



Increased Serum Ferritin and Decreased Serum Haptoglobin Levels Developing in a 40y Old Healthy Man Fasting for 3-Weeks

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Abstract

At following up a peculiar case of a healthy 40y-old man who voluntarily fasted for 21 days, we found unforeseen laboratory features suggestive of adaptive acute changes in iron metabolism, including increased serum ferritin, decreased serum haptoglobin and maintenance of normal blood hemoglobin and serum C-reactive protein levels, findings that could not be ascribed to the occurrence of infection or inflammation, but perhaps could be linked to a low-grade, sub clinical inflammation. We discuss the overall data and suggest the occurrence of some degree of intravascular hemolysis in this man during his prolonged and non-complicated fasting.

Keywords: Serum C-reactive protein; Serum haptoglobin; Serum ferritin

Introduction

In the medical context, fasting can be defined as abstaining from food during a certain period of time, which can be short (8-12h) to perform standardized basal metabolic laboratory tests (e.g. determination of blood glucose, or serum triglycerides) or a little more extended, as occur prior elective medical procedure such as general anesthesia or major surgery. Fasting can also occur involuntarily throughout time in famine, or as consequence of refusal to eat seen in physical or mental illnesses, as occur in the very old frail person, in the terminal cancer, or anorexia nervosa patients. Voluntary prolonged fast has also been described in otherwise healthy people practicing hunger strike or self-denial of food owing to a religious discipline. Comprehensible metabolic studies have been performed with normal persons fasting for five to more than 30 days [1,2].

Metabolic adaptive mechanisms in the body that permit survival for prolonged periods of time include the provision of glucose from liver glycogen in the first 18-24h, and from hepatic gluconeogenesis derived mainly from muscle amino acids thereafter. From the energy requirement point of view, increased lipolysis and ketone bodies production allow the brain to displace glucose utilization to ketone bodies, sparing muscle protein, and permitting human beings endure several days or months of fasting [3].

After following up a peculiar case of a healthy man fasting for 21 days, we found unforeseen laboratory features suggesting adaptive changes in iron metabolism. Moreover, after a literature search in Medline database using a combination of terms such as “fasting”, “starvation”, “iron deficiency”, “anemia of inflammation”, “anemia of chronic diseases”, “serum ferritin”, or “serum haptoglobin”, we could not find research with enough data to explain our main findings.

Thus, in this paper we report a case of a healthy, athletic, 40years-old man fasting during a period of 21-days, who had increased of ferritin and decreased haptoglobin serum levels suggestive of intravascular hemolysis.

Case Report

We report a case of a healthy, athletic, 40 years-old man who in the last three years submitted himself to periods of fasting lasting from 10 to 14 days. The subject asked for our medical supervision to carry out three weeks of fasting for religious reasons. After clinical evaluation and advising him about inherent risks of prolonged fasting, including eventual occurrence of electrolytes abnormalities

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Table 1: Anthropometry data, BIA parameters, and laboratory data at basal and after 7, 14 and 21 days of fasting, and 14 days after the end of fasting.

	Reference values	Basal	7th day	14th day	21st day	14days after refeeding
Body weight (kg)		83.8	77.9	73.9	70.8	75.7
Lean body mass (kg)		67.8	65.4	64.4	62.8	65.7
Body fat (kg)		16.0	12.5	9.5	8.0	10.0
Body water (%)		59.2	61.5	63.7	65.0	48.1
Urinary creatinine (mg/day)	1,696*	2,326	2,402	1,927	2,088	1,698
Serum creatinine (mg/dL)	0.4 - 1.4	1.1	1.1	1.2	1.2	0.8
Urinary urea (g/day)	15.0 - 20.0	35.8	24.7	17.9	18.6	42.9
Serum urea (mg/dL)	< 50	44	27	25	29	44
Serum albumin (g/dL)	3.5 - 5.0	4.5	4.5	4.7	4.4	4.3
Serum transferrin (g/L)	2.0 - 3.6	3.1	2.5	2.2	1.8	2.9
Serum C-reactive protein (g/L)	< 5.0	0.8	0.6	2.1	2.4	0.5
Serum acid α1 glycoprotein (g/L)	0.5 - 1.2	0.7	0.5	0.4	0.4	0.6
Serum C3 component	0.9 - 1.8	1.1	1.1	0.9	0.9	1.2
Serum ferritin (ng/mL)	30 - 400	211	690	821	794	369
Serum haptoglobin (g/L)	0.3 - 2.0	0.3	0.0	0.01	0.0	0.5
Serum iron (µg/dL)	59 - 158	100	133	109	123	97
Red blood cells (10 ⁶ /µL)	4.5 - 6.0	5.1	5.3	5.8	5.4	4.7
Blood hemoglobin (g/dL)	14.0 - 18.0	15.8	16.5	17.5	16.8	14.2
Hematocrit (%)	42 - 54	45	46	49	45	42
Mean corpuscular volume (fL)	80 - 95	88	86	85	84	89
White bloodcells (10 ³ /µL)	3.5 - 10.5	4.6	4.0	4.8	4.6	5.2
Neutrophils(10 ³ /µL)	1.7-8.0	2.7	2.5	2.8	3.1	2.7
Lymphocytes(10 ³ /µL)	0.9-2.9	1.4	1.0	1.4	0.9	1.8
Platelets (10 ³ /µL)	150 - 400	203	174	131	150	209

*23mg/kg of ideal body weight (Heymsfield, 1994).

and cardiac arrhythmias we acceded, and with his agreement, decided to perform physical examination, anthropometry, bioimpedance analysis (BIA) and blood and urinary laboratory analysis regularly at each seven days until fasting period completion.

He had a good physical condition, body weight of 83.8kg, height 1.81m, and body mass index of 25.6kg/m², with electrical bioimpedance (BIA) parameters showing lean body mass of 67.8kg, and body fat of 16kg. His daily habitual diet had about 3,000-3,500kcal, and was based on regional foods, including rice, beans, vegetables, no more than 160g of poultry, meat or fish/day, with five to six servings of fruits a day. The subject was a lifelong teetotaler, and practiced at least 40-60 minutes of aerobic exercise and about 60minutes of bodybuilding exercises by day. He did not take any medication, and his physical examination was normal, and so were his initial laboratory exams results (Table 1).

The subject stayed in rest at home most of his time, except when he left this house to light walk. He was fine without complaints all the time, except for drowsiness and slight weakness at the end of fasting period. He took nothing by mouth except about 2L of bottled mineral water each day, and refused to take omeprazole or antacids to ease an epigastric pain at the beginning of the fasting period. In table are shown anthropometry, BIA parameters and relevant laboratory data on basal, 7th, 14th, and 21st, as well as these parameters two weeks after resume feeding. The 21 days of fasting of this man was associated with a reduction of 15.5% (13kg) of body weight, with disproportionate higher loss of body fat (50%) than lean body mass (9.3%).

Discussion

Despite limitations of BIA to accurately measure body composition [4], data are in agreement with other studies showing higher weight reduction at the beginning of fasting period, with preferential lipid depletion during deprivation [5-8].

Progressive urinary and serum urea decrement, as well as the reduction of daily urinary creatinine excretion are also in accordance with decreasing body muscle mass [5,9,10]. Despite within normal laboratory reference range, a 10% increase in serum creatinine was observed. As the subject drank enough water, and maintained a normal urine output all the fasting period time, an intravascular volume contraction is not a reasonable explanation for this phenomenon, which can plausibly be associated with minor renal dysfunction [11]. In humans, the first week of fasting is associated with a marked increase in water excretion, suggesting impairment in the urinary concentrating mechanism [3,11]. In the rat, it was reported the occurrence of a decline in whole kidney glomerular filtration rate (GFR) at the beginning of fasting period, followed by an ulterior adaptive phase with normalization of GFR [3].

Despite low protein diet in humans for 7 days is associated with decreased synthesis of albumin, and increase in the synthesis of acute phase proteins such as haptoglobin and fibrinogen, the maintenance of serum albumin levels during 3-weeks of total fast is consistent with the serum albumin lifespan and the relative preservation of visceral protein synthesis [12,13].

The most remarkable findings of this case report are (i) the 60% reduction in the serum transferrin levels, with (ii) a fourfold increase in serum C-reactive protein and ferritin, and (iii) persistent reduction in the levels of serum haptoglobin, with normalization of all these laboratory data after 14 days of refeeding.

The differences in serum half-life of transferrin (5 days) and albumin (20 days) could explain the progressive reduction of the former in a 3 weeks period of fasting, but the increase in serum C-reactive protein suggest the occurrence of low-grade, sub-clinical inflammation as occur in atherosclerosis [14]. These findings are in accordance with the increase in oxidative stress in men and women submitted to nutrient and energy intake restriction for 21 days [15].

The remarkable increase in serum ferritin and decrease of haptoglobin levels suggest the occurrence of intravascular hemolysis [16]. Serum ferritin is increased in situation such as body iron excess, anemia of chronic diseases, or inflammatory diseases. Another explanation could be the occurrence of liver dysfunction as occur in non-alcoholic fatty liver, but the injury should be severe enough to decrease both albumin and haptoglobin synthesis. Haptoglobin is a protein synthesized in the liver and other tissues, such as skin, kidney and lung. She binds the free hemoglobin released by the erythrocytes. The complex haptoglobin-hemoglobin is removed from the body by mononuclear phagocyte system. Therefore, in the intravascular hemolysis, the haptoglobin serum levels are decreased [17].

As genetic and other aspects of iron metabolism were not studied, one cannot be assertive about the occurrence of hemolysis in this 40y old man fasting for 21 days. Two studies supporting this point of view: first, Wanby et al. [18] showed increase ferritin serum levels in adolescents with anorexia nervosa. An increased in ferritin serum levels in starvation may be due to hepatocyte dysfunction caused by starvation. The decreased of lean body mass, with consequent decrease in oxygen demand, combined with the limited availability of nutrients, leads to the suppression of bone marrow activity, which may explain the increased iron stores; second, Kennedy et al. [19] which described decreasing of serum ferritin levels after nutritional rehabilitation of adolescent female in patients with anorexia nervosa, suggesting that red blood cells are broken down with contraction of intravascular volume, with iron being deposited into body stores, resulting in increased ferritin.

These findings are in accordance with the concept of autophagy of red blood cells in adult starvation, as occur in liver, pancreas, kidney, skeletal muscle, and heart, and with the cell breakdown products providing substrates for both biosynthesis and energy generation, allowing survival [20].

Concluding, in this case report we described unforeseen laboratory features suggestive of intravascular hemolysis during starvation. This observation should prompt physicians to study iron metabolism in normal persons fasting for at least 7 days, and be careful in interpretation of serum ferritin levels in conditions associated with reduced food intake.

References

1. Benedict FG. A study of prolonged fasting. Carnegie Inst. Wash. Publ. 1915; 203.
2. Cahill GF, Herrera MG, Morgan AP, Soeldner JS, Steinke J, Levy PL, et al. Hormone-fuel interrelationships during fasting. *J Clin Invest.* 1966; 45: 1751-1769.
3. Amlal H, Chen Q, Habo K, Wang Z, Soleimani M. Fasting downregulates renal water channel AQP2 and causes polyuria. *Am J Physiol Renal Physiol.* 2001; 280: F513-523.
4. Piers LS, Soares MJ, Frandsen SL, O'Dea K. Indirect estimates of body composition are useful for groups but unreliable in individuals. *Int J Obes Relat Metab Disord.* 2000; 24: 1145-1152.
5. Cahill GF. Starvation in man. *N Engl J Med.* 1970; 282: 668-675.
6. Cahill GF. Starvation in man. *Clin Endocrinol Metab.* 1976; 5: 397-415.
7. Owen OE, Smalley KJ, D'Alessio DA, Mozzoli MA, Dawson EK. Protein, fat, and carbohydrate requirements during starvation: anaplerosis and cataplerosis. *Am J Clin Nutr.* 1998; 68: 12-34.
8. Cahill GF. Fuel metabolism in starvation. *Annu Rev Nutr.* 2006; 26: 1-22.
9. Consolazio CF, Matoush LO, Johnson HL, Nelson RA, Krzywicki HJ. Metabolic aspects of acute starvation in normal humans (10 days). *Am J Clin Nutr.* 1967; 20: 672-683.
10. Blackburn GL, Bistrian BR, Maini BS, Schlamm HT, Smith MF. Nutritional and metabolic assessment of the hospitalized patient. *JPEN J Parenter Enteral Nutr.* 1977; 1: 11-22.
11. Sigler MH. The mechanism of the natriuresis of fasting. *J Clin Invest.* 1975; 55: 377-387.
12. Jensen MD, Miles JM, Gerich JE, Cryer PE, Haymond MW. Preservation of insulin effects on glucose production and proteolysis during fasting. *Am J Physiol.* 1988; 254: E700-707.
13. Afolabi PR, Jahoor F, Jackson AA, Stubbs J, Johnstone AM, Faber P, et al. The effect of total starvation and very low energy diet in lean men on kinetics of whole body protein and five hepatic secretory proteins. *Am J Physiol Endocrinol Metab.* 2007; 293: E1580-1589.
14. Kivimäki M, Lawlor DA, Smith GD, Kumari M, Donald A, Britton A, et al. Does high C-reactive protein concentration increase atherosclerosis? The Whitehall II Study. *PLoS One.* 2008; 3: e3013.
15. Bloomer RJ, Kabir MM, Trepanowski JF, Canale RE, Farney TM. A 21 day Daniel Fast improves selected biomarkers of antioxidant status and oxidative stress in men and women. *Nutr Metab (Lond).* 2011; 8: 17.
16. Quaye IK. Haptoglobin, inflammation and disease. *Trans R Soc Trop Med Hyg.* 2008; 102: 735-742.
17. Jain S, Gautam V, Naseem S. Acute-phase proteins: As diagnostic tool. *J Pharm Bioallied Sci.* 2011; 3: 118-127.
18. Wanby P, Berglund J, Brudin L, Hedberg D, Carlsson M. Increased ferritin levels in patients with anorexia nervosa: impact of weight gain. *Eat Weight Disord.* 2016.
19. Kennedy A, Kohn M, Lammi A, Clarke S. Iron status and haematological changes in adolescent female inpatients with anorexia nervosa. *J Paediatr Child Health.* 2004; 40: 430-432.
20. Rabinowitz JD, White E. Autophagy and metabolism. *Science.* 2010; 330: 1344-1348.