The effects of hydration status on cardiovascular system: a review

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ABSTRACT

Fluid balance is essential for life. Some studies have shown an association between high intake of water and a low risk of cardiovascular diseases. However, the evidence is insufficient or inconsistent to draw substantial conclusions. The author's objective was to review previous studies addressing the influence of drinking water and hydration status on the cardiovascular system. The PubMed and Google Scholar databases were searched using relevant terms. Animal and human studies in the English language which were highly relevant to the topic were selected and summarized. Drinking about half a liter of water rapidly raises sympathetic activity as much as classic sympathetic stimuli such as caffeine and increases plasma norepinephrine leading to peripheral vasoconstriction. However, cardiac vagal tone enhancement with water ingestion buffers the pressor effects of sympathetic activation. Dehydration leads to mild hypernatremia which gradually causes changes such as increased blood viscosity, hemoconcentration, inflammatory signals, platelet activation and aggregation, adhesive properties of endothelial cells, thrombogenesis, and so on, all of which are harmful to the cardiovascular system. Overhydration can result in water intoxication and increase coagulability. Both dehydration and overhydration are associated with several adverse effects on the cardiovascular system. However, the data regarding how much water can reduce the risk of heart disease is limited and the results are also controversial. More research is needed to confirm the observed associations between hydration status and cardiovascular diseases.

1. Introduction

There is an association between dehydration and overhydration with morbidity and mortality (1). Therefore, adequate hydration is essential for the optimal functioning of the human body (2). The amount of fluid intake and fluid loss varies between individuals, and hydration status is not equal in the population as well. Therefore, links between water intake and health outcomes are not easy to assess. Extensive studies of dehydration in cell-culture systems and animal models have provided a wealth of information on the mechanisms by which a high-water intake may lower the risk of chronic disease in humans. High water intake may provide protection against cardiovascular disease (CVD), fatal coronary heart disease (3), hypertension, venous thromboembolism (VTE), and cerebral infarct (4). The associative evidence comes from observational and epidemiologic studies. However, some studies have demonstrated increased coagulability associated with postoperative fluid overload (5). This review summarizes the effects of water drinking, dehydration, and overhydration on the cardiovascular system. In this study, investigate electronic databases such as PubMed and Google Scholar databases were searched for relevant studies published up to 2018 using the following keywords: dehydration, overhydration, water overload, water deprivation, water restriction, water drinking, and cardiovascular. The titles of articles obtained as a result of the search were reviewed initially. If they were considered suitable, then the abstracts were reviewed and, if suitable, the full manuscripts were reviewed. Animal and human studies in the English language, which were highly relevant to the topic, were selected. The final number of articles reviewed was 100.

2. Cardiovascular responses to water drinking

The physiological response to water drinking in healthy subjects consists of activation of sympathetic and vagal

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branches of cardiovascular autonomic regulation (6, 7). Ingestion of about half a liter of water rapidly raises sympathetic activity leading to peripheral vasoconstriction lasting for up to 60 minutes. In fact, water drinking as much as classic sympathetic stimuli such as caffeine and nicotine increases plasma norepinephrine. In young healthy persons, this effect causes little or no change in blood pressure. While a moderate pressor response of 11 mmHg is caused in normal elderly subjects. However, in autonomic failure patients, blood pressure increases by more than 30 mmHg and lasts for up to 60 minutes (8, 9) (Fig. 1).
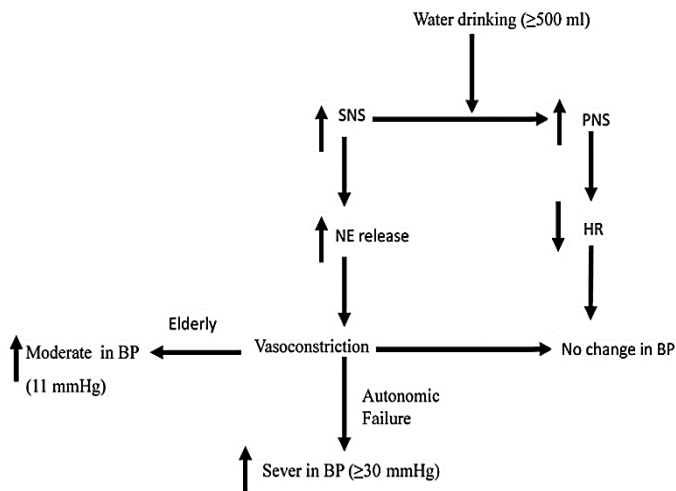

Fig 1. The effect of water drinking on blood pressure. SNS: the sympathetic nervous system; PNS: the parasympathetic nervous system; HR: heart rate; BP: blood pressure.

Decreased heart rate concurrent with increased cardiac interval variability, which is an indicator of cardiac vagal tone at resting conditions, indicate that the parasympathetic nervous system is implicated in cardiac response to water drinking (10). Therefore, in young normal subjects, water ingestion enhances cardiac vagal tone that may buffer the pressor effects of sympathetic activation. That is why no change or even a slight reduction in heart rate is observed after water drinking. Lack of this buffering mechanism is a cause for the pressor response to drinking water in older subjects and autonomic failure patients (7). Decreased rate pressure product, a simple product of systolic BP and heart rate, provides additional proof that water drinking decreases cardiac workload in young and healthy subjects (10). Although water intake causes a small increase in stroke volume, a greater reduction in heart rate provides a possible explanation for the decline in cardiac output. This concept is further strengthened by no changes in cardiac contractility post-drink in healthy subjects (10). Lu et al. found that after ingestion of 500 ml water, the cardiac index and skin blood flow immediately decreased and remained below control levels for up to 50 min (11). Different opinions have been raised about the actual stimulus setting off the cardiovascular autonomic responses to water drinking. The responses to water drinking may be triggered by gastric distension (12), water's hypo-osmotic properties (6), and water temperature (13). The findings of previous studies confirm the existence of a functional relationship between gastrointestinal distension and cardiovascular function. In young healthy subjects, gastric distension induces gastrovascular reflex causing an increase in muscle sympathetic activity, and a reflex increase in arterial pressure and heart rate (12,14). However, contrary to gastric distension, water drinking decreases heart rate. Decreases in the gut and portal osmolality induce cardiovascular reflexes (15). It has been reported that drinking water, but not the same amount of a physiological saline solution, decreases heart rate and increases TPR, cardiac interval variability, and baroreflex sensitivity, indicating the hypo-osmotic properties of water play a role in the cardiovascular responses to drinking. It appears that local stimulation of osmoreceptors in the gut or portal circulation (16) induces responses, even without any major changes in overall plasma osmolality (6). About the effect of water temperature, it has been reported that ingestion of water at 3°C (cold) and 22°C (room), but not at 37°C (body), leads to decreased heart rate and double product, and increased stroke volume, cardiac interval variability, and cardiovagal baroreflex sensitivity (13). An explanation for these results is related to the activation of thermosensitive afferent vagal nerve fibers which are distributed along the gastrointestinal tract (17). The existence of the transient receptor potential channels (TRP) in subtypes of vagal afferent neurons that project to the stomach may give temperature sensitivity on these cells (18). A sub-member of the TRP family, TRPV4 is a molecular sensor that exhibits responsiveness to both heats (at temperatures between 25 °C and 34 °C) and hypo-osmolarity (19) and, therefore, could be the link between the intestinal absorbed water and activation of vagal tone (10). The effects of dehydration on the cardiovascular system. Researchers usually use two methods to study the effects of dehydration on the body. The effects of acute dehydration have been performed in animals subjected to varying periods of water deprivation (the complete withholding of water). In chronic studies, instead of deprivation, water consumption is decreased to either a specific daily ration or planned for only a specified period per day. A physiological adaptation is produced in chronic water restriction.

3. The effects of water deprivation

Water deprivation (WD) differentially impacts on the body systems based on animal species. It significantly influences hematologic and cardiovascular indices. In mice, WD for more than 24 h results in reduced food intake with 18% body weight loss, increased plasma osmolality, sodium concentration accompanied with a decrease in plasma volume, hemoconcentration with significant increases in urea, plasma total protein, serum corticosterone, plasma renin activity (PRA), with a 3-fold increase after 24 h and 6-fold increase after 48 h, which stimulate aldosterone release (20). In response to WD for 24 hours, healthy elderly men showed

greater increased plasma osmolality, sodium concentration, vasopressin levels, and reduced thirst and water intake compared with younger men (21). During WD, hyperosmolarity directly stimulates osmosensory neurons in the forebrain lamina terminalis that project to the hypothalamic paraventricular nucleus (PVN) (22). PVN is considered as the important central site for the regulation of sympathetic nerve outflow (23). Increased sympathetic nervous activity (SNA) was reported in water-deprived rats (24-26). Therefore, plasma hyperosmolality could play a major role in the increase in sympathetic activity (22). In addition, secretion of AVP (the first hormone secreted during dehydration) and corticotropin-releasing hormone (CRH) from PVN neurons stimulates the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary, which stimulates adrenal glucocorticoids, cortisol in humans, and corticosterone in rodents (27). In rats, WD for 48 hours is associated with increased renin-angiotensin system (RAS) activity (28), elevated plasma vasopressin, and norepinephrine (29). Both WD and hyperosmolality increase the release of angiotensin II (ANG II) in PVN and circulation. ANG II influences the function of the entire adrenal gland and stimulates cortisol secretion directly from the adrenal fasciculata (30). On the other hand, ANG II through stimulation of the hypothalamic-pituitary axis during dehydration increases plasma ACTH and thence cortisol (31). Excessive cortisol is associated with hypertension, immunosuppression, and metabolic syndrome along with their morbid squeal of atherosclerosis and cardiovascular disease (32, 33). In dehydrated goats for 24 h, increased blood pressure during the act of drinking can be due to sympathetic activation (34). Dehydration was also accompanied by an increased tendency to form clots (35). It has been demonstrated an increase in adhesive properties of normal erythrocytes with increasing dehydration (36). A study showed that a few days after an acute ischemic stroke, patients with serum osmolality of more than 297 mOsm/kg had an increased rate of venous thromboembolism (VTE), indicating a highly independently associated with this marker of dehydration (37). Dehydration enhances reactive oxygen species (ROS) production (38) that triggers high lipid peroxidation resulting in an increased malondialdehyde (MDA) formation (31).

4. The effects of water restriction

Adaptation to chronic water restriction with minimal physiological disturbances has been shown in some studies. This physiological adaptation maintains plasma volume and osmolality within set limits by the release of hormones necessary to conserve water and sodium within the body (39). A study indicated that dry Awassi ewes that received water once every 2 days can withstand a water restriction regime for more than 1 month with minimal variation in physiological parameters (40). Bekkevold et al observed that chronic restriction of water consumption as much as 50% of the normal daily ration for 7 d in mice resulted in apparent physiologic adaptation, as evidenced by a minimal body weight loss of 9% with no significant changes in the physiological indices compared with ad libitum availability. However, serum corticosterone elevated significantly water-restriction protocols (20). Plasma total protein, albumin, glucose, Hct, plasma volume, and osmolality are kept at a normal level throughout the restriction period (41). It is concluded that rodents are physiologically capable to deal with chronic water restriction (20). The results of a study regarding the effect of intermittent watering also demonstrated lambs that watered ad libitum once a day could tolerate water restriction for at least 28 days without adverse effects (42). male rats restricted to 15 min access to water every 24 h did not have changes in behavior or corticosterone levels 37 days after the start of the experimental period (43). Female rats restricted to 1 hour per day access to water showed an altered circadian rhythm of pituitary-adrenal activity so that a peak of plasma corticosterone appears before the time of water presentation. For instance, water restriction in the morning leads to a significant increase in pre-water levels of circulating corticosterone without affecting evening levels (44). Therefore, according to the watering time, different patterns of adrenocortical rhythms are observed (45). Interestingly, a substantial and rapid decrease in corticosterone levels (more than 50% within 10 min) occurs post-water period in both morning and evening water restricted animals (44). For drinking-induced reduction in plasma corticosterone, an intact vagus nerve is necessary (27). In line with this finding, it has been shown that plasma cortisol, creatinine, and AVP levels are significantly higher among the habitual low drinkers (≤1.2 L water/day) compared to high drinkers (2–4 L water/day). The similarity in plasma osmolality between the groups demonstrates that physiological compromises occurred to maintain plasma osmolality despite low water consumption (46). It has been shown that the adaptations to preserve plasma osmolality have side effects over time. Evidence from the literature suggests low urinary flow rates due to a low water intake reduce the capacity of sodium excretion (47), possibly through vasopressin-mediated upregulation of epithelial sodium channels (48) and Na K-ATPase in the renal collecting duct (49). In rats, mild dehydration with sustained high levels of AVP could increase the risk of sodium retention (50). The possible deleterious effect of increased sodium retention is the development of salt-sensitive hypertension (51) in humans. Elevation of plasma sodium, even within the physiological range, induces inflammatory signaling in mouse tissues, and increases adhesive properties of endothelial cells, coagulability, and risk of thrombosis (52), and leads to vascular changes that promote atherosclerosis and thickening of the walls of coronary arteries (53). Mild dehydration increases adhesion molecules VCAM1, E-selectin, and chemoattractant MCP-1expression in mouse tissues. These molecules are involved in leukocyte-endothelial cell adhesion, transmigration, inflammation, and vascular changes and lead to the pathogenesis of CVD (53). A significantly increased serum cholesterol in water restricted mice might be an additional factor resulting in the acceleration of atherosclerosis (54). Increased sodium concentration within the physiological

range in mice subjected to water restriction stimulates production and secretion of von Willebrand factor (vWF) from endothelial cells in several tissues in vivo (52). The increase in vWF leads to platelet activation and aggregation. Platelets and vWF are key initiators of the blood clotting cascade. Given that hypercoagulability is linked to cardiovascular disease and atherosclerosis, increased vWF is considered as an important risk factor for thromboembolism, myocardial infarction, and stroke (55). It is shown that AVP infusions increase plasma factor VIII and vWF (56). On the other hand, water restriction increases plasminogen activator inhibitor 1 (PAI-1), a major inhibitor of fibrinolysis, in plasma which delays degradation of fibrin clots. Analysis of data from the Atherosclerosis Risk in Communities Study showed that serum sodium significantly contributes to the prediction of plasma level of vWF and risk of stroke in humans (52). Alteration in the expression of water channels and the RNase III enzymes in the blood and kidney of chickens under a short-term water restriction was reported (57). These results could provide new insights for the identification of the molecular mechanism involved in adaptation to water-restriction stress. The predominant water channel in the human heart is aquaporin-1 (AQP1). AQP1 protein levels on the cardiomyocyte plasma membrane were increased after water restriction (58). It is suggested that cardiovascular AQP1 has an important role in maintaining fluid balance during the hypovolemic state (59). AQP1 facilitates NO transport across cell membranes at physiological concentration ranges. Considering the importance of NO in the regulation of blood pressure and cardiac function, alterations in NO transport by AQP1 may be an alternate explanation for many diseases, especially hypertension, currently explained by inadequate NO bioavailability (60).

5. The effects of overhydration on the cardiovascular system

Excessive water intake can lead to water intoxication and death as a result of hyponatremia and cerebral edema (61). Overhydration has been seen in some psychiatric disorders (62), endurance athletes, and Army trainees (63, 64), and in individuals susceptible to water retention (65). Fluid overload most commonly results from overprescribing intravenous fluids, most notably in hospitalized surgical patients (66). This can result in heart failure, pulmonary edema, and renal impairment (1). Some cohort studies have demonstrated increased coagulability associated with postoperative fluid overload. A Possible explanation is that haemodilution reduces the activity of anticoagulant factors predisposing to thrombin generation (5).

6. Conclusion

Distinct cardiovascular changes in young and healthy subjects after water drinking are related to an increase in sympathetic vasoconstrictor activity coupled with a parallel increase in cardiac vagal activity. The existence of thermosensitive and osmoreceptive afferent vagal nerve fibers in the gut or portal circulation can influence cardiovascular autonomic regulation in humans. However, a pressor response to water drinking in elderly subjects and patients with autonomic failure is due to a deficiency in the cardiac vagal component of this integrated response. Little evidence-based data is connecting optimal hydration and cardiovascular health. Negative effects of dehydration on cardiovascular parameters are extracted from the literature. Because there is no "gold standard" for hydration markers, particularly for mild dehydration, the effects of mild dehydration on the development of cardiovascular diseases have not been well documented. Dehydration can elevate at least four independent risk factors for coronary heart disease: whole blood viscosity, plasma viscosity, hematocrit, and fibrinogen. Increased coagulability is a consequence of increased osmolality, sodium concentration, blood viscosity, and hemoconcentration. Therefore, subclinical dehydration may impair health through the increase in coagulability. Since the osmotic threshold for AVP release is lower than that for thirst, during normal living conditions AVP is constantly present in the blood, whereas the perception of thirst is intermittent. Furthermore, the sensitivity of the osmoregulatory systems is not equal in all healthy individuals, so it could be expected that some subjects tend to be continuously in a state of mild dehydration and have a high level of vasopressin to compensate. Especially in elderly persons that there are reduced thirst and water intake following dehydration and their kidneys are less able to retain water due to relative renal resistance to vasopressin. The findings suggest that elevated levels of serum sodium and vasopressin following very mild dehydration that could occur in everyday life is a risk factor for CVDs and VTE in various populations and support recommendations for adequate hydration to prevent CVDs. How much water each one needs depends on a range of factors, such as body weight, age, sex, physical activity level, and climate. Therefore, the amount of water needed differs for each individual. Some people still follow the 8 x 8 rule, but there is no scientific evidence that we need to drink at least eight 8-ounce glasses of water per day. The fact is the mean daily fluid intake of thousands of presumably healthy persons is less than the 1,900 ml prescribed by 8×8. Drinking ad libitum or by instinct may not be adequate. One needs to drink more water to improve their hydration status to better their health. Generally, because of the lack of accepted screening tools for easily performable and replicable measurements of fluid balance, further studies are required to address the challenges related to hydration status and its effect on heart health.

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