Weight loss treatment of COVID-19 in patients with NCDs: a pilot prospective clinical trial

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Abstract

Background

COVID-19 in comorbidity with non-communicable chronic diseases (NCDs) complicate the diagnosis, treatment, prognosis, and increase mortality rate.

Objective.

To evaluate the effects of the weight loss treatment on clinic/laboratory inflammation and metabolic profile, reactive oxygen species (ROS) body composition in patients with COVID-19 in comorbidity with NCDs.

Design:

A 6-week open, pilot prospective clinical trial.

Setting:

The study included 72 adult patients with COVID and influenza in comorbidity with type 2 diabetes (T2D), hypertension, and NASH.

Interventions:

The treatment involved a fast-weight-loss-method (Analimentary detoxication, ANADETO) including calorie restriction to 50–100 kcal/day, salt intake to 5–6 gr/day, hot water drinking 1000–1500 ml/day, walking > 2,000 steps/day, and sexual self-restraint.

Main outcome measures:

Primary endpoints: Clinic/infectious/inflammation tests for COVID/Influenza; weight loss during 14 days. Secondary endpoints: fasting blood glucose, HbA1c, blood insulin; systolic/diastolic BP; blood lipids; ALT/AST, chest-CT-scan.

Results

The patients weight lost from baseline (-9.14 – 12.4%; \( P<0.001 \)); COVID and Influenza were a negative in > 96.3% patients at the 14 days. Systolic/diastolic BP normalized (\( P<0.0001 \)), glucose/lipids metabolism
(P < 0.0001); ALT/AST normalized (P < 0.0001), platelets increased from baseline (P < 0.0001), chest-CT (P < 0.0001) at 6-week follow-up. The previous antidiabetic, antihypertensive, anti-inflammatory and hepatoprotective, and other symptomatic medications were adequately decreased in 2–5 days to completely stopping by 5–8 days treatment.

Conclusions

The non-pharmacological treatment including fast weight loss is clinical/laboratory benefit in treatment of patients with COVID-19 and Influenza in comorbidity with T2D, hypertension, and NASH.

Trial Registration:


1. Introduction

SARS-CoV-2, a virus which causes the disease known as COVID-19 (further – COVID), was first described in a case of pneumonia of unknown origin in Wuhan City, China but quickly evolved into a worldwide pandemic, and has changed the mortality rate.[1–3] COVID and Influenza are the most common acute respiratory diseases (ARD) in the world, which can quickly spread through the air and direct contact.[2, 4, 5] The ARDs are serious illnesses that > 100 millions of people in the worldwide get each year. It sends millions of people to the hospital and causes millions of deaths.[6, 7] Increased ranking of COVID as a leading cause of death in some age groups is consistent with a downward age shift in the distribution of COVID deaths in last years. [3, 8]

COVID and Influenza co-infection with other non-communicable chronic diseases (NCDs) complicate the diagnosis/treatment/prognosis of the ARDs emerge new concern.[9, 10] This comorbidity may even increase the disease symptoms and mortality rate. Aggravating affects of the ARDs on cardiovascular comorbidities, diabetes onset, and chronic liver and kidney diseases have long been debating.[11, 12] Older age and type 2 diabetes (T2D), hypertension, liver and kidney diseases were significantly associated with an increased likelihood of mortality.[13] NCDs are also leading cause of mortality/morbidity in the world.[14, 15]

Pharmacology treatment of ARDs and NCDs evidenced positive results, but it is still insufficiently.[14, 16, 17] Nonetheless, COVID and Influenza variants continue to evolve and emerge, resulting in significant public concerns worldwide.[3, 18]

Pharmacologic and bio-vaccine treatment are not always can help to cure the ARDs due to they have a lot of side effects during and post treatment period. Treatment of the ARDs is more difficult in patients with comorbidities as T2D, hypertension, and nonalcoholic steatohepatitis (NASH).[19–21] Therefore,
searching reliable, secure, and natural methods for treatment of COVID and Influenza are continuing in the worldwide.[3, 5, 17, 18, 22]

NCDs and COVID are spreading in countries with a higher rate of overweight.[10, 23–27] The Comprehensive Assessment of the Long-term Effects of Reducing Intake of Energy (CALERIE) phase 2 trial showed that moderate reduction of energy intake averaging approximately 12% over 2 years could improve markers of inflammation, cardiometabolic health, and oxidative stress in humans.[28, 29] Caloric restriction has been shown to extend life span and health span in many animal species.[30] There has been growing interest in evaluating related strategies, such as intermittent fasting, periodic fasting, and time-restricted eating that may achieve the putative benefits of caloric restriction with greater likelihood of sustainability.[31]

COVID affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization. Some studies reported a high prevalence of overweight and obesity in patients experiencing a severe COVID course, with serious complications requiring hospitalization and admission to intensive care units.[27] Patients with obesity require regularly taking medications for the treatment of any concurrent chronic diseases, their physicians must promptly manage any medical symptoms in the case of suspected acute respiratory syndrome infection to prevent the risk of severe outcomes.[32]

ARDs with overweight are associated with an increase in oxidative stress and a decrease in antioxidant protection.[23] Acute inflammation in patients with overweight extreme difficulties in treatment and highlight the need for preventive measures.[33]

Pharmacological treatment of ARDs with NASH is a great challenge for medicine, because the patients are often limited to take medicine due to persistent progression, increasing of hepatocellular injury/inflammation, and medicinal overloading.[20]

In previous studies we showed a significant impact of overweight/obesity prevalence on the increase in COVID morbidity/mortality,[26] and beneficial role of our weight loss method in improving glycemic, lipid and hormone profiles, electrolyte and biochemical indices, blood pressure, reactive oxygen species and bone mineral density in patients with T2D/hypertension/severe NASH.[34, 35] The aim of the study was: to evaluate the effects of our fast weight loss method on clinic and laboratory inflammation profile, metabolic profile, reactive oxygen species (ROS) level and body composition in patients with COVID in comorbidity with T2D/hypertension/NASH.

2 Study Design And Participants

Study Design. A 6-week, open, pilot prospective clinical trial with the intention-to-treat principle.

2.1 Participants The study enrolled 72 adults (38 women) aged 25–80 years with moderate-to-severe cases COVID and Influenza in comorbidity with T2D, hypertension, NASH; 6 patients were excluded due to
noncompliance of inclusion and exclusion criteria. Of the remaining 66 patients 4 (6.5%) dropped out prior to the study completion: 2 refused the treatment method in 3 days after starting, and 1 moved to another city, 1 was excluded due to noncompliance. (Fig. 1) A control pharmacology group was not used because medicinal treatment was unacceptable due to NASH in most of the patients.

Thus, 62 patients (36 women) included for the analysis; 27 with COVID and 35 with Influenza. Overweight in 33 patients (53.2%) with body mass index (BMI) 28.14 ± 0.39 kg/m², and 29 without overweight with BMI 23.37 ± 0.38 kg/m². T2D in 26 (41.9%); Hypertension in 38 (61.3%) (incl. 12 with T2D); NASH in 51 (82.2%) (incl. 8 with NASH/T2D/Hypertension; 6 with NASH/T2D; 18 with NASH/Hypertension; 19 only NASH). Thus, all patients with the ARDs had in comorbidity with one or more NCDs. All patients with T2D were on Metformin, Sulfonylurea, DPP-4 inhibitors, GLP-1 receptor agonists, Glitazones in different combinations. All patients with hypertension received antihypertensive treatment.

All patients refused for pharmacology therapy due to: either previous unsuccessful drug results; or an antimicrobial resistance profile; or drug allergy; or reluctance to take medication; or iatrogenic fear (iatrophobia); or a rich failed experience in drug treatment; and NASH.

All the patients were admitted into the out-patient department in 3–5 days after illness onset.

**Inclusion criteria**

1) written informed consent form; 2) patients with fever; 3) patients refused for pharmacology therapy; 4) weight loss treatment for 12–14 days and + 4 weeks follow-up (total 6 weeks).

**Exclusion criteria**

1) patients with acute respiratory failure and assisted ventilation requirement; 2) respiratory rate ≥ 30 times/minute; 3) oxygen saturation ≤ 93% by finger oximetry at resting status.

Outcome measures *Primary endpoints*: Clinic and infectious tests for COVID/Influenza; weight loss during 14 days; inflammation profile. *Secondary endpoints*: fasting blood glucose, glycosylated hemoglobin A1c (HbA1c), blood insulin; systolic/diastolic blood pressures (BP); blood lipids; alanine aminotransferase (ALT), aspartate aminotransferase (AST), chest computed tomography (CT) scan.

**2.2 Analytical Assessment**

**Pathogen detection methods.**

*Infection detection*. COVID was diagnosed primarily by direct detection of SARS-CoV-2 RNA by nucleic acid amplification tests with a real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay using nasal or pharyngeal swab specimens from the upper respiratory tract. A health care professional collected a fluid sample by inserting a long nasopharyngeal swab into a nostril and taking fluid from the back of a nose.
To diagnosis of the flu was used a RT-PCR test called the Flu SC2 Multiplex Assay. Sputum DNA was extracted using Chemagic DNA kits (PerkinElmer, Turku, Finland) and PCR assays were performed using Seegplex Pneumobacter ACE Detection kits (Seegene Inc., Seoul, South Korea) according to the manufacturer protocol.[36]

Sputum specimens collection, samples transport, samples storage, diagnostic test procedures environment, to tests results reporting, every step were strictly performed under the standard guidelines. [37, 38]

All the tests were performed in two independent laboratories in Astana: BioLab and OLIMP laboratories. Positive results were considered when both laboratories give equal results.

**Biochemical laboratory assessments** consisted of a complete blood cell count, white blood cells (normal: 3.5-9.0×10^9/L), neutrophil-to-lymphocyte ratio (NLR) is calculated by dividing the absolute count for neutrophils by the absolute count for lymphocytes (normal: 1–2), blood chemical analysis, erythrocyte sedimentation rate, urea (normal: 2.1–7.7 mmol/L), creatinine (normal: 53–115 μmol/L), glucose, cholesterol (normal: <5.4 mmol/L), triglyceride (normal: <1.69 mmol/L), high-density lipoprotein (HDL) (normal: >1.55 mmol/L), fibrinogen (normal: 2.0–4.0 g/L), hepatic enzyme levels (ALT, norm < 36 U/L, AST, norm < 40 U/L), assessment of liver and renal function, and measures of inflammation level, C-reactive protein (normal: ≤10.0 mg/L), and HbA1c (normal: <5.7%; prediabetes: 5.7–6.5%, diabetes: ≥6.5%). All the data of enrolled cases, including demographic information, clinical symptoms or signs, clinical outcomes and laboratory findings on admission, were included in electronic medical records.

**Hormonal assays.** Fasting serum insulin was determined by immunoassay (Immunotech Insulin Irma kit, Prague, Czech Republic). Hyperinsulinemia was considered >12.5 nU/L. The Homeostasis Model Assessment insulin resistance indexes (HOMA-IR) was used as surrogate measure of insulin sensitivity as follows: HOMA-IR = ((fasting insulin in nU/L) × (fasting glucose in mmol/l)/22.5). Insulin resistance was considered if the index was >2.

Diagnostic criteria for T2D were used the standards of American Diabetes Association in 2017.[39] Hypertension was diagnosed by BP readings and from medical records. Physical activity of patients was assessed by the number of steps measured by pedometers (Hoffmann-La Roche Ltd, Basel, Switzerland).

The Nonalcoholic Steatohepatitis Clinical Research Network criteria was used to diagnose NASH and from medical records.[40]

**Anthropometrical data.** Anthropometrical indicators included age (years), weight (kg), BMI (kg/m^2). Body composition parameters including fat mass (in % of total body weight and total kg), fat free mass (kg), total body water (%), muscle and bone mass (%) were measured using Tanita-SC330S Body Composition Analyzer (Tanita Corp., Tokyo, Japan).
For ROS we measured malondialdehyde (MDA), superoxide dismutase (SOD) and catalase (antioxidant enzymes), and advanced oxidation protein products (AOPP).

Imaging. Ultrasound images (GE-Vivid-9-Ultrasound; GE-Healthcare-Worldwide-USA, Michigan) and chest-CT (Siemens-Somatom-Sensation-32) were obtained. The key imaging finding in the pneumonia were ground-glass opacity, distribution and extent of lung abnormalities, including consolidation, cavitation and pleural effusion.

Chest-CT assessment of the severity of lung changes. Each lung field was divided into three equal zones. Each zone was assigned a score from 0–4 based on the percentage of lung involved (0 = no abnormality, 1 = < 25% of the zone involved, 2 = 25–50% involved, 3 = 51–75% involved and 4 = > 75% involved). The scores for all six zones of each CT examination were summed to provide a cumulative chest radiographic score (range, 0–24). Baseline and follow-up CT-scans were reviewed in consensus by two radiologists with 10–25 years of experience. Laboratory tests, ultrasound/CT images, and an electrocardiogram were performed, and sputum and blood samples were collected on the inclusion day.

Intervention. We used the “Analimentary detoxication” (ANADETO) fast-weight-loss-method, including calorie restriction to 50–100 kcal/day with fat-free vegetables (tomatoes and cucumbers) with mandatory salt intake to 5–6 gr/day, hot water drinking 1000–1500 ml/day, walking at least 2,000 steps/day after normalized body temperature, and sexual self-restraint. The walking provided to promote of blood circulation and decrease in metabolic intoxication. The weight loss method lasted 14 days. Then the patients followed for 4-week diet where they ate one meal/day without any food restriction. A combination of in-person conversations and telephone calls were conducted during whole 6-week study period.

Statistics The two-side Student’s t-test and Odds ratios (ORs) with 95% Confidence intervals (CIs) were used. The study data were tested against the normal distribution and are presented in Tables as Mean±Standard Error of the Mean (M ± SEM). P-value of < 0.05 was set as significant and < 0.0001 was set as highly significant. Statistical analysis was performed using SPSS ver.23.0 for Windows (SPSS: An IBM Company, Armunk, NY) and Microsoft Excel-2021. All analyses were intention-to-treat.

3 Results

The symptoms of COVID/Influenza were the common typical such as fever in 62 patients (100%), cough in 48 (77.4%), runny or stuffy nose in 51 (82.2%), fatigue in 49 (79%), chills in 30 (48.4%), sore throat in 14 (22.6%), headache in 22 (35.4%), body aches in 18 (29%). Loss of taste or smell was in 21 patients (33.8%): 9 with COVID; 12 with Influenza. This symptom did not differ between these diseases (95%; OR:0.96, CI:0.34–2.73, P = 0.46). Loss of appetite and smell irritability were in 51 patients (82.3%): 24 with COVID; 26 with Influenza (95%; OR:1.19, CI:0.81–1.77, P = 0.92). Other clinical symptoms of the diseases did not also differ from each other.
Baseline/7-day/14-day treatment and to 6-week follow-up results concerning anthropometrical data, body composition, and metabolic data are shown in Table 1. Patients with overweight lost 8–11 kg (-12.4% from baseline), and it was higher than patients without overweight (-9.14% from baseline; -9.7 ± 0.7 kg vs. -6.4 ± 0.6 kg, respectively; \( P < 0.001 \)) at 14-day of the treatment. In patients with overweight BMI at 14-day was highly significantly decreased (-4.2 kg/m\(^2\)) than without overweight (-2.2 kg/m\(^2\)) (\( P < 0.001 \)).
Table 1
Anthropometrical data, body composition in patients (with/without overweight) with COVID and Influenza in comorbidity with the Non-communicable diseases before (baseline), during treatment, and 6-week follow-up (M ± SEM)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Baseline</th>
<th>Treatment days</th>
<th>6-Week follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weight in patients with overweight (n = 33) (kg)</td>
<td></td>
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<tr>
<td></td>
<td>83.15 ± 0.74</td>
<td>76.24 ± 0.79**</td>
<td>72.84 ± 0.72**</td>
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<td></td>
<td>BMI (kg/m$^2$)</td>
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<tr>
<td></td>
<td>28.14 ± 0.39</td>
<td>26.07 ± 0.37*</td>
<td>24.91 ± 0.34**</td>
</tr>
<tr>
<td></td>
<td>Fat mass (%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>29.73 ± 0.45</td>
<td>22.90 ± 0.41**</td>
<td>19.54 ± 0.51**</td>
</tr>
<tr>
<td></td>
<td>Fat free mass (kg)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>58.21 ± 0.43</td>
<td>58.09 ± 0.41</td>
<td>58.08 ± 0.41</td>
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<tr>
<td></td>
<td>Total body water (%)</td>
<td></td>
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<tr>
<td></td>
<td>53.47 ± 0.43</td>
<td>57.32 ± 0.42**</td>
<td>62.13 ± 0.44**</td>
</tr>
<tr>
<td></td>
<td>Muscle mass (%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>65.45 ± 0.98</td>
<td>69.89 ± 1.02*</td>
<td>74.67 ± 1.06**</td>
</tr>
<tr>
<td></td>
<td>Bone mass (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.61 ± 0.09</td>
<td>3.68 ± 0.09</td>
<td>3.83 ± 0.09</td>
</tr>
<tr>
<td></td>
<td>Weight in patients without overweight (n = 29) (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>71.33 ± 0.81</td>
<td>67.98 ± 0.83*</td>
<td>64.81 ± 0.83**</td>
</tr>
<tr>
<td></td>
<td>BMI (kg/m$^2$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>23.37 ± 0.38</td>
<td>23.80 ± 0.37</td>
<td>21.23 ± 0.35*</td>
</tr>
<tr>
<td></td>
<td>Fat mass (%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>25.81 ± 0.43</td>
<td>23.43 ± 0.41*</td>
<td>19.81 ± 0.43**</td>
</tr>
<tr>
<td></td>
<td>Fat free mass (kg)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>52.92 ± 0.52</td>
<td>52.05 ± 0.51</td>
<td>51.77 ± 0.48</td>
</tr>
<tr>
<td></td>
<td>Total body water (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>53.97 ± 0.46</td>
<td>55.22 ± 0.46</td>
<td>59.32 ± 0.48**</td>
</tr>
<tr>
<td></td>
<td>Muscle mass (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>67.84 ± 0.97</td>
<td>68.76 ± 0.99</td>
<td>72.67 ± 0.98*</td>
</tr>
<tr>
<td></td>
<td>Bone mass (%)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>3.78 ± 0.08</td>
<td>3.80 ± 0.09</td>
<td>3.97 ± 0.08</td>
</tr>
</tbody>
</table>

* P-value of < 0.05, and
** P < 0.0001 were set as significant from baseline.
**Abbreviations:** BMI, body mass index; M, mean; SEM, standard error of the mean.

Weight loss in both groups was due to reduction of fat mass ($P < 0.0001$). Percentages of total body water and muscle mass tended to increase significantly in both groups at 7-day/14-day of the treatment, and the percentage of bone mass increased significantly too (in patients with overweight $P < 0.0001$; without overweight $P < 0.05$). Lean body mass (fat free mass) did not change significantly during weight loss in both groups, patients with and without overweight ($P = 0.82–0.97$). These trends persisted at 6-week of follow-up.

Starting from 2–3 days of the treatment, in almost patients is increased a sputum production to 1.0-1.5 liters/day. A sputum production decreased by 7–9 days of the treatment.

Body temperature decreased starting from 3–4 days of treatment, and it is normalized to 6–9 days, and also was normal at 6-week follow-up (Table 2). Begin from 3–5 days of the treatment, in most patients their urine became turbid, muddy and intensively darkly colored, which persisted for several days. Urine microscopy showed organic and non-organic salts such as oxalates/urates/phosphates/carbonates of calcium/magnesium, and leukocyturia (20–35 per in sight). Starting from 5–7 days, the patients noticed a physical relief, increase in physical/mental workability, and exercise tolerance. Infection detection at 14-day of treatment was a negative in 26 patients of 27 with COVID, and 34 patients of 35 with Influenza. Redetection on the next two days showed a negative in both patients.
### Table 2

Body temperature, Blood pressures, Inflammation level, Glucose and Lipids metabolism, Lipid and protein oxidative products, and chest CT in patients with COVID and Influenza in comorbidity with the Non-communicable diseases at baseline, during treatment, and 6-week follow-up (M ± SEM)

<table>
<thead>
<tr>
<th>Variables (n)</th>
<th>Baseline</th>
<th>Treatment days</th>
<th>6-Week follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>7 day</td>
<td>14 day</td>
</tr>
<tr>
<td>Body temperature, °C (62)</td>
<td>39.34 ± 0.08</td>
<td>37.86 ± 0.08**</td>
<td>36.7 ± 0.05**</td>
</tr>
<tr>
<td>Systolic BP in patients with hypertension, mmHg (38)</td>
<td>161.3 ± 1.31</td>
<td>116.2 ± 0.77**</td>
<td>118.3 ± 0.46**</td>
</tr>
<tr>
<td>Diastolic BP in patients with hypertension, mmHg (38)</td>
<td>101.6 ± 0.85</td>
<td>78.92 ± 0.67**</td>
<td>80.89 ± 0.66**</td>
</tr>
<tr>
<td>Total protein, g/l (62)</td>
<td>62.41 ± 0.63</td>
<td>--</td>
<td>66.92 ± 0.65**</td>
</tr>
<tr>
<td>Hemoglobin, g/L (62)</td>
<td>128.6 ± 0.71</td>
<td>--</td>
<td>131.7 ± 0.72*</td>
</tr>
<tr>
<td>White blood cells, ×10⁹/L (62)</td>
<td>12.29 ± 0.17</td>
<td>11.83 ± 0.16</td>
<td>7.68 ± 0.12**</td>
</tr>
<tr>
<td>Neutrophil, ×10⁹/L (62)</td>
<td>7.128 ± 0.012</td>
<td>6.389 ± 0.010**</td>
<td>3.610 ± 0.009**</td>
</tr>
<tr>
<td>Lymphocytes, ×10⁹/L (62)</td>
<td>2.581 ± 0.008</td>
<td>3.256 ± 0.009**</td>
<td>2.918 ± 0.009**</td>
</tr>
<tr>
<td>Neutrophil-to-lymphocyte ratio (62)</td>
<td>2.762 ± 0.009</td>
<td>1.962 ± 0.009**</td>
<td>1.237 ± 0.009**</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate, mm/Hour (62)</td>
<td>33.4 ± 0.56</td>
<td>--</td>
<td>13.76 ± 0.24**</td>
</tr>
<tr>
<td>Total Fibrinogen, g/L (62)</td>
<td>4.83 ± 0.07</td>
<td>5.25 ± 0.09*</td>
<td>3.81 ± 0.08**</td>
</tr>
<tr>
<td>C-reactive protein, mg/L (62)</td>
<td>34.86 ± 1.26</td>
<td>26.35 ± 1.37**</td>
<td>12.39 ± 0.79**</td>
</tr>
<tr>
<td>Glucose in patients with T2D, mmol/L (26)</td>
<td>12.86 ± 0.19</td>
<td>6.75 ± 0.11**</td>
<td>4.60 ± 0.09**</td>
</tr>
<tr>
<td>HbA1c, % (26)</td>
<td>7.03 ± 0.09</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Immunoassay Insulin, nU/L (26)</td>
<td>22.38 ± 0.58</td>
<td>--</td>
<td>9.61 ± 0.22**</td>
</tr>
</tbody>
</table>

* P-value of < 0.05, and

** P < 0.0001 were set as significant from baseline.
<table>
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<tr>
<td></td>
<td></td>
<td>7 day</td>
<td>14 day</td>
</tr>
<tr>
<td>HOMA-IR index (26)</td>
<td>12.79 ± 0.35</td>
<td>--</td>
<td>1.96 ± 0.17**</td>
</tr>
<tr>
<td>Platelets, ×10⁹/L (51)</td>
<td>186.5 ± 4.6</td>
<td>196.6 ± 4.7</td>
<td>238.5 ± 5.8**</td>
</tr>
<tr>
<td>ALT, U/L (51)</td>
<td>134.3 ± 5.4</td>
<td>102.6 ± 5.7*</td>
<td>78.4 ± 4.2**</td>
</tr>
<tr>
<td>AST, U/L (51)</td>
<td>166.5 ± 5.5</td>
<td>126.3 ± 5.9**</td>
<td>92.4 ± 4.9**</td>
</tr>
<tr>
<td>Urea, mmol/L (62)</td>
<td>5.17 ± 0.07</td>
<td>7.54 ± 0.07**</td>
<td>5.62 ± 0.06**</td>
</tr>
<tr>
<td>Creatinine, µmol/L (62)</td>
<td>75.58 ± 1.27</td>
<td>109.73 ± 1.59**</td>
<td>62.86 ± 1.07**</td>
</tr>
<tr>
<td>Cholesterol, mmol/L (62)</td>
<td>5.82 ± 0.07</td>
<td>6.83 ± 0.08**</td>
<td>6.19 ± 0.09*</td>
</tr>
<tr>
<td>Triglyceride, mmol/L (62)</td>
<td>2.52 ± 0.07</td>
<td>5.94 ± 0.09**</td>
<td>5.73 ± 0.08**</td>
</tr>
<tr>
<td>HDL, mmol/L (62)</td>
<td>0.96 ± 0.03</td>
<td>1.02 ± 0.03</td>
<td>1.06 ± 0.03*</td>
</tr>
<tr>
<td>MDA, µmol/L (62)</td>
<td>60.74 ± 1.84</td>
<td>--</td>
<td>41.51 ± 0.87**</td>
</tr>
<tr>
<td>AOPP, µmol/L (62)</td>
<td>295.6 ± 9.2</td>
<td>--</td>
<td>206.3 ± 11.1**</td>
</tr>
<tr>
<td>SOD, U/mg (62)</td>
<td>34.58 ± 1.07</td>
<td>--</td>
<td>57.72 ± 1.06**</td>
</tr>
<tr>
<td>Catalase, U/g (62)</td>
<td>26.52 ± 0.67</td>
<td>--</td>
<td>46.83 ± 0.65**</td>
</tr>
<tr>
<td>Chest CT scan, score (44)</td>
<td>13.12 ± 0.38</td>
<td>--</td>
<td>1.72 ± 0.12**</td>
</tr>
</tbody>
</table>

* P-value of < 0.05, and 
** P < 0.0001 were set as significant from baseline.

**Abbreviations:** AOPP, Advanced oxidation protein products; BP, blood pressure; CT, Computed tomography; HDL, high density lipoprotein; HOMA-IR, Homeostasis Model Assessment for Insulin Resistance; M, mean; MDA, Malondialdehyde; SOD, Superoxide dismutase; SEM, standard error of the mean; T2D, type 2 diabetes.
The weight loss treatment evoked significantly rising of serum urea and creatinine on 7-day. We noticed normalization levels of serum urea and creatinine on 14-day. (Table 2)

During weight loss there was no protein lost because total serum protein level significantly increased from baseline (62.41 ± 0.53 g/l) to 14-day treatment (66.92 ± 0.65 g/l, \(P<0.0001\)), and 6-week follow-up (71.43 ± 0.67 g/l, \(P<0.0001\)). Hemoglobin level also significantly increased from baseline (128.6 ± 0.71 g/l) to 14-day treatment (131.7 ± 0.72 g/l, \(P<0.05\)), and 6-week follow-up (136.9 ± 0.78 g/l, \(P<0.0001\)). HDL significantly increased from baseline (0.96 ± 0.03 mmol/L) to 14-day treatment (1.06 ± 0.03 mmol/L, \(P=0.02\)), and 6-week follow-up (1.68 ± 0.04 mmol/L, \(P<0.0001\)). (Table 2)

White blood cells were gradually decreased on the 14 day. Relative lymphocyte count increased that the NLR was significantly decreased (\(P<0.0001\)). Total fibrinogen, C-reactive protein, and Erythrocyte sedimentation rate were significantly decreased to normal at 14-day of treatment (\(P<0.0001\)) and 6-week follow-up (\(P<0.0001\)). (Table 2)

The weight loss treatment led to a normal systolic/diastolic BP starting from 7-day of treatment, and it were normalized at 14-day and 6-week follow-up (Table 2) reaching the levels recommended by the American Heart Association (2014).

The positive changes in glucose metabolism in patients with T2D (n = 26) were at 14-day of treatment and also at 6-week follow-up. Fasting Glucose and Immunoassay Insulin, and HOMA-IR index quickly decreased at 14-day of treatment. Insulin decreased 2.3-fold from baseline at 14-day of treatment, whereas 3.5-fold from baseline at 6-week follow-up. HbA1c decreased to the normal by 6-week (4.86 ± 0.08) by 31% (\(P<0.05\)).

Cholesterol and triglycerides are significantly increased by 17.2–6.4% and 68.8–62.7% from baseline at 7 and 14 days, respectively.

In patients with NASH (n = 51) ALT/AST levels significantly decreased from baseline (134.3±5.4 and 166.5±5.5 U/L, respectively) at 7-day (102.6±5.7 (\(P<0.05\)) and 126.3±5.9 U/L (\(P<0.0001\)), respectively); and 14-day (78.4±4.2 (\(P<0.0001\)) and 92.4±4.9 U/L (\(P<0.0001\)), respectively). On the 6-week follow-up ALT/AST levels returned to normal (\(P<0.0001\)). (Table 2)

Platelets in patients with NASH (n = 51) significantly increased from baseline 186.5 ± 4.6, \(\times10^9/L\) at 14-day of treatment by 238.5 ± 5.8, \(\times10^9/L\) (\(P<0.0001\)), and at 6-week follow-up by 278.3 ± 6.9, \(\times10^9/L\) (\(P<0.0001\)).

\textit{Abnormal chest imaging.} CT-scans were abnormal in 44 patients (70.97%) aged > 40 years, including 8 patients with NASH/T2D/Hypertension; 6 patients with NASH/T2D; 12 patients with T2D/Hypertension; 18 patients with NASH/Hypertension.

CT findings included multiple small patchy shadows, centrilobular nodules and bronchial wall thickening, interstitial inflammation, predominantly distributed in the peripheral of the lungs, ground glass opacities...
and infiltrates in the lungs, bronchopneumonia patterns. The most common finding was ground glass opacity (n = 39; 88.6% including 25 patients with COVID), not followed by consolidation. Pleural effusion and cavitation was not detected. Unilateral lung involvement (n = 36; 81.8%) was more common than bilateral involvement (n = 6; 13.6%). The right/ left lower zones (n = 34; 77.3%) were more commonly affected than the right/ left middle (n = 9; 20.5%). Multifocal distribution was more common (n = 24, 54.5%) than unifocal distribution (n = 19, 43.2%). Chest CT-scans were non-specific for the ARDs.

The mean score of chest-CT for the patients (n = 44) was 13.12 ± 0.38. A significant positive changes was found on 14-day treatment with the score 1.72 ± 0.12 (P < 0.0001). There were not found the lung abnormalities at 6-week follow-up (Table 2). By 14-day of treatment CT-scans showed that the scope of the lesions had been reduced, the density was gradually decreased, the number of lesions decreased, and the ground glass opacities were absorbed.

There was no 6-week risk of arterial thromboembolism and venous thromboembolism among the patients with COVID/Influenza.

The oxidative products of lipids/proteins had a trend to normalize at 14-day treatment and 6-week follow-up, where MDA decreased by 31.7% at 14-day (P < 0.0001) and by 48.4% at 6-week from baseline (P < 0.0001), AOPP decreased by 30.2% at 14-day (P < 0.0001) and by 36.3% at 6-week from baseline (P < 0.0001), and SOD increased by 66.9% (P < 0.0001) and Catalase by 76.6% at 14-day (P < 0.0001), and by 92.4% and 85.8%, respectively, at 6-week from baseline (P < 0.0001) (Table 2).

As clinical status of the patients was improving, the previous antidiabetic (with T2D, n = 26), antihypertensive (hypertension, n = 38), anti-inflammatory and hepatoprotective (NASH, n = 51), and other symptomatic conventional medications were adequately decreased starting from 2–5 days of the treatment. By 5–8 days after treatment starts, the drugs were stopped completely. There were no recurrence of T2D, hypertension, and NASH at 6-week follow-up.

### 4. Discussion

Our data showed that the fast weight loss method at 14-day treatment and at 6-week follow-up had a clinical, laboratory and imaging effectiveness in patients with COVID/Influenza in comorbidity with T2D/hypertension/NASH.

The weight loss in patients with overweight goes faster than in patients without overweight. The finding in weight loss physiology might be explained by different structure of fat in people with/without overweight.[49] People who quickly weight gain can accumulate a lightweight body-fat, and people who slowly weight gain can accumulate a dense bod- fat. Some people cannot weight gain due to genotype, different fat structure, metabolic equivalent.[50, 51]

The weight loss improved a patients immunity by significantly increase in lymphocyte count and decrease in NLR. In fact, lymphopenia is also associated with severe illness and poorer survival in COVID.
In clinical practice, “divergence” between absolute value of neutrophils and lymphocytes, that NLR, may be correlated with progression/prognosis of COVID.[54]

Our clinical study confirmed that weight loss significantly reduces inflammation biomarkers.[55, 56] Inflammation reducing by weight loss could be associated with a reduced risk for NCDs.[28, 57] The weight loss had immunomodulatory effect, insulin resistance repealed, blood insulin and BP decreased, blood hemoglobin increased.[58, 59] Blood cholesterol/triglyceride, lipid/protein oxidative products also decreased, and anti-oxidative enzymes increased.

Increase in serum urea/creatinine levels during 14-day weight loss can testify about endogen intoxication related to active lipolysis. In adipocytes adsorbed endogen organic metabolites was eliminating through blood system during lipolysis.[60, 61] Increase in lipids (cholesterol/triglyceride) from baseline at 7–14 weight loss days confirms the activity of lipolysis.

Patients with acute respiratory inflammation in comorbidity with NCDs lose a lot of sodium ions through urine.[62, 63] In our study blood and urine sodium levels became a normal, possibly, due to elimination of metabolic pollutants.

Weight loss improves liver health, cardiovascular risk, and quality of life, therefore studies offer it as feasible treatment of NASH.[64, 65]

Our study evidenced that chest-CT in the patients with COVID and Influenza are highly variable and nonspecific, that is considered with other authors.[66] Chest-CT has been widely using during COVID-pandemic, which has a sensitivity with 60–97%, but low specificity (20–50%).[66, 67] Many radiology professional societies recommend against performing chest-CT as a primary technique for COVID pneumonia diagnosis.[68] In patients with ARDs, CT findings should be interpreted in combination with a clinical context.

Overweight is a biological burden for the body, which consumes additional immunological, antitoxic, trophic, excretion function.[69] ANADETO method metabolizes ‘old lipids’ with fat loss, decreases in inflammation, increases in immune response, improves of glucose/lipid metabolism, and liver functions. The method had side effects related to symptoms of metabolic intoxication that is a common problem during weight loss. Adipose tissue absorbs persistent organic pollutants,[70] and plays an important role in storing of many pollutants.[71]

The ability to accumulate adipose tissue is one of the most important adaptive mechanisms for survival, but now we observe a steady increase in obesity-related-diseases.[72, 73]

The fast weight loss method was a safe, well tolerated, and acceptable therapy option for patients with the ARDs in comorbidity with the NCDs. The optimal mix of caloric restriction, sodium intake, walking, and sexual self-restraint behavior is the effective treatment method for COVID/Influenza in comorbidity with the NCDs.
The strengths of this study are that it was presented a positive role of restriction diet and weight loss in patients with COVID-19 in comorbidity with non-communicable diseases in a prospective clinical trial. The limitations of this study are that it was a single-center study, the study was short duration, we did not study T-cell and B-cell subpopulation, and the study was non-controlled trial. Further randomized controlled trials with longer-term follow-up are needed to confirm and extend the results of the study.

5. Conclusions

Thus, the fast weight loss healed up clinical and laboratory/instrumental data of inflammation, improved glucose/lipids metabolism, systolic/diastolic BPs and NASH’s biochemical outcomes, reactive oxygen species, and allowed to stop drugs in patients with COVID/Influenza in comorbidity with T2D/hypertension/NASH. The weight loss was achieved due to decrease in fat mass. Chest CT-scans were non-specific for COVID and Influenza.

Abbreviations

ALT – alanine aminotransferase
ANADETO – ‘Analimentary detoxication’ weight loss method
AOPP – advanced oxidation protein products
AST – aspartate aminotransferase
BMI – body mass index
BP – blood pressure
CT – Computed tomography
COVID – SARS-CoV-2, a virus which causes the disease known as COVID-19
HbA1c – glycosylated hemoglobin A1c
HDL – high density lipoprotein
HOMA-IR – Homeostasis Model Assessment for Insulin Resistance
M±SD – Mean ± standard deviation
M±SEM – Mean ± standard error of the mean
MDA – malondialdehyde
NASH – Nonalcoholic steatohepatitis
Declarations

The study was carried out in the Republic of Kazakhstan from November, 2020, through July, 2022. The participants were recruited gradually as they come in the Republican Diagnostic Center at University Medical Center (Astana) and ANADETO medical center from November 2020 to March 2022.

Consent for publication. All authors of the manuscript affirm that they had access to the study data and reviewed and approved the final version.

Conflict of Interest Disclosures: The authors declare that they have no any competing interests (financial, professional, or personal) that are relevant to the manuscript. We have read and understood the journal policy on declaration of interests and have no interests to declare. Dukenbayeva Bibazhar, coauthor, she is a director of the Medical center ‘ANADETO’, who participated in the study design, data interpretation, writing of discussion, bibliography and paper review.

Ethics approval and consent to participate. The Local Ethics Committee of the University Medical Center (phone: +71272-692586; e-mails: mirgul.bayanova@umc.org.kz; https://umc.org.kz/en/?ethics-commission) approved a study “The fast weight loss in patients with acute and chronic respiratory infections in comorbidity with non-communicable diseases” (approval protocol number is #7 of 26.09.2019).

Availability of data and materials. First, the data is too large (>2.8 GB). Secondly, we will make our data available to any investigator/reviewer on their own request, so that the personal privacy of our patients cannot be compromised.

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Author contributions:

KO: study design, collection of the clinical data, diagnosis and treatment of the patients, bibliography review, statistical analysis, data interpretation, writing of the paper. AD: study design, data collection,
diagnosis and treatment of the patients, data interpretation, bibliography and paper review. Al: study
design, data collection, writing the Introduction and Methods, data interpretation, paper review. ZZ and
MG: preparation of the statistical data in Excel, collection of the clinical data, bibliography and paper
review, data interpretation, statistical analysis, writing of the Methods and Discussion, paper review.
GB: study design, data collection, writing the results and discussion, and paper review. AN: collection of
the clinical data, preparation of statistical data in Excel, patient diagnosis, bibliography search and
review. AT: writing of the discussion, statistical analysis, paper review. BD: study design, data collection
and interpretation, writing the discussion, bibliography and paper review.

All authors read and approved the final manuscript.

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Figures

Figure 1. Participant Flow Diagram

Enrollment

Assessed for eligibility (n= 72 )

Excluded (n= 6)
  ♦ Excluded due to noncompliance of inclusion and exclusion criterion

Allocation

Allocated to intervention (n= 66)
  ♦ Received allocated intervention (n= 66 )
  ♦ Did not receive allocated intervention (n= 0)

Follow-Up

Lost to follow-up (n= 4)
Reasons: 1 patient moved to another place, 2 patients refused to treat, 1 patient was excluded due to noncompliance of recommendations.

Analysis

Analysed (n= 62 )
  ♦ Excluded from analysis (n= 0)

Figure 1

See image above for figure legend

Supplementary Files

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