screening (**Fig. 1** shows the CONSORT diagram). The key selection criteria were as follows: age 18–59 years, BMI between 25 and 29.9, nondiabetic, no history of metabolic disease (cardiovascular, renal, hepatic, etc.), apparently healthy (i.e., no fever or illness at that time), light to moderately active (i.e., 3–5 hours/week of light-intensity exercise), not fasted any day in the last two weeks and not taking weight loss or glucose-lowering medications.

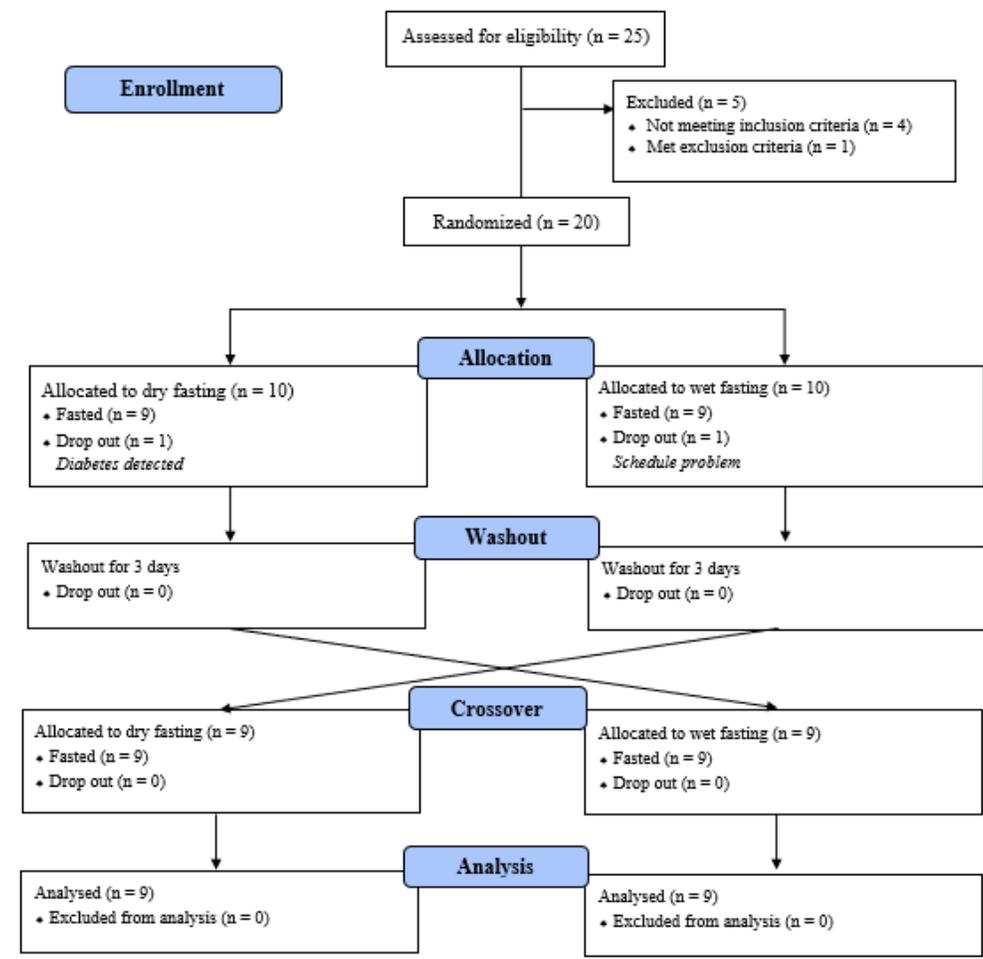


Figure 1. The CONSORT diagram

Several anthropometric and biochemical parameters were measured for each subject. However, the number of data collection points was different, as shown in **Table 1**. The subjects were instructed to avoid exercise, water, tea, and coffee 2h before each measurement.

Table 1. Summary chart for dietary and data collection protocol

Day	Diet	Data collection	
		Anthropometric and hemodynamic	Blood
0	ad libitum intake	9 a.m. (empty stomach)	9 a.m. (empty stomach)
1	wet or dry fasting from 4:30 a.m. to 6:30 p.m.; 50% of ER in feeding time	-	-
2	same as in day 1	-	-
3	same as in day 1	4:30 p.m. (fasting state)	4:30 p.m. (fasting state)
4	ad libitum intake	-	-
5	ad libitum intake	-	-
6	ad libitum intake	9 a.m. (empty stomach)	-
7	another fasting from 4:30 a.m. to 6:30 p.m.; 50% of ER in feeding time	-	-
8	same as in day 7	-	-
9	same as in day 7	4:30 p.m. (fasting state)	4:30 p.m. (fasting state)

The anthropometric and hemodynamic parameters were: (a) Bodyweight or BW (in kg); (b) Body mass index or BMI (in kg/m²); (c) Waist circumference or WC (in cm); (d) Systolic blood pressure or SBP (in mm of mercury); (e) Diastolic blood pressure or DBP (in mm of mercury). The biochemical parameters were: (a) Complete serum lipid profile, i.e., total cholesterol or TC, high-density lipoprotein cholesterol or HDL-C, low-density lipoprotein cholesterol or LDL-C, triglycerides or TG (all in mg/dL); (b) Atherogenic coefficient or AC; and (c) Fasting plasma glucose or FPG (in mg/dL). Other parameters were: (a) Compliance percentage and (b) Clinical features and feedbacks of the subjects.

Analyses

(A) Anthropometric: Body weight measurements were taken to the nearest 0.05 kg wearing light clothing and without shoes using a digital weight machine (Beurer Wellbeing PS240, Germany). The height and waist circumference was taken in triplicate by a measuring tape according to the WHO protocol was followed.

(B) Hemodynamic: Blood pressure (SBP and DBP) were measured by a Sphygmomanometer (ALRK2, 500-v, made in Japan) and stethoscope in triplicate with the subject in a seated position after a 10-min rest.

(C) Biochemical: The fasting plasma glucose, TC, HDL-C, and TG concentrations were measured by using enzymatic kits, standardized reagents, and standards (Atlas Medical,

Cambridge, UK) and analyzed by using an auto biochemistry analyzer (Dimension Xpand Plus Chemistry Analyzer, Siemens Healthcare GmbH, Erlangen, Germany) in the Biochemistry Laboratory of Dhaka Medical College Hospital, Bangladesh. The concentration of LDL cholesterol was calculated using the Friedewald equation (Fontana, 2008). The atherogenic coefficient was calculated by the formula (Olamoyegun, Oluyombo and Asaolu, 2016)-

$$\text{Atherogenic coefficient (AC)} = \frac{\text{Total cholesterol} - \text{HDL cholesterol}}{\text{HDL cholesterol}}$$

(D) Dietary data: On fasting days, the subjects were instructed to follow the 'diet chart' customized for each. The energy requirement was determined by the Mifflin equation (Mifflin *et al.*, 1990). The subjects were also instructed to report the names, portions, and times of food consumed in the provided 'food log'.

Percentage compliance for each subject was calculated by applying the following formula:

$$\% \text{ Compliance} = \frac{(\% \text{ Duration compliance} + \% \text{ Caloric compliance})}{2}$$

Results were presented as means \pm standard error of mean (SEM). Test for normality, namely Kolmogorov-Smirnov (K-S) test, was included in the model. Paired sample t-test for normally distributed data and a Wilcoxon test for non-normally distributed data were performed to determine the *p*-value for each variable. Dietary data were analyzed following the National Research Council (NRC) method (NRC, 1986).

Data were analyzed using the SPSS software (version 21.0 for Windows 10; SPSS Inc, Chicago, IL). In all cases, $P < 0.05$ was considered significant.

Ethical Approval

Prior approval for the human trial was obtained from the Institutional Review Board (IRB) of the Faculty of Biological Science, University of Dhaka. A written informed participation consent was obtained from each participant upon agreeing to participate in the study. All of the research participants' information was kept confidential. This study was registered in UMIN-CTR (UMIN000041481).

Results

Baseline characteristics

After screening, 20 participants were randomly assigned to the interventions, and 18 participants (90% of assigned) completed the study. One subject dropped out due to her time constraint, whereas another dropped out as she was diagnosed with pre-diabetes after the initial screening. **Table 2** shows the baseline characteristics of the subjects completing the trial (N = 18).

Table 2. Subject characteristics at baseline (N = 18)

Characteristics	Mean \pm SEM	Range
Age (y)	34.00 \pm 2.10	19-53
Height (cm)	168.71 \pm 6.73	147.3-175.3
Weight (kg)	69.23 \pm 2.91	58.95-91.85
Body mass index, BMI (kg/m ²)	27.61 \pm 1.51	25.12-29.80
Waist circumference (cm)	64.09 \pm 5.85	59.44-84.07
Systolic blood pressure (mmHg)	110 \pm 2	90-130
Diastolic blood pressure (mmHg)	79 \pm 2	60-90
Fasting blood glucose (mmol/L)	5.20 \pm 1.50	4.80-8.20

Note. SEM= Standard error of mean.

Anthropometric and hemodynamic parameters

The anthropometric and hemodynamic changes were all significantly different between interventions ($P < 0.05$ to < 0.001), except systolic blood pressure in dry fasting, as shown in **Table 3**. Wet and dry fasting, both resulted in the reduction of body weight 0.77 ± 0.09 kg ($P < 0.001$) and 1.00 ± 0.11 kg

($P < 0.001$) respectively. When two interventions were compared, the waist circumference (WC) showed a significant reduction in dry fasting ($P < 0.001$). There were no changes in blood pressure measurements (systolic and diastolic) between interventions.

Table 3. Anthropometric and hemodynamic changes due to 3 days of wet fasting plus 3 days of dry fasting (N = 18)

Risk factors	Type	At baseline (Mean \pm SEM)	After 3 days (Mean \pm SEM)	Change in 3 days (Mean \pm SEM)	P^1	P^2
BW (kg)	Wet	69.20 \pm 2.09	68.42 \pm 2.10	-0.77 \pm 0.09	<0.001**	0.045*
	Dry	69.20 \pm 2.13	68.20 \pm 2.13	-1.00 \pm 0.11	<0.001**	
BMI (kg/m ²)	Wet	27.60 \pm 0.36	27.29 \pm 0.35	-0.43 \pm 0.55	<0.001**	0.048*
	Dry	27.60 \pm 0.34	27.19 \pm 0.34	-0.56 \pm 0.06	<0.001**	
WC (cm)	Wet	64.09 \pm 1.37	63.62 \pm 1.37	-0.46 \pm 0.05	<0.001**	0.001*
	Dry	63.62 \pm 1.37	62.93 \pm 1.37	-0.62 \pm 1.37	<0.001**	
SBP	Wet	110 \pm 2	106 \pm 2	-4 \pm 2	0.042*	0.386

(mmHg)	Dry	110 ± 3	108 ± 2	-2 ± 2	0.449	
DBP (mmHg)	Wet	79 ± 2	71 ± 2	-8 ± 2	0.002*	0.369
	Dry	79 ± 8	73 ± 6	-6 ± 2	0.025*	

Note. SEM = Standard error of mean; BW = Body weight; BMI = Body mass index; WC = Waist circumference; SBP = Systolic blood pressure; DBP = Diastolic blood pressure

¹Within intervention *P*: Paired t-test

²Between intervention *P*: Paired t-test

*significant difference from baseline at *P* < 0.05; **significant difference from baseline at *P* < 0.001

Biochemical parameters

For the biochemical parameters, namely- TG, TC, HDL-C, LDL-C, and FPG, neither the individual effect of each fasting intervention nor the between intervention difference was statistically significant (Table 4).

Table 4. Biochemical changes due to 3 days of wet fasting and 3 days of dry fasting (N = 18)

Risk factors	Type	At baseline (Mean ± SEM)	After 3 days (Mean ± SEM)	Change in 3 days (Mean ± SEM)	<i>P</i> ¹	<i>P</i> ²
HDL-C (mg/dL)	Wet	40 ± 1	38 ± 2	-2 ± 2	0.237	0.227
	Dry	40 ± 1	40 ± 2	0 ± 1	0.867	
TC (mg/dL)	Wet	181 ± 8	184 ± 8	2 ± 6	0.715	0.377
	Dry	181 ± 8	191 ± 10	10 ± 8	0.229	
TG (mg/dL)	Wet	98 ± 10	86 ± 7	-11 ± 7	0.134	0.784
	Dry	98 ± 10	88 ± 9	-9 ± 6	0.172	
LDL (mg/dL)	Wet	121 ± 7	128 ± 8	7 ± 5	0.174	0.418
	Dry	121 ± 7	133 ± 8	7 ± 4	0.066	
AC	Wet	0.34 ± 0.06	0.33 ± 0.05	-0.00 ± 0.03	0.820	0.411
	Dry	0.34 ± 0.06	0.31 ± 0.05	-0.03 ± 0.03	0.329	
FPG (mg/dL)	Wet	82.35 ± 5.29	72.35 ± 3.19	-10.00 ± 5.97	0.113	0.521
	Dry	82.35 ± 5.29	74.98 ± 3.46	-7.36 ± 6.43	0.268	

Note. SEM = Standard error of mean; HDL-C = High density lipoprotein; TC = Total cholesterol; TG = Triglyceride; LDL-C = Low density lipoprotein; AC = Atherogenic coefficient; FPG = Fasting plasma glucose

¹Within intervention *P*: Paired t-test or Wilcoxon test

²Between intervention *P*: Paired t-test or Wilcoxon test

Dietary Data analysis

The compliance percentage calculated shows that there was no significant change between wet and dry fasting, i.e., *P* > 0.05 (wet: 93.81%; dry: 92.30%) (Table 5). The percentages of macronutrient intakes were neither significantly different between interventions nor with the prescribed percentages, i.e., *P* > 0.05.

Table 5. Compliance percentage of the subjects (N = 18)

Type	Category	Prescribed value	Obtained value (Mean ± SEM)	Compliance %	<i>P</i> ^a
Wet	Duration (h)	14.0	13.6 ± 0.30	93.81 ± 2.11	0.473
	Energy (kcal)	50% of ER	1172 ± 120		
Dry	Duration (h)	14.0	13.2 ± 0.20	92.30 ± 3.21	
	Energy (kcal)	50% of ER	1075 ± 134		

Note. SEM = Standard error of mean; ER = Energy requirement per day.

^aPaired t-test

Clinical features and feedbacks

The subjects showed no severe signs like fatigue, nausea, headache, muscle pains, etc., during each fasting intervention. Some subjects reported a few mild complaints; two were the same in both interventions—slight weakness (wet: 1 and dry: 5) and hunger (wet: 3 and dry: 4). The unique complaint after wet fasting was stomach rumbling by 7 and after dry was thirst by 2. When asked about the continuation of IF in the future (other than religious fasts), 17 answered positively, and 16 out of them preferred dry fasting over the wet one. After 1 week of the end of the trial, 9 subjects gave feedback that they felt less hungry than before.

Discussion

Our findings suggest that even short-term IF can result in weight loss. Herein we have reported a total of 776 ± 90 g and $1,002 \pm 110$ g (i.e., 1.1% and 1.5%) reduction in body weight for 3 days of each wet and dry fasting, respectively. Although dry fasting results in more weight loss as reported in the previous study (Papagiannopoulos *et al.*, 2013), we cannot confirm if the whole of lost weight was attributed to the loss of body water or not. We did not have access to any instrument which could measure either the percent body fat or water content. This randomized clinical trial demonstrated that dry fasting produced weight loss, but no significant difference in risk indicators for cardiovascular disease than wet fasting.

The most notable results in this study were observed in anthropometric and hemodynamic parameters. Both fasting interventions induced statistically significant anthropometric changes in the 3-day intervention period (i.e., $P < 0.001$ for both). However, with weight loss of $1,002 \pm 110$ g in 3 days, dry fasting seems to be the more effective dietary protocol since the magnitude of weight reduction is more than that of wet fasting, i.e., 776 ± 90 g in 3 days ($P < 0.05$). The weight loss finding is similar to previous studies (Johnson *et al.*, 2007; Varady and Bhutani, 2009; Varady *et al.*, 2009; Horne *et al.*, 2013; John F. Trepanowski *et al.*, 2017) on water-only alternate day fasting (ADF) with 20-25% caloric restriction for several weeks. It is also identical to the findings of the studies done on dry fasting and one-day water-only fasting (Horne *et al.*, 2013; Papagiannopoulos *et al.*, 2013). The decrease in body weight may be due to breaking down adipose tissue to provide energy when all glycogen level is depleted to produce glucose. The greater weight loss in dry fasting was not only water weight due to dehydration. It can be justified as researchers have found that during dry fasting, the body can compensate for dehydration by minimizing water losses (Molla, 2003).

Besides weight, waist circumference (WC) changed significantly ($P < 0.001$). The total decrease in body weight, together with WC during the trial, corresponds to a considerable reduction in the abdominal volume within 6 days. Such a rapid volume decrease may be attributed to reducing

visceral fat and eliminating oedema fluids from the abdominal organs (Papagiannopoulos *et al.*, 2013). The total

anthropometric changes, particularly the degree of weight loss achieved by the prescribed regimen, are comparable to short-

term calorie restriction (CR) trials (Harp, Henry and DiGirolamo, 2002; Cameron *et al.*, 2008; Chaston and Dixon, 2008). Because of these similar effects on body weight, IF may be considered a suitable alternative to CR diets to help obese individuals lose weight. However, whether obese individuals can adhere to regimens over the long term and experience sustained weight loss will be an important focus of future research.

Findings from the study also showed that both wet and dry fasting in overweight individuals might significantly reduce systolic and diastolic blood pressure. Blood pressure reductions by 5 to 10 mmHg are commonly reported in fasting studies after a few months of an intervention (Varady and Bhutani, 2009; Bhutani *et al.*, 2013). Thus, the present findings align with what has been demonstrated previously, though they were extended periods. Because of the strong association of high blood pressure with the risk of cardiovascular diseases, this finding further supports the protective actions of IF (Brindle *et al.*, 2006; Kannel, 2009).

Both types of fasting acutely increased TC and LDL-C; whereas TG and atherogenic coefficients AC in 3 days. The change of HDL-C was variable. However, the intervention difference was not significant for any of them. It is surprising, but the negative modulations in LDL-C and TC concentrations are precisely similar to those observed by a previous short-term study (Horne *et al.*, 2013). During Ramadan fasting, some studies also found similar results at the beginning of the month (Saleh *et al.*, 2005; Mansi, 2007; Kamal *et al.*, 2012). One study also reported that the decrease in LDL-C cholesterol was significantly evident after 21 days (Saleh *et al.*, 2005). The fact behind this may be that stored TG in the adipose tissue is broken to free fatty acids and goes to the liver, which increases VLDL-C secretion and, in turn, LDL-C in the blood. The change of TG was as expected and by almost all the studies on fasting. The HDL-C change was variable between two interventions in our research and other studies also. This lack of effect of fasting on HDL-C cholesterol is not surprising because this cardioprotective lipid parameter is generally augmented only in response to exercise training (Ellison *et al.*, 2004). Reduction in AC is associated with decreased morbidity and mortality from coronary heart disease, so it is another beneficial side of IF. Fasting plasma glucose decreased on fasting intervention, slightly higher during wet fasting. This could be attributed to the interruption of food intake during fasting.

The blood parameters did not change significantly; this may be due to the body's hormonal contra-regulation or homeostasis. However, this is a positive finding that the body did not suffer negatively due to wet or dry fasting combined with a considerable dietary restriction. The risk factors were mostly improved, even in a noticeably short period. Dry fasting posed more significant beneficial effects than wet fasting, though not enough to be substantial.

The overall compliance level was almost similar for two: 93.81% in wet and 92.30% in dry fasting. The percentage is very satisfactory compared to that of other similar studies, mainly because the intervention did not occur in a controlled environment. This may have happened because the calorie and

time restrictions on fasting days were much less than other studies; also, because the subjects knowing that they were enrolled in a trial, ate less than usual.

This study had some limitations. First, the sample size was short, and all of the subjects were overweight women who were free of metabolic diseases, and so the outcomes of the study may not be extrapolated to the whole population. Second, in such a short period, the blood parameters are unlikely to change expectedly. Despite these limitations, this study had some strengths: the study's cross-over design helped nullify the effect of individual differences, and the 1:1 randomization of the subjects minimized the carry-over effect. Additionally, the anthropometric, clinical, biochemical, and dietary data combined with subject feedback altogether enabled us to perceive the effectiveness of IF better.

In summary, the findings of this study indicate that IF, especially the dry one, could be an effective diet strategy to assist overweight individuals in losing weight and modulating blood pressure, which may confer protection against cardiovascular diseases in the long term. However, biochemical parameters did not change significantly in the short study period. While this study's preliminary results are promising, they still require confirmation by more extended-length clinical trials in the future.

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