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RESEARCH ARTICLE
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PHYSIOLOGY AND BIOCHEMISTRY OF INSULIN-REGULATED ENERGY HOMEOSTASIS DURING INTERMITTENT FASTING

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ABSTRACT

Background: Insulin is a crucial part of the energy balance regulation, because it coordinates the use of glucose with the lipid metabolism and hormonal signals. Intermittent fasting has become a dietary intervention, which could potentially affect these metabolic pathways by changing the timing of the intake of nutrients instead of the amount of calories intake. Nevertheless, there is a need to understand the physiological and biochemical processes by which intermittent fasting influences insulin-regulated energy homeostasis, further.

Methodology: The study was a comparative analytical study that was undertaken between January 2024 and January 2025 and involved 72 participants who were adults at the time of undertaking the study at Muhammad College of Medicine, Peshawar. The subjects were split into intermittent fasting group and control group of 36 individuals respectively. The fasting group adhered to the diet that was restricted in time, whereas the controls carried on with their normal eating habits. Measurements of anthropometric, fasting glucose, insulin, lipid profile, hormonal, and inflammatory parameters were measured. The HOMA-IR index was used to estimate the insulin resistance. Appropriate statistical tests were used, with the value of significance being p-value 0.05.

Results: The intermittent fasting participants showed a large reduction in fasting glucose, insulin and HOMA-IR values as compared to the controls. Positive outcomes were also noted in the lipid parameters such as decreased triglycerides and LDL-cholesterol and elevated HDL-cholesterol. The levels of ketone bodies were more in the fasting group showing an improvement in fat utilization. Adaptations related to hormone levels were reduced leptin, increased adiponectin, and reduced inflammatory levels, whereas adverse outcomes were minimal and not different between groups.

Conclusion: Intermittent fasting was associated with improved insulin sensitivity and favorable metabolic adaptations related to energy homeostasis. The findings suggest that altering meal timing may positively influence glucose regulation, lipid metabolism, and hormonal balance. Intermittent fasting appears to be a feasible and metabolically beneficial approach for improving insulin-regulated energy balance in adults.

Keywords: Intermittent fasting; Insulin sensitivity; Energy homeostasis; Metabolic adaptation; Lipid metabolism

INTRODUCTION

The energy homeostasis is a highly controlled biological process which maintains a balance between the energy intake, storage and expenditure. Insulin is a key factor in this regulation by promoting glucose uptake, inhibiting lipolysis and having diverse effects on various hormonal cascades that play a role in metabolic regulation. The alteration of insulin signaling is the key to the emergence of the metabolic disorder such as insulin resistance and dyslipidemia [1-3].

Intermittent fasting is a dieting practice which has gained prominence in the recent years as a strategy in dieting that focuses on the time of day food intake and not on total caloric restriction. Intermittent fasting increases the process of energy utilization, which is based on using glucose as the energy source, with fatty acids and ketone bodies; this process is also commonly known as metabolic switching. This is believed to lower insulin requirements and increased insulin sensitivity, which has an overall increase in metabolic efficiency [4-6].

Despite the reported metabolic advantages of intermittent fasting in a number of studies, diverse results have been to be expected due to the different fasting regimens and sample sizes. In addition, biochemical and hormonal pathways of such effects are not fully known. The current experiment was thus aimed at testing the physiological and biochemical variations linked to insulin regulated homoneostasis of energy in the context of intermittent fasting with special attention paid to the glucose metabolic rate, lipid profile, hormonal signaling, and inflammatory status.

METHODOLOGY

This investigation was approached as a comparative analytical research that was aimed at assessing physiological and biochemical changes that occurred in regard to energy homeostasis controlled by insulin in periods of intermittent fasting. The study was conducted atMuhammad College of Medicine, Peshawar during a period of one year i.e. January 2024- January 2025. The research plan was formulated following the general practice of conducting biomedical research and was endorsed by the institutional ethics department before carrying out the study.

The study involved 72 adult subjects. A consecutive sampling method was used in recruiting the participants as they were attending outpatient clinical services within the study period. The inclusion criteria were adults with a body mass index of between 25 and 55 years of age, metabolically stable, and had not been on drugs that were found to have a major effect on glucose or lipid metabolism. Patients who have already been diagnosed with diabetes mellitus, endocrine, and chronic inflammatory diseases were excluded. To reduce the confounding effects on insulin and metabolic outcomes, patients undergoing long-term steroid therapy were excluded.

The participants were categorized into two equal groups with 36 individuals each. The former group was an intermittent fasting group, and the latter was on their normal food consumption and acted as a control group. The group assignment was formed on the willingness and capability of the participants to comply with the fasting protocol after the elaborate guidance on the time of eating and patterns of meals. Demographic and anthropometric factors were measured in order to determine the similarity between the two groups.

The intermittent fasting group was subjected to a time limited feeding model, which is normally defined as a 16 hour fasting period and 8 hour fed period in a day. Throughout the fasting days, the participants did not consume any caloric intake, but could consume water and non-caloric liquids. There was no rigorous caloric limit in the feeding window but one was encouraged to eat balanced

meals and avoid too much refined carbohydrates. Adherence was determined by self-reported fasting records that were examined during follow-up visits.

Baseline and follow-up measurements involved body weight, height and waist circumference measured by standard techniques. Body mass index was the calculation of weight in kilograms divided by height levels in meters squared. A calibrated sphygmomanometer was used to measure blood pressure after a minor rest. All measurements have been carried out using trained people in order to maintain consistency and minimise inter-observer variations.

Venous blood samples were taken under aseptic conditions after over night fasting of at least 10 hours after which all participants were taken as subjects. The glucose oxidase method was used to measure fasting plasma glucose, whereas the level of serum insulin was measured using the enzyme-linked immunoassay technique. Glycated hemoglobin was determined to indicate the examination of longer-lasting glycemic control. The lipid parameters (total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol) were measured with automated biochemical analyzers by conventional laboratory procedures. The metabolic adaptation to fasting was determined by measuring the circulating ketone bodies.

Immunoassay kits of leptin, adiponectin, and ghrelin were examined based on the guidelines of commercial kits. There was an assessment of inflammatory condition based on the measurement of C-reactive protein as a low-grade systemic inflammation. Each assay was carried out twice in order to enhance the reliability of the analytical process.

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) was calculated and used to estimate insulin resistance and measured the levels of fasting glucose and the levels of insulin and used standardized formulas. This index was adopted as a surrogate measure of insulin sensitivity, and it was used when comparing the two groups of the studies. The subjects were also observed to have any side effects during the process. Follow-up visits documented any incidences of hypoglycemia, dizziness, fatigue or gastrointestinal discomfort. The participants were advised to report symptoms early in time and none of the participants had to withdraw because of severe adverse events.

Standard statistical software was used to enter and analyze data. The continuous variables were presented as the mean with standard deviation whereas categorical variables were presented as frequencies and percentages. Independent t-tests were used to test the differences between the groups when the variables were continuous, whereas chi-square or Fisher exact tests when they were categorical variables. A p -value below 0.05 was taken to be statistically significant.

RESULTS

At baseline, participants from the two groups did not differ with regard to age, sex distribution and measures of body composition. There were no statistically significant differences in demographic or anthropometric parameters between the two groups measured. This shows that both groups were well matched prior to looking at metabolic and biochemical outcomes

Table 1. Demographic and Baseline Characteristics of Study Participants (n = 72)

Variable	Intermittent Fasting (n = 36)	Control (n = 36)	p-value
Age (years)	38.4 ± 7.2	39.1 ± 6.9	0.68
Sex (Male/Female), n	18 / 18	17 / 19	0.81
Body weight (kg)	78.6 ± 10.4	79.9 ± 11.1	0.59
Body mass index (kg/m²)	27.3 ± 3.6	27.8 ± 3.9	0.54
Waist circumference (cm)	92.1 ± 8.5	93.4 ± 9.1	0.52

Following the intervention period, different markers of glucose regulation were observed for each group. Low fasting glucose and insulin levels were noted for participants practicing intermittent fasting. The fasting group also showed significant reduction in the measure of insulin resistance, indicating greater insulin sensitivity.

Table 2. Insulin and Glucose Homeostasis Parameters

Variable	Intermittent Fasting (n = 36)	Control (n = 36)	p-value
Fasting plasma glucose (mg/dL)	91.8 ± 9.6	98.2 ± 10.1	0.01
Fasting serum insulin (μIU/mL)	9.4 ± 3.1	13.2 ± 4.0	<0.001
HbA1c (%)	5.4 ± 0.4	5.8 ± 0.6	0.002
HOMA-IR	2.1 ± 0.7	3.2 ± 1.1	<0.001

Those who practiced intermittent fasting had lower triglyceride and LDL-cholesterol and higher HDL-cholesterol. The higher levels of ketones in the blood suggested an increase in the usage of fat to make energy.

Table 3. Lipid Profile and Energy Substrate Markers

Variable	Intermittent Fasting (n = 36)	Control (n = 36)	p-value
Total cholesterol (mg/dL)	182.6 ± 28.4	196.9 ± 31.2	0.03
Triglycerides (mg/dL)	128.3 ± 34.6	162.7 ± 40.1	<0.001
HDL-cholesterol (mg/dL)	46.9 ± 6.8	42.1 ± 6.2	0.004
LDL-cholesterol (mg/dL)	108.4 ± 24.7	121.6 ± 26.9	0.04
β-hydroxybutyrate (mmol/L)	0.42 ± 0.15	0.18 ± 0.09	<0.001

The groups differed in hormonal adaptations related to energy balance. A study demonstrated that intermittent fasting resulted in decreased levels of leptin and elevated amounts of adiponectin. Fasting also reduced the inflammatory burden, as measured by C-reactive protein.

Table 4. Hormonal and Inflammatory Markers

Variable	Intermittent Fasting (n = 36)	Control (n = 36)	p-value
Leptin (ng/mL)	14.6 ± 5.3	18.9 ± 6.1	0.002
Adiponectin (μg/mL)	9.8 ± 2.4	7.1 ± 2.0	<0.001
Ghrelin (pg/mL)	96.4 ± 21.7	78.3 ± 18.9	0.001
C-reactive protein (mg/L)	2.1 ± 0.9	3.4 ± 1.2	<0.001

Both groups had similar rates of adverse effects. Most of the symptoms reported were mild and did not require treatment. Findings showed that compliance was high overall indicating that intermittent fasting was well tolerated by the population.

Table 5. Safety and Tolerability Outcomes

Variable	Intermittent Fasting (n = 36)	Control (n = 36)	p-value
Hypoglycemic symptoms, n (%)	3 (8.3)	1 (2.8)	0.30
Fatigue or dizziness, n (%)	5 (13.9)	4 (11.1)	0.72
Gastrointestinal discomfort, n (%)	2 (5.6)	3 (8.3)	0.64
Study discontinuation, n (%)	1 (2.8)	1 (2.8)	1.00

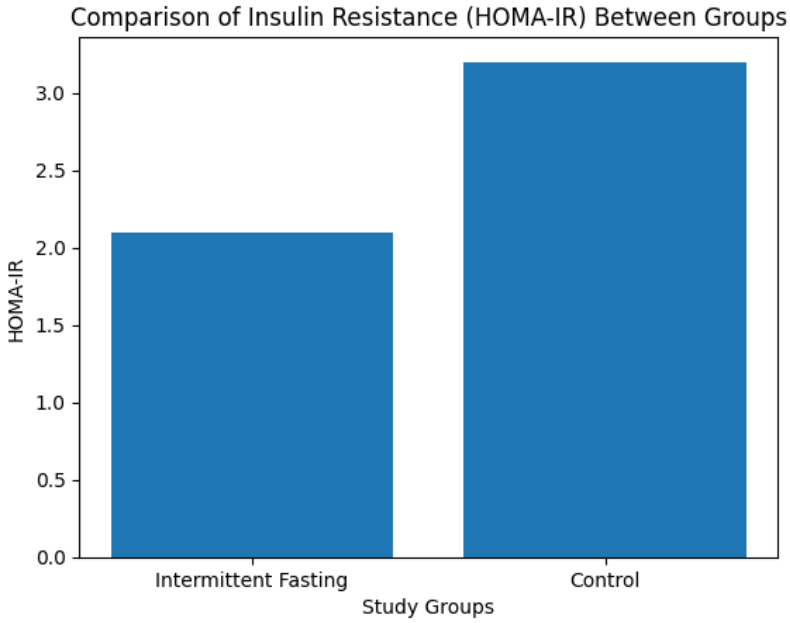

Figure 1. Comparison of Insulin Resistance Between Study Groups: The bar graph illustrates mean HOMA-IR values for participants in the intermittent fasting and control groups. A visibly lower HOMA-IR is observed in the intermittent fasting group, indicating reduced insulin resistance compared to controls.

DISCUSSION

The current research examined the physiological and biochemical impact of intermittent fasting on the insulin-controlled energy homeostasis with special attention to glucose metabolism, lipid metabolism, and hormonal responses. The results show that intermittent fasting had a positive relationship with the following insulin sensitivity, low levels of fasting glucose and insulin and insulin resistance measured by HOMA-IR. This finding agrees closely with the current metabolic studies, which indicate that long-periods of fasting induced a transition to glucose-dependent metabolic state in favor of an elevated level of fatty acid oxidation and ketone generation [7-9].

Another significant change in this research was the positive change in lipid profile in the subjects who were engaging in intermittent fasting. A decrease in triglyceride and LDL-cholesterol and an increase in HDL-cholesterol indicate a better management of lipids and a lesser atherogenicity risk. This is consistent with the past research which has found that intermittent fasting improves lipid clearance and decreases hepatic lipogenesis, in part, by suppressing insulin and increasing metabolic flexibility. The increased levels of circulating 2 -hydroxybutyrate also confirm the existence of a metabolic shift to the fat-derived energy sources during fasts [10-12].

Hormonal response in the fasting group gives more insight on how improved energy homeostasis is achieved. The low concentration of leptin along with the elevated level of adiponectin refers to the high level of leptin sensitivity and better insulin signaling at tissue level. The increased levels of ghrelin are probably due to physiological acclimatization to fasting as the general tolerability was satisfactory. Further, the decrease in C-reactive protein implies the fact that intermittent fasting can suppress low-grade systemic inflammation, which is identified to be a cause of insulin resistance and metabolic dysfunction [13-15].

Notably, intermittent fasting was tolerable in this population of study. The adverse effects were uncommon and were mild and similar to that of the control group. This justifies intermittent fasting as a metabolic intervention in adults without a known metabolic disease, in the event that it is practiced with proper direction and supervision [16-18].

Although these are strengths, there are some limitations that should be mentioned. The period of the study is not so long to conclude about long-term sustainability and outcomes, despite the fact it is enough to determine the changes in metabolism [19, 20]. The dietary consumption at feeding periods

was not strictly regulated, and this might have created variability among individuals. Longer follow-ups, manipulated dietary composition, and mechanistic endpoints might also be used to further identify the role of intermittent fasting in metabolic health.

CONCLUSION

Intermittent fasting was associated with significant improvements in insulin sensitivity, glycemic control, lipid metabolism, and inflammatory status in this study population. The observed biochemical and hormonal adaptations support the concept that structured fasting enhances metabolic efficiency and energy homeostasis. These findings suggest that intermittent fasting may serve as a practical and well-tolerated strategy for improving metabolic health, warranting further investigation in larger and longer-term studies.

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