### **Review Article**

## Impact of High NaCl Concentration in Drinking Water on Health of Different Human Organs; Review Article

Majid Zamani beidokhti1, Daryoush Yousefi Kebria1, Shima Mehrabadi2\*.

- 1. Environmental Engineering Department, Faculty of Civil Engineering, Babol Noshirvani University of Technology, Babol, Iran
- 2. Department of Medical Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

\*correspondence: **Shima Mehrabadi**, Department of Medical Physiology, Faculty of Medicine, Tehran University of Medical Sciences, Tehran, Iran. Email: sh-mehrabadi@razi.tums.ac.ir

#### Abstract:

Sodium chloride (NaCl) that commonly named dietary salt is most important electrolyte in our body. NaCl has many role in health of many human organs. Normal function of CNS, cardiovascular system, kidney and other organs are dependent to NaCl concentration. NaCl controlled blood. small changes NaCl concentration is very conscious Any in in concentration in blood can cause major changes in blood volume and may lead many conditions like: heart disease, kidney failure, encephalopathy, pathophysiology stroke, high with blood pressure. Due to geographical diversity, in different region, people are exposed different range of NaCl concentration. This is a novel issue that how much of the health of people from different region is related to salt level. Because of the importance of this issue, advantages and the aim of this study is to review studies that performed about in this issue, disadvantages of different level of NaCl in health of people from different region and in each of region which disease more common due to impaired NaCl homeostasis.

Keywords: NaCl, kidney, heart, CNS, water drinking.

#### **Introduction:**

The major salt that exists in human body is NaCl. So in human, around 0.4 per cent of the body's weight is NaCl. A concentration that pretty equivalent to that in seawater(1). In addition of NaCl, other salt exists in drinking water. Total salt in drinking water measured by: 1- Total Dissolved Solids (TDS) and 2- Electrical Conductivity (EC).TDS in drinking water should not exceed 500 mg/L(1). Although water with a TDS content of up to 1000 mg/L is acceptable in water scarce regions. Water will become undrinkable up to 1000 mg/L(2)(3). NaCl is crucial for body hemostasis maintenance. Function of our nervous system, our muscles to contract and

relax, and fluid balance is related to blood NaCl concentration(4). Also if we intake more salt it can be harmful for health of different body organs(5). So the level of NaCl in extracellular fluids is carefully maintained by the kidney and determines the volume of fluids. Na+ is most important cation in body. The level of Na+ controlled by nervous system and many hormones(6). It has been estimated that daily intake of 120-400 mg need to grow of infants and children, and 500 mg also need for adults(7). Nonetheless, people around the world exposes with different concentration of NaCl based on their dietary plan and water. There is a lot of diseases that associated with imbalance of NaCl hemostasis in our body(8). We classified water based on TDS to 5 group: 1- Fresh water: Less than 1000 ppm, 2- Slightly saline water: from 1000 ppm to 3000 ppm, 3- Moderately saline water: from 3000 ppm to 10000 ppm, 4-Highly saline water: from10000 ppm to 35000 ppm, 5- Ocean water contains about 35000 ppm of salt, also there is an extensive amount of very salty water in a round of the world(3)(9). We assess change of NaCl concentration in different region how can effect on health of different organs.

### NaCl concentration and kidney function:

NaCl concentration is regulated by kidney precisely. Regulation of NaCl and also water is highly regulated by vasopressin (antidiuretic hormone or ADH) this hormone secretes by posterior pituitary gland to response of many conditions like: dehydration, hypovolemia, hyper osmolality and circadian rhythmicity(10)(11). Serum osmolality is an exquisitely sensitive but less potent AVP stimulant. A small rise in osmolality, even within physiological range (280-295 mOsm/kg), can trigger a high rise of circulating AVP. Actually high salt and lower -water intake increase the level of ADH in circulatory system and these hormone may lead many pathogenic conditions in body especially hypertension and chronic kidney disease(12). Excessive salt intake lead to increase of extracellular volume and high blood pressure(13)(14). Increase of blood pressure also can damage Glomeruli and nephrons(15). So high salt intake are very dangerous for kidney disrupt kidney function and may damage kidney tubular and nephrons(16). Also hyposmolality of circulatory system as a

result of losing NaCl (hyponatremia) in many conditions like sweating too much, hemorrhage or low salt intake also cause disruption in kidney function(17). In central part of kidney, there is hyper-osmolality fluids that is responsible for concentration of urine in dehydration conditions(18)(19). When NaCl concentration disrupt in central part of kidney, we lose a lot of water. Basically in all around of world, drinking water and nutrients have NaCl even more than we need (20). Hyponatremia happens more when someone sweets a lot(21). In tropical regions, level of NaCl in drinking water is high and can support need the body(22)(23). So nature meets the needs of body to NaCl and does not need to consume more NaCl by our regime. Also there is a lot of NaCl in nutrients that we consume every day(24). But in vegetarian people, due to their diets, they consume less salt in their life.So they must be regulate their diet to consume NaCl needs from other resource, like water (25) (Figure 1).

### NaCl concentration and heart failure:

Changes in level of NaCl concentration in blood also can make important and vital problems for heart function and circulatory system(26)(27). Studies indicated excess dietary salt is an important cause of hypertension. When we use NaCl more, plasma volume are also increased especially in salt sensitive people. So it resulted to high blood pressure(27). Hypertension can make disaster for heart. Heart work increase according with elevating of blood pressure (BP)(28). The initial BP elevation in response to a high-salt diet is due to plasma volume expansion and an increase in cardiac output (CO), where  $BP = CO \times TPR$  (total peripheral resistance)(29)(30). Also when NaCl concentration increase in BP, it can result to elevate NaCl in CSF (cerebrospinal fluid) that can activate sympathetic center in CNS and induce the secretion of hormones. When Na+ increase in CSF, hypothalamic signaling chain includes adrenocorticotropic hormone- aldosterone, angiotensin II (ANG II) activate more(31). All these hormones involved in Na+ homeostasis but also directly interact with hypothalamic neurons, kidneys, adrenals, and arteries(31)(32). Also increase of Na+ concentration can increase sympathetic drive and in the periphery to augment arterial Ca2+ signaling and vasoconstriction as a result of different effects on the myocytes and endothelium(33)(34).So increase of sympathetic drive and ANG II increase vasoconstriction, and this phenomena increase resistance in circulatory system that lead to high blood pressure(34) (Figure 2). Increase of blood pressure cause increase of over load to heart and so increase heart work. These problems cause myocardial damage, risk of heart attack, and myocardial infarction(35). So we expect that in region, that people intake more salt from drinking water and regime they more susceptible for heart attack and other disorder associated with heart and circulatory systems. So many studies indicated that high salt intake seriously aggravates chronic congestive heart failure, and ill effects due to high levels of sodium in drinking-water.

#### NaCl concentration and CNS disorder:

Many studies suggest that changes in level of NaCl concentration can induce many

pathological disorders in CNS(36)(37). High-salt intake may contribute to the (MS) Multiple sclerosis and other autoimmune disease development(38)(39). Studies indicated excessive consumption of especially in developed countries may increase in incidence of MS and other autoimmune diseases. Moreover high-salt concentration results in growth of pathogenic phenotype of (T helper -17) Th17 cells. The Th17 cells can upregulate the production of many pro-inflammatory cytokines(40). These pro-inflammatory cytokines can also induce neurodegeneration in spinal cord and brain. The reninangiotensin-aldosterone system that mentioned has important role in regulation of NaCl balance and a major regulator of blood pressure, also significantly affects autoimmunity in many diseases. It is also well-established that even a short-term excessive in salt intake can activate many immune cell against our body cells(41).

Also in other studies discovered that excessive salt intake can promote risk of stroke in adults. Actually, increase in NaCl concentration in CSF can make endothelial disruption, vascular fibrosis and arterial hypertension in CNS(42)(43). So Risk of stroke may increase in people with salt intake even in short- term consumption(43). Actually, high salt intake by drinking water can cause endothelial dysfunction by suppression of the endothelial nitric oxide (NO) production(43). Nitric oxide can dilate cerebral artery, so NO can increase CNS blood stream(44). So cerebral hypoperfusion by decrease of NO is an important cause of stroke by high salt intake(45)(46). Hypo-perfusion disrupt circulation in CNS and reduce the oxygen and glucose supply to CNS(47).

Recent research suggests that a diet high in salt also may promote some cognitive decline by destabilizing of tau protein. In Alzheimer disease (AD) as a common cognitive disorder(48). tau protein phosphorylated destabilize and pathologically. Also high diet sodium also can contribute destabilizing of tau protein as important factor in AD pathogenesis.(49) Excessive levels of tau are a hallmark of dementia(50). Studies indicated NaCl consumption decrease blood stream of CNS. Reduction in perfusion of CNS increase many pro-inflammatory cytokines(51)(52). All these events lead to tau destabilization and neurodegeneration in CNS(53). Decrease of Sodium intake is the most important ways to prevent CNS disorders to have a healthy brain. So we must decrease our sodium consumption in our diet and importantly our drinking water (Figure 3).

# **Conclusion:**

Na+ is most important electrolyte in our body. It helps to body manage hemostasis. Many important function can disrupt easily with slight changes in Na+ even concentration. Recent studies indicated we consume salt more than we need. It can cause Na+ concentration increase in our blood stream. We must manage our dietary sodium in our foods and also water we consume. We must reduce consumption of western diets and use more traditional diets that more healthy. Also we can use desalination ways to improve quality of drinking water, to decline high NaCl intake side effects.

## **References:**

1. 1. Beidokhti M, Naeeni S, AbdiGhahroudi M. 2019. Biosorption of Nickel (II) from aqueous solutions onto Pistachio Hull waste as a low-cost biosorbent. Civ Eng J 1.

2. Whelton AJ, Dietrich AM, Burlingame GA, Schechs M, Duncan SE. 2007. Minerals in drinking water: impacts on taste and importance to consumer health. Water Sci Technol 55:283–291.

3. Van der Aa M. 2003. Classification of mineral water types and comparison with drinking water standards. Environ Geol 44:554–563.

4. Munteanu C, Iliuta A. 2011. The role of sodium in the body. Balneo Res J 2:70–74.

5. Frohlich ED, Varagic J. 2004. The role of sodium in hypertension is more complex than simply elevating arterial pressure. Nat Rev Cardiol 1:24.

6. Hamm LL, Feng Z, Hering-Smith KS. 2010. Regulation of sodium transport by ENaC in the kidney. Curr Opin Nephrol Hypertens 19:98.

7. Karppanen H, Mervaala E. 2006. Sodium intake and hypertension. Prog Cardiovasc Dis 49:59–75.

8. Kirabo A. 2017. A new paradigm of sodium regulation in inflammation and hypertension. Am J Physiol Integr Comp Physiol 313:R706–R710.

9. Butler M, Wallace J, Lowe M. 2002. Ground-water quality classification using GIS contouring methods for Cedar Valley, Iron County, Utah. Digit Mapp Tech 207.

10.CuzzoB,LappinSL.2019.Vasopressin(antidiuretichormone,

ADH)StatPearls [Internet]. StatPearls Publishing.

11. Stockand JD. 2010. Vasopressin regulation of renal sodium excretion. Kidney Int 78:849–856.

12. Sanders PW. 2004. Salt intake, endothelial cell signaling, and progression of kidney disease. Hypertension 43:142–146.

13. Mohan S, Campbell NRC. 2009. Salt and high blood pressure. Clin Sci 117:1–11.

14.Gómez-SánchezEP,ZhouM,Gomez-SanchezCE.1996.Mineralocorticoids, saltandhighbloodpressure.Steroids 61:184–188.

15. Hoy WE, Hughson MD, Bertram JF, Douglas-Denton R, Amann K. 2005. Nephron number, hypertension, renal disease, and renal failure. J Am Soc Nephrol 16:2557–2564.

16. Langley-Evans SC, Langley-Evans AJ, Marchand MC. 2003. Nutritional programming of blood pressure and renal morphology. Arch Physiol Biochem 111:8– 16.

17. Palmer BF, Gates JR, Lader M.2003. Causes and management of hyponatremia. Ann Pharmacother 37:1694–1702.

18. Qian Q. 2018. Salt, water and nephron: Mechanisms of action and link to hypertension and chronic kidney disease. Nephrology 23:44–49.

19. Ghanem M, Zeineldin M, Eissa A, El Ebissy E, Mohammed R, Abdelraof Y. 2018. The effects of saline water consumption on the ultrasonographic and histopathological appearance of the kidney and liver in Barki sheep. J Vet Med Sci 17– 596. 20. Scheelbeek PFD, Chowdhury MAH, Haines A, Alam DS, Hoque MA, Butler AP, Khan AE, Mojumder SK, Blangiardo MAG, Elliott P. 2017. Drinking water salinity and raised blood pressure: evidence from a cohort study in coastal Bangladesh. Environ Health Perspect 125:57007.

21. Murray B, Eichner ER. 2004. Hyponatremia of exercise. Curr Sports Med Rep 3:117–118.

22. Chau PH, Chan KC, Woo J. 2009. Hot weather warning might help to reduce elderly mortality in Hong Kong. Int J Biometeorol 53:461.

23. Wexler RK. 2002. Evaluation and treatment of heat-related illnesses. Am Fam Physician 65:2307–2313.

24. Rakova N, Kitada K, Lerchl K, Dahlmann A, Birukov A, Daub S, Kopp C, Pedchenko T, Zhang Y, Beck L. 2017. Increased salt consumption induces body water conservation and decreases fluid intake. J Clin Invest 127:1932–1943.

25. Dwyer J. 2013. Vegeterian Diets. sic) Encycl Hum Nutr 4:316–322.

26. Mahtani KR, Heneghan C, Onakpoya I, Tierney S, Aronson JK, Roberts N, Hobbs FDR, Nunan D. 2018. Reduced Salt Intake for Heart Failure: A Systematic Review. JAMA Intern Med 178:1693–1700.

27. Kong YW, Baqar S, Jerums G, Ekinci EI. 2016. Sodium and its role in cardiovascular disease–the debate continues. Front Endocrinol (Lausanne) 7:164.

28. Meneton P, Jeunemaitre X, de Wardener HE, Macgregor GA. 2005. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev 85:679–715. 29. Elkinton JR, Danowski TS, Winkler AW. 1946. Hemodynamic changes in salt depletion and in dehydration. J Clin Invest 25:120–129.

30. Kurtz TW, DiCarlo SE, Pravenec M, Morris RC. 2018. The pivotal role of renal vasodysfunction in salt sensitivity and the initiation of salt-induced hypertension. Curr Opin Nephrol Hypertens 27:83–92.

31. Hall JE, Guyton AC, Smith Jr MJ, Coleman TG. 1980. Blood pressure and renal function during chronic changes in sodium intake: role of angiotensin. Am J Physiol Physiol 239:F271–F280.

32. Drenjančević-Perić I, Jelaković B, Lombard JH, Kunert MP, Kibel A, Gros M. 2011. High-salt diet and hypertension: focus on the renin-angiotensin system. Kidney blood Press Res 34:1–11.

33. Zhu Z, Zhu S, Zhu J, van der Giet M, Tepel M. 2004. Effect of Sodium on Vasoconstriction and Angiotensin II Type 1 Receptor mRNA Expression in Coldinduced Hypertensive Rats. Clin Exp Hypertens 26:475–483.

34. Crestani S, Júnior AG, Marques MCA, Sullivan JC, Webb RC, da Silva-Santos JE. 2014. Enhanced angiotensin-converting enzyme activity and systemic reactivity to angiotensin II in normotensive rats exposed to a high-sodium diet. Vascul Pharmacol 60:67–74.

35. Forechi L, Baldo MP, de Araujo IB, Nogueira BV, Mill JG. 2015. Effects of high and low salt intake on left ventricular remodeling after myocardial infarction in normotensive rats. J Am Soc Hypertens 9:77–85. 36. Diringer MN. 1992. Management of sodium abnormalities in patients with CNS disease. Clin Neuropharmacol 15:427–447.

37. Kim DK, Joo KW. 2009.
Hyponatremia in patients with neurologic disorders. Electrolytes Blood Press 7:51–57.
38. Farez MF, Fiol MP, Gaitán MI, Quintana FJ, Correale J. 2015. Sodium intake is associated with increased disease activity in multiple sclerosis. J Neurol Neurosurg Psychiatry 86:26–31.

39. Mehrabadi S. 2019. Interaction
between Gut Microbiota Dysbiosis and
Multiple Sclerosis. Int J Med Investig 8:21–
28.

40. Mehrabadi S, Karimiyan SM. 2018. Morphine Tolerance Effects on Neurotransmitters and Related Receptors: Definition, Overview and Update. J Pharm Res Int 1–11.

41. Zostawa J, Adamczyk J, Sowa P, Adamczyk-Sowa M. 2017. The influence of sodium on pathophysiology of multiple sclerosis. Neurol Sci 38:389–398.

42. Campese VM, Mozayeni P, Ye S, Gumbard M. 2002. High salt intake inhibits nitric oxide synthase expression and aggravates hypertension in rats with chronic renal failure. J Nephrol 15:407–413.

43. Ni Z, Vaziri ND. 2001. Effect of salt loading on nitric oxide synthase expression in normotensive rats. Am J Hypertens 14:155–163.

44. Calabrese V, Mancuso C, Calvani M,
Rizzarelli E, Butterfield DA, Stella AMG.
2007. Nitric oxide in the central nervous system: neuroprotection versus neurotoxicity. Nat Rev Neurosci 8:766.

45. Strazzullo P, D'Elia L, Kandala N-B, Cappuccio FP. 2009. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. Bmj 339:b4567.

46. Turlova E, Feng Z. 2013. Dietary salt intake and stroke. Acta Pharmacol Sin 34:8.

47. Perry IJ, Beevers DG. 1992. Salt intake and stroke: a possible direct effect. J Hum Hypertens 6:23–25.

48. Mehrabadi S, Motevaseli E, Sadr SS, Moradbeygi K. 2020. Hypoxic-conditioned medium from adipose tissue mesenchymal stem cells improved neuroinflammation through alternation of toll like receptor (TLR) 2 and TLR4 expression in model of Alzheimer's disease rats. Behav Brain Res 379:112362.

49. Fyfe I. 2020. High-salt diet promotes Alzheimer disease-like changes. Nat Rev Neurol 16:2–3.

50. Mehrabadi S, Sadr SS, Hoseini M.2019. Stem Cell Conditioned Medium as a

Novel Treatment for Neuroinflamation Diseases. Int J Med Investig 8:1–12.

51. Goldstein B, Speth RC, Trivedi M. 2016. Renin–angiotensin system gene expression and neurodegenerative diseases.

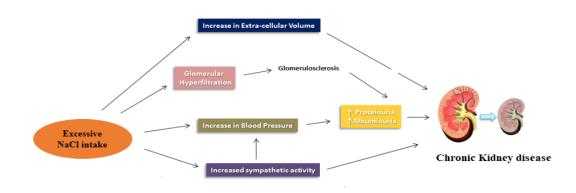
J Renin-Angiotensin-Aldosterone Syst 17:1470320316666750.

52. Faraco G, Brea D, Garcia-Bonilla L, Wang G, Racchumi G, Chang H, Buendia I, Santisteban MM, Segarra SG, Koizumi K. 2018. Dietary salt promotes neurovascular and cognitive dysfunction through a gutinitiated TH17 response. Nat Neurosci 21:240.

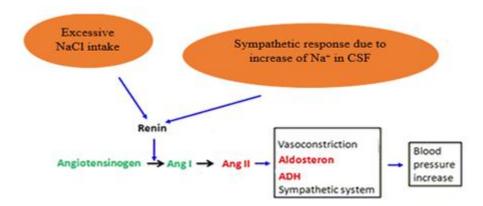
53. Fiocco AJ, Shatenstein B, Ferland G, Payette H, Belleville S, Kergoat M-J, Morais JA, Greenwood CE. 2012. Sodium intake and physical activity impact cognitive maintenance in older adults: the NuAge Study. Neurobiol Aging 33:829-e21.

# **Tables and Charts:**

**Figure 1**: Effects of high NaCl intake and kidney function. Excessive NaCl intake can cause chronic kidney disease by changing of kidney function.



**Figure 2**: Effects of high NaCl intake and heart function. Excessive NaCl intake can induce high blood pressure by increasing level of Angiotensin II.



**Figure 3**: Relationship between NaCl concentration and CNS disorders. High salt intake can activate many pathological pathways.

