Original Article

The effect of drinking cold water on fasting blood glucose, urea, uric acid, creatinine, liver transaminase enzymes activities, lipid profiles and thyroid hormones in rats

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Abstract

Background: The current study was designed to investigate the changes of fasting blood glucose (FBG), urea, uric acid, creatinine, aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), very low-density lipoprotein cholesterol (VLDL-c), high-density lipoprotein cholesterol (HDL-c), thyroid-stimulating hormone (TSH), thyroxin (T4) and triiodothyronine (T3) of rats after long-term drinking of cold water. **Materials and Methods:** In this experimental study, 12 adult male Wistar rats weighting 220-200 g were used. The rats were divided into 2 equal groups including, control and experimental groups. The control and experimental groups received normal water (20 ° C) and cold water (4 ° C) for 60 days, respectively. At the end of the 60 days, blood was taken from the heart of animals. After separating the serum, concentration of FBG, urea, uric acid and creatinine, ALT, AST, TG, TC, HDL-c were assayed by spectrophotometer and LDL-c, VLDL-c were calculated by the Friedewald formula. The serum concentrations of TSH, T4 and T3 were identified by ELISA. **Results:** Results showed that cold water significantly increased the levels of ALT,AST,TG, LDL,VLDL,TSH,T4 and T3 ($P<0.05$) and had no significant effect on urea, uric acid, creatinine, TC and HDL levels in experimental group compared to control group. **Conclusion:** Cold water can have a devastating effect on the metabolism of the body in the long-term. Although more studies are needed.

Keywords: Cold water, liver enzymes, thyroid hormones

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Introduction

Ibn Sina (also known as Avicenna in the West), the most famous physician of the medieval era, has a book of Canon. The Canon is compiled on the basic sciences of medicine, diseases and their treatment (1). Water and its importance in maintaining health are important parts of the book of Canon. Classification of water types is important in terms of harvesting method, water quality, extraction sources and water temperature(2). According to Avicenna, the cold water and water in the direct or indirect vicinity of the ice are, harmful to the neural tissues of the body and internal organs, and continuous intake is associated with the several dysregulations such as lower body energy, liver function damage, heart rate drops, constipation and headache. Due to increasing public access to water and cold drinks cold

water on the negative impact health it became an important issue in medical written sources (2). Despite its daily usage, metabolic responses to water ingestion in humans are not well understood. However, some study reported, the drinking water induces short-term cardiovascular and metabolic changes (3). Clive and et al. reported drinking cold water in healthy subjects increase energy expenditure compared to healthy subjects who drink water at room temperature (4). It has been shown that immersion rats with metabolic syndrome in cold water induced adipose and cardiac tissue abnormality as well as abnormal glucose and lipid metabolism (5). Today, the application of cryotherapy or localized cold is widely used to reduce the inflammatory response in injured tissue (6). In general, studies suggest that osmotic changes occur in the body by water consumption, which changes the function of the autonomic nervous system and the endocrine system (7).

The aim of this study was to evaluate the effects of cold water compared to water at room temperature on fasting blood glucose (FBG), urea, uric acid, creatinine, aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), very low-density lipoprotein cholesterol (VLDL-c), high-density lipoprotein cholesterol (HDL-c), thyroid-stimulating hormone (TSH), thyroxin (T4) and triiodothyronine (T3) of rats after long-term drinking of cold water.

Methods

Animals, Chemicals and Devices. In this experimental study, 12 male Wistar rats (200-250 g) were supplied from the central animal house, Arak University of Medical Sciences. All rats were kept 12 hours of darkness and 12 hour of light conditions, temperature 25 ± 2 ºC, appropriate humidity and conditions standard laboratory inside special cages. Animals were received standard food (prepared from the Pars Animal Feed Company) and had free access to water. The protocol of the present study was approved by the Animal Care and Use Committee of the Arak University of Medical Sciences and Ministry of Health. The serum concentrations of fasting blood glucose (FBG), urea, creatinine, total cholesterol (TC), triglycerides (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-c) were measured enzymatically using commercial kits (Pars Azemoon, Tehran, Iran) and spectrophotometer (JENWAY 6505, Europe Union). The serum low-density lipoprotein cholesterol (LDL-c) and very low-density lipoprotein cholesterol (VLDL) were calculated by the Friedewald formula (12) as follows: LDL-c = Total cholesterol – [HDL-c + (TG/5)] and VLDL-c = TG/5. Hormonal tests included thyroid-stimulating hormone (TSH), thyroxin (T4) and triiodothyronine (T3) in the study groups were identified by Enzyme-linked immunosorbent (ELISA) by an ELISA reader (ELX 800 TM ELISA reader Bio Tek, Winooski, VT, U.S.A). This kits were purchased from the Bioassay technology laboratory (Shanghai, China).

Experiment design. The rats were randomly assigned (simple randomization) to the control and treatment groups; 6 rats in each group. These two groups were received the following regimens for 60 days: The first group (group I) was the control group receiving water at room temperature and food, the second group (group II) was the treatment group receiving cold water and food. In order to create the same conditions with daily consumption of cold water by people, water bottles were frozen at a temperature below 4 ° C and placed in available to the experimental group. By gradually melting water and consuming it for 6 hours at an animal's house temperature, the average water temperature was estimated to be 4 degrees in the experimental group. At the end of study, blood sample was collected by cardiac puncture and serum was separated immediately. All samples were stored at -70°C. It should be noted that all serum samples were aliquoted in a separate microtube and then coded for biochemical and ELISA tests.

Statistical analysis. The normal distribution of data was assessed using the D'Agostino test. Since the data had been normally distributed, the Student-T-test was employed to calculate and compare the means and standard error deviations (SEM) [data is expressed as means ± SEM] of serum parameters separately for each group. Significant level was defined as less than 5% ($p < 0.05$). The data were analyzed by Graph Pad Prism software (Version 6.00).

Table1. Effect drinking of cold water and water at room temperature on serum FBG, ALT, AST, urea, creatinine and uric acid in studied rats a,b.

Group	FBG (mg/dl)	ALT(U/l)	AST(U/l)	Urea(mg/dl)	Creatinine (mg/dl)	Uric acid(mg/dl)
I	157.8±10.7	172.8±11.7	61.8±1.4	48.1±2.5	2±0.16	1.23±0.15
II	116.3±8.4C	231.2±16.2C	73±2.2C	28.6±4.6D	3.8±0.28D	1.27±0.2 D

[a]Each value is mean ± SEM of 6 rats in each group.

[b]Abbreviations: FBG, triglycerides; ALT, low-density lipoprotein cholesterol; AST, high-density. Group I: received water at room temperature; Group II: received cold water.

[C] P < 0.05 in comparison with Group I.

[D] P > 0.05 in comparison with Group I.

Table2. Effect driking cold water and water at room temperature on serum lipids profile in studied rats a,b.

Group	TG (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	TC (mg/dl)	HDL (mg/dl)
I	59.6±4.3	37.8±7	2±0.16	75.6±5.7	48.1±2.5
II	177.8±33.9C	46.6±7.5C	3.8±0.28D	79,5±0,2 D	42,1±4,6 D

[a] Each value is mean ± SEM of 6 rats in each group

[b]Abbreviations: TG, triglycerides; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol and VLDL-c, very-low-density lipoprotein cholesterol. FBG, triglycerides; ALT, low-density lipoprotein cholesterol; AST, high-density. Group I: received water at room temperature; Group II: received cold water.

[C] P < 0.05 in comparison with Group I.

[D] P > 0.05 in comparison with Group I.

Table3. Effect drinking cold water and water at room temperature on serum TSH, T4 and T3 in studied rats a,b.

Group	TSH(µg/dl)	T4(µg/dl)	T3(µg/dl)
I	3,4±0,3	2.9±0.2	2.6±0.3
II	5.3±0.4C	5.4±0.2C	3.5 ± 0.2 C

[a]Each value is mean ± SEM of 6 rats in each group

[b]Abbreviations: TSH, Thyroid-stimulating hormone; T4, Thyroxin; T3, Triiodothyronine, Group I: received water at room temperature; Group II: received cold water.

[C] P < 0.05 in comparison with group I.

Results

FBG, ALT, AST, urea, creatinine and uric acid levels. Table 1 presents the effect of cold water compared to water at room temperature on changes of FBG in two group. The FBG of the group I was significantly less than the group II (P< 0.05). The data showed that serum ALT and AST of the group II were significantly higher than the group I (P< 0.0 01). However, data showed that cold water did not significantly affect the serum creatinine, urea and Uric acid levels in group II (P> 0.0 5).

Serum lipid profile levels. The effect of cold water and water at room temperature drinking on lipid profile was shown in table 2. The TC and HDL-c concentrations in the serum were no significant between group I and group II (p>0.05). But, the drinking of cold water caused significantly increased in the serum TG, VLDL-c and LDL-c in group II than group I (p<0.001).

Level of TSH, T4 and T3 hormones. As shown in Table 3, Serum TSH, T4 and T3 were significantly increased by drinking cold water (p<0.05).

Discussion

This study was conducted for the first time to investigate the effect of long-term drinking cold water on metabolic indices. Generally, our data showed that long-term usage of cold water can alter the body's metabolic activity pattern. The major cause of these changes can be attributed to cold water due to changes in thyroid hormones. The regulation of the body temperature involves a part of the brain, the pituitary gland, the thyroid gland, and conversion of thyroid hormones in the tissues of the body (8). Some previous studies indicated that patients with hyperthyroidism

(an overactive thyroid) or hypothyroidism (an underactive thyroid) often feel that they are too hot or too cold, respectively (9). As well as, exposure to cold environments has been shown to result in higher rates of thyroid hormones turnover. The cause of this phenomenon has so far been attributed to the thyroid hormones' general effect on the metabolism in the cells themselves (10). In this regard, our data demonstrated that the TSH, T4 and T3 significantly increased in group receiving cold water than the group receiving water at room temperature, this result shows that cold water can effect on thyroid function and metabolism. This increase has probably occurred to increase body temperature due to long-term drinking cold water. Increased thyroid hormone can increase metabolism and energy expenditure in the body (11). Our results showed that the FBG levels in serum has significantly decreased in the group II than the group I. These results suggest that the cold water in the long term raises energy consumption, this is probably due to increased thyroid hormone levels. It has been reported that thyroid hormones can affect the metabolism of the liver (12). Upadhyay et al (13), shows that elevated levels of T3 induces apoptosis of hepatocytes and causes hepatic dysfunction through the activation of the mitochondrial dependent pathway. The results of our study showed that the serum levels of the ALT and AST were significantly higher in the group II than the group I. These findings propose that cold water has a harmful effect on liver function. Extensive thyroid hormone activity regulates the body's metabolic, today it has been proven that thyroid dysfunction (both hypo- and hyperthyroidism) are associated with alternations in lipid and glucose metabolism (8, 14). Studies have shown, hyperthyroidism leads to an increase in lipolysis and thus reduces body weight, reduces HDL, LDL and leptin levels (14). Conversely, hypothyroidism has the opposite effects: hypothyroid patients are presented with higher plasma TG, total cholesterol, and LDL cholesterol levels (14, 15) . This study showed that the lipids metabolism could be changed by the long-term effects of cold water consumption, so that significantly increased TG, VLDL and LDL but does not affect the amount of TC and HDL. This is probably due to increased thyroid hormones and increase in lipid release into the bloodstream. The kidneys also participate in the metabolism of thyroid hormones and also a target of some of its actions (16). Some effects of thyroid dysfunction on kidney which include changes in water and electrolyte metabolism, notably hyponatremia and hypernatremia , remarkable changes in glomerular and tubular functions (16). However, the results of this study showed that cold water had no effect on uric acid, urea and creatinine levels and therefore probably did not affect the function of the kidneys. Our study was the first report about evaluating effects of drinking cold water on metabolic indices, however, there is a need for extensive study on more metabolic parameters.

Conclusion

In conclusion, our results indicate that drinking cold water changes in the pattern of liver function, thyroid hormones and lipid profiles, and ultimately changes the other organ function. Although more studies are needed for confirming these effects.

Conflict of interest

The authors declare that they have no conflict of interests.

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References

1. Mazengenya P, Bhikha R. A critical appraisal of 11th century treatise by Ibn Sina (Avicenna) on the anatomy of the vascular system: Comparison with modern anatomic descriptions. Morphologie. 2018;102(337):61-8.
2. Ibn-e-Sina AH. Al-qanun fit-tib [The canon of medicine]. Beirut, Lebanon: Alaalami Beirut lib Press; 2005.
3. Girona M, Grasser EK, Dulloo AG, Montani JP. Cardiovascular and metabolic responses to tap water ingestion in young humans: does the water temperature matter? Acta Physiol. 2014;211(2):358-70.
4. Brown CM, Dulloo AG, Montani JP. Water-induced thermogenesis reconsidered: the effects of osmolality and water temperature on energy expenditure after drinking. J Clin Endocrinol

Metab. 2006;91(9):3598-602.
5. Nagasawa K, Matsuura N, Takeshita Y, Ito S, Sano Y, Yamada Y, et al. Attenuation of cold stress-induced exacerbation of cardiac and adipose tissue pathology and metabolic disorders in a rat model of metabolic syndrome by the glucocorticoid receptor antagonist RU486. Nutr Diabetes. 2016;25(6):14.
6. Zhang J, Pan T, Wang JHC. Cryotherapy suppresses tendon inflammation in an animal model. Journal of orthopaedic translation. 2014;2(2):75-81.
7. Stocker SD, Osborn JL, Carmichael SP. Forebrain osmotic regulation of the sympathetic nervous system. Clin Exp Pharmacol Physiol. 2008;35(5-6):695-700.
8. Mullur R, Liu Y-Y, Brent GA. Thyroid Hormone Regulation of Metabolism. Physiological Reviews. 2014;94(2):355-82.
9. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology. 2018;14:301.
10. Ribeiro MO, Carvalho SD, Schultz JJ, Chiellini G, Scanlan TS, Bianco AC, et al. Thyroid hormone–sympathetic interaction and adaptive thermogenesis are thyroid hormone receptor isoform–specific. The Journal of clinical investigation. 2001;108(1):97-105.
11. Kim B. Thyroid hormone as a determinant of energy expenditure and the basal metabolic rate. Thyroid. 2008;18(2):141-4.
12. Khemichian S, Fong T-L. Hepatic Dysfunction in Hyperthyroidism. Gastroenterology & Hepatology. 2011;7(5):337-9.
13. Upadhyay G, Singh R, Kumar A, Kumar S, Kapoor A, Godbole MM. Severe hyperthyroidism induces mitochondria-mediated apoptosis in rat liver. Hepatology. 2004;39(4):1120-30.
14. Chen Y, Wu X, Wu R, Sun X, Yang B, Wang Y, et al. Changes in profile of lipids and adipokines in patients with newly diagnosed hypothyroidism and hyperthyroidism. Scientific reports. 2016;6:26174.
15. Harvey CB, Williams GR. Mechanism of thyroid hormone action. Thyroid. 2002;12(6):441-6.
16. Iglesias P, Diez JJ. Thyroid dysfunction and kidney disease. Eur J Endocrinol. 2009;160(4):503-15.