

# Is Water-Only Fasting Safe?

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## Abstract

**Background:** Water-only fasting (WF) is a practice used to improve and maintain health.

**Objective:** The aim of the study was to show whether WF performed for 8 days may be a threat to the health and/or life of people undergoing this practice.

**Methods:** Twelve middle-aged men participated in the study. During the 8-day WF, the subjects ate no food except for drinking mineral water. Before and after WF, all subjects had a series of tests performed, beginning with the level of perceived stress and somatic measurements. The concentrations of creatinine, sodium (Na<sup>+</sup>), potassium (K<sup>+</sup>), total calcium (Ca), magnesium (Mg<sup>++</sup>), urea (U), uric acid (UA) and total protein were determined in this urine and in the serum. For these substances, the values of clearance, renal filtration and fractional excretion were calculated. The osmotic clearance and free water clearance as well as the amount of daily urinary excretion of creatinine, Na<sup>+</sup>, K<sup>+</sup>, Ca, Mg<sup>++</sup>, U and UA were also calculated. Moreover, the concentration of glucose in the serum and the concentration of β-hydroxybutyrate in the plasma were determined. In urine, specific gravity, pH and osmolality were also measured.

**Results:** After 8 days of WF, the study showed a significant reduction in the level of perceived stress, weight loss, changes in body composition, dehydration, increased ketogenesis, hyperuricemia, decreased serum glucose concentration, and hyponatremia. These changes were accompanied by Na<sup>+</sup>, K<sup>+</sup> and protein sparing, decreased serum Ca and Mg<sup>++</sup> concentrations, and reduced daily volume of more acidic urine with elevated specific gravity.

**Conclusions:** After 8 days of WF, all subjects were found to remain safe and feel the sense of well-being. However, the appearance of the above-mentioned adverse metabolic effects, despite partially effective renal compensations, suggests that the further continuation of fasting intervention by the subjects would be detrimental to their body.

## Keywords

men, water-only fasting, kidney function, stress

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## Introduction

Water-only fasting (WF) is an absolute cessation of food consumption while consuming water *at libitum*. This type of fasting is believed to improve health and can help motivate a healthy diet and lifestyle changes.<sup>1,2</sup> It has been found that this type of intervention stimulates physiological effects that are potentially favorable to health. They include enhanced ketogenesis, modulated hormone activity, reduced inflammation and oxidative stress symptoms, lipolysis, autophagy, and improved physical and emotional well-being.<sup>3,4</sup> When taking into account the above data, it can be concluded that even prolonged fasting may not deteriorate health condition, and even have therapeutic values. The WF intervention is defined as a “zero calorie diet”.<sup>5–7</sup>

When using WF, it is crucial to remember to maintain the safety of people participating in such experiments. They should be monitored for possible adverse effects caused by WF, such as: increased uric acid and

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creatinine blood concentrations, decreased glomerular filtration, or other serious health complications.<sup>8,9</sup> Ketosis, which develops from the first days of fasting, is its metabolic consequence. In the early days of starvation, which is considered a mild and stable state, ketone bodies are an alternative source of energy substrates for the nervous system and other body cells, the metabolism of which depends on glucose.

The concentration of ketone bodies, such as  $\beta$ -hydroxybutyrate ( $\beta$ -HB), increases after just a few days of fasting. They show neuroprotective effects by increased mitochondrial respiration ensuring the production of adenosine triphosphate (ATP).<sup>10–12</sup> Moreover, ketone bodies can promote the excitability of neuronal membranes, the occurrence of autophagy, while reducing inflammation and inhibiting the production of free radicals.<sup>13</sup> Conversely, acidosis stimulates the unfavorable process of calcium release from bones.<sup>14</sup> In addition, ketones that persist in the body for an extended period of time can prevent or reverse abnormalities in heart energy metabolism that occur during fasting.<sup>15</sup> The disadvantageous effect of short-term total fasting is the deterioration of bone formation markers. However, the most noticeable change that occurs during fasting or caloric restriction is weight loss, this reduction applies to both fat-free mass and body fat.<sup>16,17</sup>

When undertaking WF, it is recommended that an individual drink 2–3 liters of fluid daily, especially in the form of mineralized water. This partially covers the body's needs to keep the balance of particular minerals.<sup>18,19</sup> It should be emphasized that the minerals contained in these waters are well absorbed, often much better than those from food, which is an important attribute in times of fasting. On the other hand, the low water consumption accompanying WF, in the absence of nutrients supplied with food, can lead to a significant loss of sodium and potassium from the body and the occurrence of hypovolemia, which threatens the safety of people using this type of intervention.<sup>20</sup> Therefore, in order to assess the clinical status and safety of WF individuals, the levels of natremia, kaliemia and volemia should be monitored.<sup>5</sup>

### Study Objective

The presented study was aimed at determining whether the 8-day WF undertaken by a group of men was a safe practice for their body. This thesis was verified by examining somatic changes, water-mineral and protein balance, kidney function and the intensity of perceived stress before and after the 8-day WF.

## Material and Methods

### Subjects

Twelve healthy male volunteers aged  $50.25 \pm 14.18$  years were enrolled in the study. The subjects were non-smokers with no history of chronic diseases. The study was carried out at the Department of Health Sciences at the Jan Długosz University in Czestochowa and registered at the Urology and Andrology Clinic “Urogen” in Tarnowskie Góry (Poland). Before starting the study, each subject had medical examinations with the determined blood levels of sodium, potassium, calcium, magnesium, creatinine, urea, uric acid,  $\beta$ -hydroxybutyrate, glucose and a basic urine test. Those who had no contraindications to undergo 8-day WF were admitted to further research.

All subjects were white collar workers and had already practiced WF before. The number of previously conducted WF by individual subjects ranged from 3 to a dozen or so. However, none of the subjects had undertaken such interventions over the period of 6 months before the study. The study was approved by the Ethical Committee of the Scientific Research of Jan Długosz University in Czestochowa - Poland, in accordance with the requirements of the Helsinki Declaration.

All participants were enrolled in the study after receiving a verbal explanation of the research procedures and providing both oral and written informed consent.

The inclusion criteria were: (1) previous experience in undertaking WF of more than three days; (2) age range of 30–70; (3) body weight between 60–95 kg; (4) body mass index – BMI 20–29.9 kg/m<sup>2</sup>; (5) no chronic diseases; (6) systolic blood pressure in the range of 100–140 mmHg and diastolic blood pressure in the range of 60–90 mmHg. The Exclusion criteria were: (1) the presence of chronic diseases; (2) smoking cigarettes; (3) the use of medications, strong stimulants or psychoactive substances; (4) failure to complete the research procedure.

### Procedure

Prior to the study, the participants were on a mixed diet, during which the research procedures described below were performed. After completing this stage of the study, the subjects began a fasting procedure, during which they did not eat any food, but only drank of the same, moderately mineralized water *ad libitum*. The fasting procedure was completed after the tests were repeated on the 8th day of its duration. During the fasting intervention, male respondents were in constant contact with a qualified health professional who also instructed them about the eating strategy 7 days immediately after the end of fasting.

All study participants were informed about the conditions they had to fulfill prior to the research procedure (no alcohol consumption or high-intensity exercise for 48 hours prior to measurements; no food or beverages intake for 12 hours prior to measurements). All tests were performed in the morning. On the first and eighth day of WF, all subjects had the following tests performed: The Perceived Stress Scale-10 (PSS-10) psychological test, somatic measurements, biochemical blood and urine analysis.

### Psychological Test

In order to assess the intensity of perceived stress, the Perceived Stress Scale-10 (PSS-10)<sup>21</sup> was used, which contains 10 questions about different subjective feelings related to personal problems and events, behaviors, and ways of coping with various situations. All respondents provided their answers by selecting the correct number (0 - never, 1 - almost never, 2 - sometimes, 3 - quite often, 4 - very often). The overall score on the scale is the sum of all points, the theoretical distribution of which ranges from 0 to 40. The higher the score, the greater the intensity of perceived stress. The general test score was expressed in standard units called sten.

The results between 1-4 sten scores are regarded as a low stress level, between 7-10 sten scores as a high stress level, and between 5 - 6 sten scores as an average stress level.

### Bioelectrical Impedance Analysis (BIA)

At the beginning of the somatic measurements, age was recorded, and Body Height (BH) was determined using the A-226 anthropometer (Tristom, Olomouc, Czech Republic).

Body Weight (BW) and body composition (Body Fat - BF, Fat Free Mass - FFM, total body water - TBW, Body Mass Index - BMI) were measured by means of the bioelectrical impedance analysis using a commercially available body composition analyzer (Type BF-300, TANITA Corporation, Tokyo, Japan) based on the manufacturer's instructions. The subjects were asked to wipe out the soles of their feet with a wet tissue and stand on the electrodes of the analyzer to record all data. The Body Surface Area (BSA) was calculated using the Du Bois and Du Bois equation.<sup>22</sup>

### Urine and Blood Tests

Before the first and after the eighth day of WF, blood was drawn from the cubital vein under laboratory conditions and urine samples were collected to determine specific gravity and pH. The concentration of sodium ( $\text{Na}^+$ ), potassium ( $\text{K}^+$ ), total calcium (Ca), magnesium ( $\text{Mg}^{++}$ ), protein, urea (U), uric acid (UA), protein and

creatinine (Cr) was determined in the serum and urine samples collected during the 24-hour collection.

Additionally, the osmolality of plasma and urine, the plasma concentration of  $\beta$ -hydroxybutyrate ( $\beta$ -HB), serum concentration of glucose (G), pH and urine specific gravity were measured.

### Methods

Based on the data obtained from the blood and urine tests, the following indicators were calculated:

- clearance of sodium ( $C_{\text{Na}^+}$ ), potassium ( $C_{\text{K}^+}$ ), total calcium ( $C_{\text{Ca}}$ ), magnesium ( $C_{\text{Mg}^{++}}$ ), endogenous creatinine ( $C_{\text{Cr}}$ ), urea ( $C_{\text{U}}$ ), and uric acid ( $C_{\text{UA}}$ );
- filtration of sodium ( $F_{\text{Na}^+}$ ), potassium ( $F_{\text{K}^+}$ ), total calcium ( $F_{\text{Ca}}$ ), magnesium ( $F_{\text{Mg}^{++}}$ ), urea ( $F_{\text{U}}$ ), and uric acid ( $F_{\text{UA}}$ );
- fractional excretion of filtered sodium ( $\text{FE}_{\text{Na}^+}$ ), potassium ( $\text{FE}_{\text{K}^+}$ ), total calcium ( $\text{FE}_{\text{Ca}}$ ), magnesium ( $\text{FE}_{\text{Mg}^{++}}$ ), urea ( $\text{FE}_{\text{U}}$ ), and uric acid ( $\text{FE}_{\text{UA}}$ );
- osmolar clearance,
- free water clearance.

The osmolality of plasma and urine was determined using the Osmometer Os3000 by Marcel sp. z o. o. (Poland). The concentration of sodium and potassium in both serum and urine were measured by direct potentiometry - with an ion-selective electrode (ISE) by the ABBOTT's ARCHITECT c SYSTEM 4000 analyzer. The plasma concentration of  $\beta$ -HB was determined enzymatically using the RANBUT diagnostic kit by RANDOX (UK). The concentration of urea, uric acid, total calcium and magnesium in both serum and urine was determined by enzymatic methods using the ABBOTT's ARCHITECT c SYSTEM 4000 analyzer. The serum concentration of total protein was measured by means of the biuret method using the ARCHITECT/AEROSSET 4000 device by ABBOTT, while protein concentration levels in urine were determined by the turbidimetric method using the ABBOTT's ARCHITECT c SYSTEM 4000 device. Creatinine concentration levels in both serum and urine were checked by means of the kinetic method with the use of the ABBOTT's ARCHITECT c SYSTEM 4000 analyzer. Urine specific gravity and pH were determined with the BIOMAXIMA BM URI apparatus.

### Statistical Analyses

Both arithmetic means ( $\bar{x}$ ) and standard deviations ( $\pm$  SD) were calculated for studied variables. At the beginning, the Shapiro-Wilk test was utilized to examine the normality of the distribution of individual variables. The Student's t-test or the Wilcoxon test was applied. Values

**Table 1.** Age and Somatic Variables for Studied Men (n=12) Before and After 8 Days of Water-Only Fasting.

Variable	Before		Significance (p)
	Mean ±SD	Mean ±SD	
Age	50.25±14.18	50.25±14.18	NS
BW [kg]	79.38±10.79	73.42±10.26	p<0.001
BH [cm]	178.67±4.54	178.67±4.54	NS
BF [%]	18.68±5.04	17.37±5.72	p<0.001
BF [kg]	15.27±5.42	13.21±5.33	p<0.001
FFM [%]	81.31±5.06	82.38±5.63	p<0.01
FFM [kg]	64.11±5.87	60.07±5.88	p<0.001
TBW [%]	59.54±3.71	60.50±4.21	p<0.001
TBW [kg]	46.94±4.29	44.08±4.11	p<0.001
BMI [kg/m <sup>2</sup> ]	24.89±3.52	23.02±3.35	p<0.001
BSA [m <sup>2</sup> ]	1.98±0.12	1.90±0.13	p<0.001

BW-body weight; BH-body height; BF-body fat; FFM-fat free mass; TBW-total body water; BMI-body mass index; BSA-body surface area.

at  $p < 0.05$  were considered statistically significant. The obtained values were subjected to statistical analysis using the SPSS Statistics 20.

## Results

The mean value of perceived stress measured with the PSS-10 was found to be higher on the first day of WF than after the 8<sup>th</sup> day of the intervention in question. The average result obtained in the PSS-10 for the entire group was  $23.83 \pm 4.73$ , which is classified on the borderline of 7<sup>th</sup> and 8<sup>th</sup> sten score as high values. However, after 8 days of WF, the average score obtained in the PSS-10 for this group was  $12.76 \pm 3.45$ , which is classified on the borderline of 4<sup>th</sup> and 5<sup>th</sup> sten score as low and average values.

Table 1 presents the age of studied men and their somatic data. The results indicate a significant influence of WF especially on: Body Weight (BW); Body Height (BH); Body Fat (BF); Fat Free Mass (FFM); Total Body Water (TBW); Body Mass Index (BMI) and Body Surface Area (BSA).

The volume of urine before fasting amounted to 2353.75 [ml/24h] and 1.63 [ml/min], and it was reported to have significantly decreased after 8 days of WF to 1378.33 [ml/24h] and 0.96 [ml/min].

Urine specific gravity and pH were found to have changed significantly, while urine osmolality did not change after the 8-day WF intervention (Table 2).

It was shown that the 8-day WF caused a considerable and statistically significant increase in the plasma concentration of  $\beta$ -HB and a smaller but also statistically significant increase in the serum concentration of  $K^+$  and UA, and a significant decrease in the concentration of G,  $Na^+$ , Ca, and  $Mg^{++}$ .

Also, plasma osmolality was reported to be significantly decreased after 8 days of WF, and the concentration of serum protein, Cr and U did not change significantly during this time when compared to the values prior to the discussed intervention (Table 3).

After 8 days of WF, decreased levels of  $Na^+$  and  $K^+$  in urine and lower daily excretion of  $Na^+$ ,  $K^+$ , U and UA were observed compared to the values obtained before the intervention (Table 4).

Table 5 shows changes in the renal function indices, which show that the clearance of  $Na^+$  and  $K^+$  as well as U ( $p < 0.001$ ) and UA ( $p < 0.01$ ) decreased significantly after 8 days of WF, while UA filtration was found to be significantly increased ( $p < 0.001$ ).

A significant reduction in the fractional excretion of  $Na^+$ ,  $K^+$ , U and UA after 8 days of WF was also reported versus the values of these variables observed before the intervention.

## Discussion

The stress burden is considered to be the risk of developing civilization diseases, and thus pro-health activities can be used, such as fasting.<sup>23</sup> After performing the PSS-10, it was found that 8-day WF reduced the level of perceived stress from  $23.83 \pm 4.73$  (classified as high stress level) to  $12.76 \pm 3.45$  (classified on the border of moderate and low stress level). The 8-day WF can be considered an acute form of stress for the body that increases immunity, while chronic stress impairs the body's ability to produce a strong immune response.<sup>24</sup> Among the many other effects of fasting on the body, one should mention its therapeutic impact on neurological diseases or the activation of autophagy.<sup>25</sup> The effects of fasting are modified by various factors and it has been shown that in the group of amateur athletes, it improved mental flexibility, increased anger and intensified cognitive functions.<sup>26</sup> In turn, in the group of obese elderly women, fasting was found to cause fatigue and prolonged reaction time in the two-choice reaction time test, decrease mental flexibility and activate the hypothalamic-pituitary-adrenal axis.<sup>27</sup> In addition, fasting reduced negative affect and led to the withdrawal of symptoms in drug users.<sup>28</sup>

In addition to modifying changes in the nervous system that occur during fasting, there is also a reduction in glucose consumption and an increased metabolism of ketone bodies. With regard to our subjects, after 8 days of WF, a significant increase in the plasma concentration of  $\beta$ -HB was found, which largely supplies energy to the brain during fasting.<sup>17,29</sup> It is an efficient energy system due to the fact that  $\beta$ -HB possesses an intrinsic high heat of combustion. In addition, this compound reduces the production of reactive oxygen species and inflammation.<sup>30,31</sup>  $\beta$ -HB also plays a crucial role in

**Table 2.** General Characteristics of Urine for Studied Men (n=12) Before and After 8 Days of Water-Only Fasting.

Variable	Before	After	Reference Range
Volume [ml/24h]	2353.75±788.14	1378.33±751.36###	~1500
Volume [ml/min]	1.63±0.55	0.96±0.52###	~1,04
Specyfic weight [g/ml]	1.01±0.004	1.02±0.004###	1,015–1,030
pH	6.04±0.84	5.29±0.40#	4,8–8,0
Osmolality [mmol/kg/H <sub>2</sub> O]	398.67±201.31	532.17±301.13	100–1200

**Table 3.** Blood Content of Metabolites and Ions Together With Plasma Osmolality for Studied Men (N=12) Before and After 8 Days of Water-Only Fasting.

Variables	Before	After	Reference Range
Glucose – serum [mmol/L]	4.84±0.35	3.66±0.27####	5.0–5.5
Creatinine – serum [mmol/L]	0.08±0.008	0.08±0.01	0.06–0.13
Na <sup>+</sup> – serum [mmol/L]	139.25±2.34	133.83±2.37####	136–146
K <sup>+</sup> – serum [mmol/L]	3.89±0.26	4.18±0.44#	3.5–5.1
Ca – serum [mmol/L]	2.39±0.10	2.28±0.09#	2.1–2.6
Mg <sup>++</sup> – serum [mmol/L]	0.85±0.07	0.80±0.10#	0.66–1.03
Urea – serum [mmol/L]	4.81±0.86	5.41±1.59	3.0–9.2
Uric acid – serum [mmol/L]	0.38±0.05	0.85±0.10####	0.18–0.42
Osmolity-plasma [mmol/kgH <sub>2</sub> O]	286.92±5.09	278.08±4.74###	285–295
Protein – serum [g/l]	74.31±4.32	74.93±4.50	60–80
β-HB – plasma [mmol/L]	0.30±0.21	4.77±0.70####	0.03–0.3

β -HB- β-hydroxybutyrate; Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>++</sup>, and Ca – sodium, potassium, magnesium and total calcium.

**Table 4.** Content of Metabolites and Ions in Urine for Studied Men (N=12) Before and After 8 Days of Water-Only Fasting

Variables	Before	After	Reference Range
Creatinine [mmol/L]	6.68±3.00	11.01±6.49	10.0–18.0
Creatinine [mmol/24h]	15.71±4.53	15.18±4.49	~7.07–14.14
Urea [mmol/L]	207.07±69.08	235.81±71.91*	249–566
Urea [mmol/24h]	485.38±160.96	322.76±133.31#	333–582.75
Uric acid [mmol/L]	1.30±0.52	1.22±0.98	< 4.8
Uric acid [mmol/24h]	3.06±0.81	1.69±0.82*####	1.49–4.50
Protein [mg/dL]	9.07±2.41	10.44±3.07*	10–30
Protein [g/24h]	0.15±0.10	0.11±0.05*	<0.15
Na <sup>+</sup> [mmol/L]	80.06±45.03	30.94±13.03####	–
Na <sup>+</sup> [mmol/24h]	189.69±157.11	42.54±21.64####	80–240
K <sup>+</sup> [mmol/L]	47.04±25.23	25.87±16.51*#	20–40
K <sup>+</sup> [mmol/24h]	110.86±44.97	34.44±18.43####	25–100
Ca [mmol/L]	3.03±1.59	4.95±3.16*	2.5–5.0
Ca [mmol/24h]	7.06±3.14	6.72±3.21	1.25–7.7
Mg <sup>++</sup> [mmol/L]	2.43±1.08	3.06±1.73	–
Mg <sup>++</sup> [mmol/24h]	5.64±2.88	4.31±2.91	0.99–10.04

Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>++</sup>, and Ca – sodium, potassium, magnesium and total calcium.

cell signaling that may have important implications for the pathogenesis and treatment of metabolic diseases.<sup>10,11</sup> Based on the results of the presented research and the results of studies by other authors cited above, it is impossible to explain the mechanism of reducing the perceived stress by the 8-day WF. However, this is a positive adaptive change that helps to consciously continue fasting for many days.

The use of WF for 8 days also affected the dehydration of studied men, which translated into water sparing (reduced water content in the body as well as reduced urine volume) and has been described by other authors.<sup>32,33</sup> The occurring dehydration was also manifested as a significant reduction of plasma osmolality. However, it should be acknowledged that this dehydration takes a mild form, as urine osmolality, osmotic

**Table 5.** Kidney Function Indices for Studied Men (N=12) Before and After 8 Days of Water-Only Fasting.

Variables	Before	After	Reference Range
C Creatinine [ml/min/1.73m <sup>2</sup> ]	119.23±32.21	119.91±53.90	80–150
C <sub>Na<sup>+</sup></sub> [ml/min/1.73m <sup>2</sup> ]	0.80±0.48	0.19±0.08####	0.08–0.70
C <sub>K<sup>+</sup></sub> [ml/min/1.73m <sup>2</sup> ]	16.92±6.54	5.33±2.30####	7.70–14.00
C <sub>Ca</sub> [ml/min/1.73m <sup>2</sup> ]	1.83±1.04	1.87±1.07	0.63–1.50
C <sub>Mg<sup>++</sup></sub> [ml/min/1.73m <sup>2</sup> ]	3.99±1.75	3.29±1.78	1.50–3.20
C Urea [ml/min/1.73m <sup>2</sup> ]	60.94±10.74	37.32±10.41##	50.00–90.0
C Uric acid [ml/min/1.73m <sup>2</sup> ]	4.90±1.82	1.27±0.56*###	4.00–9.00
F <sub>Na<sup>+</sup></sub> [mmol/24h/1.73m <sup>2</sup> ]	23911.04±5706.64	23107.09±1002.34	19thous. –27thous
F <sub>K<sup>+</sup></sub> [mmol/24h/1.73m <sup>2</sup> ]	670.14±161.70	720.71±313.36	600–900
F <sub>Ca</sub> [mmol/24h/1.73m <sup>2</sup> ]	412.53±98.95	392.20±135.91	300–450
F <sub>Mg<sup>++</sup></sub> [mmol/24h/1.73m <sup>2</sup> ]	147.07±39.61	136.32±59.09	120–450
F Urea [mmol/24h/1.73m <sup>2</sup> ]	823.46±219.52	936.76±348.56	600–1500
F Uric acid [mmol/24h/1.73m <sup>2</sup> ]	65.87±21.42	146.22±67.23####	45–65
FE <sub>Na<sup>+</sup></sub> [%]	0.66±0.70	0.16±0.13##	0.05–0.60
FE <sub>K<sup>+</sup></sub> [%]	14.37±7.49	4.46±1.04####	6.00–11.00
FE <sub>Ca</sub> [%]	1.53±0.94	1.54±0.73	0.50–1.20
FE <sub>Mg<sup>++</sup></sub> [%]	3.34±1.01	2.75±1.02	1.20–2.60
FE Urea [%]	50.55±18.87	31.58±14.25#	35.00–75.0
FE Uric acid [%]	4.20±1.58	0.99±0.36####	3.80–9.00
Osmolar C [ml/min/1.73 m <sup>2</sup> ]	1.92±0.84	1.59±0.52	1.00–4.00
Free Water C [ml/min/1.73 m <sup>2</sup> ]	–0.28±0.94	–0.63±0.86	–2.5–1.5

C-clearance; F-filtration; FE- fractional excretion; Na<sup>+</sup>, K<sup>+</sup>, Mg<sup>++</sup>, and Ca – sodium, potassium, magnesium and total calcium.

clearance and free water clearance were unchanged after 8 days of WF versus the pre-intervention study.

In terms of ion metabolism in the body among studied men, it was reported that the concentration levels of sodium, total calcium and magnesium in the serum decreased significantly after 8 days of WF. With regard to calcium and magnesium, this adverse effect in the serum was completely compensated by the kidneys, as no differences were noticed in their concentration or daily excretion, nor in the clearance, filtration or fractional excretion in the urine after the 8-day CWF versus the values recorded before the fasting intervention. A different picture of changes was observed in relation to sodium, as its serum concentration decreased below the reference value (hyponatremia) after the fasting intervention. An effective response to this unfavorable change was sodium sparing in the body, as its concentration levels in urine, clearance, daily and fractional urinary excretion were significantly reduced after 8 days of WF, with unchanged filtration. This indicates increased reabsorption of this mineral in nephron tubules. The occurrence of hyponatremia in conditions of fasting has also been described by other authors.<sup>34</sup> Hyponatraemia is defined as serum sodium below 136 mmol/L, which occurred after 8 days of WF.<sup>35</sup> Hyponatraemia is considered a serious clinical complication that can even be fatal and should therefore be properly diagnosed and treated.<sup>36</sup> In our study, hyponatremia, along with hypoglycaemia, were the main factors

in reducing plasma osmolality. Accompanying hyponatremia and sodium sparing, decreased daily and fractional urine excretion of potassium, urea and uric acid, with reduced volume of more acidic urine excreted during the 8-day WF, was an attempt to compensate and maintain the water-mineral balance of the body. On the other hand, it must be pointed out that maintaining the water-mineral balance after 8-days of WF was not possible, although urine osmolality, osmotic clearance and free water clearance did not change statistically when compared to the state before the application of the 8-day WF.

Being aware that changes in the water-mineral balance may have extensive negative effects on the body, it is necessary to increase medical supervision over the safety of fasting men already at this stage of fasting.

Other unfavorable effects of the 8-day WF included elevated serum uric acid concentration levels, which significantly exceeded the upper limit of the reference value.<sup>37</sup> At the same time, no compensatory reaction of the kidneys was observed, as the daily and fractional urinary excretion of this compound, as well as its clearance during the 8-day WF, were significantly reduced, despite its increased filtration versus the values reported before this intervention. Although uric acid acts as a strong antioxidant, which determines the antioxidant potential of plasma in humans in about 60%,<sup>38</sup> when it enters the cellular environment, it activates oxidative

stress.<sup>39,40</sup> This promotes the oxidation of lipids, proteins, DNA and carbohydrates.<sup>41</sup> As a result of the intensification of oxidative stress in hyperuricemia, both nephritis and systemic inflammation may also occur.<sup>42,43</sup> Moreover, it has been shown that hyperuricemia causes significant changes in systemic and renal hemodynamics, resulting in a loss of renal autoregulation.<sup>44</sup> Also, it leads to hypertension, insulin resistance, obesity, hypertriglyceridemia, and metabolic syndrome.<sup>45</sup>

In the light of the above data, it should be concluded that the 8-day WF leading to hyperuricemia is an absolute contraindication for use in patients with renal diseases. On the other hand, no negative acute events that could be associated with hyperuricemia were observed in healthy men participating in this study. However, it does not mean that such effects may become apparent at a later time. Therefore, it would be justified to undertake further research in this direction.

Although the 8-day WF resulted in a significant reduction in body weight and the absolute values of BF, FFM, TBW, BMI and BSA ( $p < 0.001$ ), no significant, adverse changes in the serum or in urine concentration of creatinine, protein or urea were observed. In addition, it was noticed that the daily urea excretion was significantly reduced after this intervention. It should also be noted that although the urea filtration did not change, its clearance and fractional excretion decreased significantly. These data indicate an increased reabsorption of urea in the renal tubules, which together led to the beneficial phenomenon of sparing the body's protein reserves. Therefore, it can be concluded that the protein balance after the 8-day WF was still maintained. In this respect, it should be recognized that the 8-day WF was not yet a dangerous intervention for the body, because in such earlier stages of fasting, processes like increased lipolysis, fat oxidation, ketone bodies synthesis, controlled glucose production and uptake, and less glucose oxidation protect the protein mass against catabolism.<sup>46</sup> It was found that only in the final phase of starvation was there a significant loss of muscle mass and protein content, inhibition of its synthesis and increased breakdown of muscle proteins.<sup>47,48</sup> It is during this late stage of starvation that the degraded proteins provide the carbon chains to the synthesis of newly formed glucose.<sup>46</sup>

Some of the results of biochemical and physiological tests underwent statistically significant changes under the influence of the applied 8-day WF and exceeded the reference values for healthy people whose diet met physiological criteria, but at the same time no acute, negative clinical changes were observed. The literature suggests that negative health effects caused by WF are extremely rare.<sup>49</sup> The lack of reference values for individual biochemical and physiological variables occurring

during this type of starvation necessitates increased clinical control or discontinuation of this type of intervention. Clinical experience shows that staying in the conditions of hyponatraemia, hyperuricemia or low blood glucose levels caused by WF for many days is unfavorable.

Certain scientific reports can be found in the literature on the beneficial use of WF for the health.<sup>50</sup> In order for prolonged, several days or longer, fasting to bring benefits to the body, participants need to master the art of leading the body out of the state of fasting to the ability of tolerating physiological nutrition. This is as important as the fasting process itself, and an inept return to physiological nutrition can lead to serious health consequences and even death.<sup>51</sup> Therefore, the men participating in the present study were instructed on the principles of nutrition for the next 7 days after stopping WF.

## Conclusions

The positive and negative reactions of the 8-day WF, observed during the presented research, suggest that more caution should be given during such intervention and subjects need to be under constant medical care. It should also be taken into account that despite reduced perceived stress and maintained protein balance among studied males, the symptoms of dehydration, increased ketogenesis, hyponatremia, hypoglycemia, hyperuricemia, and a significant reduction in body weight were reported. Therefore, for the safety of middle-aged people subjected to 8-day WF, it is recommended to discontinue such intervention, as it is a drastic form of fasting that already begins to generate unfavorable symptoms for a healthy person.

At the same time, bearing in mind the favorable adaptive changes observed during the 8-day WF, future studies should consider the possibility of even longer fasting, but in a less stringent form, e.g., caloric restriction or the use of intermittent fasting, during which the above-described adverse effects should not occur. Perhaps, with such milder forms of intervention, it will be easier to indicate in which fasting stage the threshold of homeostasis is reached, namely the balance between the long-term benefit of fasting and the harm due to insufficient food consumption.

## Study Limitation

Due to the small number of men participating in the study and the comparison of the obtained results with the reference values for healthy people using the "mixed diet", the conclusions drawn have a limited application value and cannot be generalized to a wider population.

Our results concern only healthy middle-aged men adapted to prolonged fasting.

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