PERSPECTIVE

3(10), April - June, 2017

ISSN 2394-3750 EISSN 2394-3769

Science & Technology

Salt Intake: Cardiovascular Concerns and Controversies

Shashi K Agarwal

Agarwal Health Center, Edison, NJ, USA

Corresponding author: Shashi K. Agarwal, MD, FACP, FACC, FCCP; Email: usacardiologist@gmail.com

Publication History
Received: 11 May 2017
Accepted: 19 June 2017
Published: April- June 2017

Citation
Shashi K Agarwal. Salt Intake: Cardiovascular Concerns and Controversies. *Science & Technology,* 2017, 3(10), 140-145

ABSTRACT

Compelling epidemiological, experimental and clinical data has established that excess salt intake is associated with a higher cardiovascular morbidity and mortality. Several prospective cohort studies and clinical outcome trials have recognized the reduced risk of cardiovascular disease associated with a lower salt intake. The major benefits appear to accrue from a reductions in blood pressure as a result of salt restriction. As a result, efforts are being made by several countries to reduce the salt intake from the current level of 9-12 g/day to less than 5-6 g/day. Population based reduction in salt intake is expected to result in a substantial decline in major cardiovascular events, prevention of millions of premature deaths and massive healthcare savings worldwide. Two recent reports have however questioned the validity of severe salt restriction and present persuasive data recommending a restrained restriction.

Keywords: hypertension, salt, sodium, sodium chloride, heart failure

Abbreviations: ASH: American Society of Hypertension; BMI: Body mass index; HIV: Human Immunodeficiency Virus Infection; BP: Blood pressure; HTN: Hypertension; JNC-7: The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; NACL: Sodium Chloride

1. INTRODUCTION

There is overwhelming evidence from animal, epidemiological and human interventional studies that dietary salt is the major contributor to high blood pressure (Elliott et al, 1996) Elevated blood pressure is a major cause of cardiovascular disease and is estimated to be responsible for 62% of stroke and 49% of coronary heart disease worldwide, (WHO, 2002) and 10% of all global healthcare spending. Since cardiovascular disease is the leading cause of death and disability worldwide, (WHO) reduction in blood pressure should positively impact the scourge of cardiovascular events and deaths. (Stamler, 1997) Emerging data suggests that a reduction in salt intake results in mild decreases in blood pressure (Sacks et al, 2001) and the resultant decreases in cardiovascular morbidity and mortality. (Taylor et al, 2001) Although these reductions are modest, the benefits accrued in reduced cardiovascular events and deaths in large populations could be enormous. (He et al, 2002) A 10% reduction in salt intake will translate to an almost 3% reduction in cardiovascular deaths worldwide. (Gaziano, 2012) It would also reduce millions of non-fatal heart attacks and strokes. There are also the added benefits of an enhanced blood pressure control and the reduced need for pharmaceuticals. (Whelton et al, 1998; MacGregor et al, 1987) The quality of life would improve for millions. The anticipated healthcare savings are also tremendous. (Palar et al, 2009) However individual restrictions have been difficult to adhere to, and some reports have questioned the benefit of universal intensive salt restriction. (Alderman, 2004, Stolarz-Skrzypek et al, 2011) Overall, the overwhelming data does favor a modest dietary salt reduction, and this could be achieved by regulations aimed at a gradual decrease in salt in processed and cooked foods sold in grocery stores and restaurants.

2. DISCUSSION

The association between sodium intake and health has been noticed over a century ago. (Ambard et al, 1904) The major source of sodium in the diet is from common salt (NaCl). The terms salt and sodium are often used synonymously, although, on a weight basis, salt comprises 40% sodium and 60% chloride; 1 g of sodium is equivalent to 2.55 g of salt; 1 mmol of sodium is equivalent to 23 mg of sodium; and 1 g of salt is equivalent to 17 mmol of sodium (SACN, 2003; Eaton et al, 1985) The easy commercial availability of salt has increased the daily intake from less than 0.25g to almost 10 g and has greatly contributed to the growing scourge of cardiovascular diseases worldwide. (Chockalingam et al, 1999) Restricting salt intake in the industrialized countries from 8–12 g/d to 5–6 g/d has been recommended for hypertensive individuals for many years by the World Health Organization (WHO, 2006) and many medical societies. (Chobanian et al, 2003; ESC, 2003)These recommendations are now being extended to the general non-hypertensive population, (Dickenson et al, 2007) while stricter restrictions are being mulled for hypertensives.

2.1. Salt and Hypertension

Animal studies have shown that increasing salt intake results in an increase in blood pressure. (Denton et al, 1995; Elliott et al, 2007) The main evidence for the association between high intakes of salt and BP relates to sodium content of the salt. (Stamler, 1997) Several epidemiological studies in human populations have revealed that populations with little salt intake have lower blood pressures and do not develop hypertension as they age. (Uzodike, 1993; Mancilha-Carvalho et al, 1989; Page et al, 1981; Pavan et al, 1999) Migration studies have also established an association with increased salt intake with the development of hypertension. (He et al, 1991; Poulter et al, 1990) A large prospective international study has confirmed the salt intake-hypertension relationship. (Stamler, 1997) Overall, consensus dictates that salt restriction has a salutary effect on hypertension. (Ebrahim et al, 1998)

2.2. Salt and IHD

Several studies have found an association with excess salt intake and an increase in coronary heart disease. (Strazzullo et al, 2009) Studies also demonstrate a reduction with a restriction in salt intake. (Fung et al, 2008) It has been estimated that the reductions in systolic/diastolic blood pressure of 7/4 mm Hg in people with hypertension and 4/2 mm Hg in those without hypertension would result from a salt reduction to 6 g per day. (He et al, 2002) At the population level these reductions in blood pressure could predict an average lower rate of 18% for coronary heart disease. (He et al, 2003)

2.3. Salt and Stroke

Higher stroke events have been linked to an increase in salt intake. (Nagata et al, 2004; Yamori et al, 1994) At the population level, reductions in blood pressure associated with salt restriction are expected to lower the stroke rate by about 24%. (He et al, 2003)

2.4. Salt and Left Ventricular Hyperterophy

Excess salt intake has been associated with increases in left ventricular muscle mass. (Schmieder et al, 1988)

2.5. Salt and Heart Failure

Salt restriction is traditionally recommended in patients with heart failure. (Hunt, 2005) However, a normal salt intake appears to improve outcomes in patients with compensated congestive heart failure and sodium depletion may result in detrimental renal and neuro-hormonal effects. (Paterna et al, 2008) The role of sodium restriction in heart failure patients is under question. (Michael et al, 2010)

2.6. Salt and Arterial Stiffness

Excess salt intake is associated with a reduction in arterial compliance and raised pulse pressure. (Cailar et al, 2004)

2.7. Salt and Edema

A high sodium intake may actually reduce edema by inducing a relative fluid shift from the interstitial into the intravascular space. (Heer et al, 2000) However, most recommendations are to decrease salt intake to relieve edema.

2.8. Salt and Other diseases

Salt intake has also been associated with some non-cardiovascular adverse effects. (Antonios, 1996)

2.8.1. Salt and the kidneys

Salt has multiple effects on the renal system. Excess intake is initially associated with increased glomerular filtration rate, and later with glomerulosclerosis. (Mallamaci et al, 1996) There is an increased micro-albuminuria, (Ribstein et al, 2002) while rat studies have shown a tendency towards the development of renal fibrosis (Yu et al, 1998)

2.8.2. Salt and stomach cancer

Salt and salt preserved foods increase the risk of gastric cancer. (Takahashi et al, 1985; Negri et al, 1990) Salt increases gastric irritation and this may increase the risk of infection by Helicobacter pylori. (Beevers et al 2004) H. pylori infection has been linked to an increase in the risk of gastric cancer. (Kato et al, 2006; Nozaki et al, 2002)

2.8.3. Salt and other conditions

A high salt intake has been associated with a weakened baro-receptor reflex (Creager et al, 1991) and decreased myocardial fibrosis in experimental rat studies. (Yu et al, 1998) A high salt intake affects urinary calcium excretion and this may have implications on bone health. (Nordin et al, 1993)

2.9. Salt and mortality

An inverse relationship was seen by the NHANES II Study between salt intake and mortality. (Cohen et al, 2006) This was also suggested in the NHANES III Study. (Cohen et al, 2008) Some models also suggest that in large population groups consisting of normotensive, pre-hypertensive and hypertensive people, salt restriction leads to an improvement cardiovascular and all cause mortality. (Bibbins-Domingo et al, 2010)

2.10 Benefits of salt restriction

Several well-controlled clinical trials have provided strong evidence that reduction of sodium intake lowers arterial pressure in hypertensive, prehypertensive and normotensive people, (Sacks et al, 2001; He et al, 2004; Whelton et al, 1998) reducing the need for anti-hypertensive medications. The benefits also stretch to cardiovascular outcomes: prospective epidemiological studies have shown that a lower salt intake is related to a lower risk of stroke, (Nagata et al, 2004) coronary heart disease, (Tuomilehto et al, 2001) LV hypertrophy (Kupari et al, 1994; Simpson, 1988) and renal disease. (Kayikcioglu et al, 2009; Ozkahya et al, 3006; Maduell et al, 2001) Salt reduction also decreases aortic stiffness. (Avolio et al, 1986) Although the effect of salt reduction on cardiovascular deaths is extrapolated from blood pressure data, (He et al, 2003; PSC, 2002) there is some evidence that increased salt intake may be independently contributing to a higher cardiovascular mortality. (He et al, 1999; Tuomilehto et al, 2001) Salt restriction also helps chronic renal disease and proteinuria. (Cianciaruso et al, 1998; Swift et al, 2005; Ritz et al, 2008)

2.11 Dangers of severe salt restriction

A recent report from Dr. Staessen and colleagues revealed that the association between systolic pressure and sodium excretion did not translate into less morbidity or improved survival. On the contrary, low sodium excretion predicted higher cardiovascular

mortality. (Stolarz-Skrzypek et al, 2011) Restricting salt may also result in neuro-hormonal stimulation and lead to the detrimental progression of heart failure. (Nakasato et al, 2010) Extreme salt restriction may therefore be associated with detrimental effects. Harmful effects of excessive salt reduction include sodium deficiency during periods of excessive heat exposure or diarrhea. It may also lead to hypovolemia in the elderly. Extreme salt restriction could potentially stimulate the sympathetic nervous system and the renin-angiotensin-aldosterone system. There may be increases in LDL cholesterol, triglycerides and uric acid levels in the blood and the insulin sensitivity may be lowered. Salt restriction could also lead to an increased consumption of sugar, with its deleterious consequences on obesity, diabetes and heart disease. (Stamler et al, 1997)

3. CONCLUSIONS

The effect of salt restriction on long term health outcomes is positive but only mild. Data is also mixed (Taylor et al, 2011, Stolarz-Skrzypek et al, 2011) and this may be due to differential effects on blood pressure and the neuro-hormonal system. (Frohlich, 2007) The benefits noted in clinical studies demonstrate only a small reduction in blood pressure. Overall reduction in cardiovascular morbidity and mortality remains questionable. (Stolarz-Skrzypek et al, 2011) In some analysis, salt restriction in some cardiac condtions may actually be detrimental. (Paterna et al, 2008) However, most computer models suggest that a widespread reduction of salt intake should reap significant population benefits, with a decrease in major cardiovascular events (Bibbins-Domingo et al, 2010) Reduced salt intake in treated individuals may also help reduce the number and dose of drugs or obviate the need for treatment. (Stamler et al, 1987; Neaton et al, 1993) The economic benefits to the world health care system will also be tremendous.(Bibbins-Domingo et al, 2010; Cappuccio et al, 2011) Since individual salt restrictions are difficult to adhere to, (Kumanyika et al, 2005) salt intake should be reduced to about 5-6 g/day from the current intake of 9–12 g/day. This appears to be a more prudent approach and should still achieve major beneficial effects on health, along with major cost savings. Health outcomes do not appear to be consistent with extreme lowering of dietary sodium in the general population. Since the major source of salt is processed foods in the western countries (James et al, 1987) and from salt added during cooking in sauces or added at the table in the eastern countries, an effective collaborative partnership between the food industry, government and healthcare organizations is needed.

REFERENCE

1. Alderman MH. Dietary sodium and cardiovascular health in hypertensive patients: the case against universal sodium restriction. J Am Soc Nephrol. 2004 Jan;15 Suppl 1:S47-50.
2. Ambard L, Beaujard E. Causes de l'hypertension arterialle. Arch Gén Med. 1904; 1: 520–533.
3. Antonios TF, MacGregor GA.Salt--more adverse effects. Lancet. 1996 Jul 27; 348(9022):250-1.
4. Avolio, A. P., Clyde, K. M., Beard, T. C. et al. (1986) Improved arterial distensibility in normotensive subjects on a low salt diet. Arteriosclerosis 6, 166-169.
5. Beevers G, Lip G, Blann A (2004) Salt intake and Helicobacter pylori infection. Journal of Hypertension 22:1475-1477.
6. Bibbins-Domingo K, Chertow GM, Coxson PG, et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med. 2010; 362(7):90–599.
7. Cailar G, Mimran A, Fesler P, et al. Dietary sodium and pulse pressure in normotensive and essential hypertensive subjects. J Hypertens. 2004;22:697–703.
8. Cappuccio FP, Capewell S, Lincoln P et al. Policy options to reduce population salt intake. BMJ 2011; DOI:10.1136/bmj.d4995.
9. Carvalho JJ, Baruzzi RG, Howard PF, et al. Blood pressure in four remote populations in the Intersalt study. Hypertension. 1989;14:238–246.
10. Chobanian AV, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;43:1206–1252.
11. Chockalingam, A. and Balaguer-Vintro, I. (1999) Impending Global Pandemic of Cardiovascular Diseases: Challenges and Opportunities for the Prevention and Control of Cardiovascular Diseases in Developing Countries and Economies in Transition. The World Heart Federation, Prous Science, Barcelona.
12. Cianciaruso, B., Bellizzi, V., Minutolo, R. et al. (1998) Salt intake and renal outcome in patients with progressive renal disease. Miner. Electrolyte Metab. 24, 296-301.
13. Cohen HW, Hailpern SM, Alderman MH. Sodium intake and mortality follow-up in the Third National Health and Nutrition Examination Survey (NHANES III). J Gen Intern Med. 2008 Sep; 23(9):1297-1302.
14. Creager MA, Roddy M, Holland KM, et al. Sodium depresses arterial baroreceptor reflex function in normotensive humans. Hypertension. 1991;17:989–996.
15. Denton D, Weisinger R, Mundy NI et al. The effect of increased salt intake on blood pressure of chimpanzees. Nat Med 1995;1:1009–1016.
16. Dickinson BD, Havas S. Council on Science and Public Health, American Medical Association. Reducing the

population burden of cardiovascular disease by reducing sodium intake: a report of the Council on Science and Public Health. Arch Intern Med. 2007;167:1460–1468.
17. Eaton, S. B. and Konner, M. (1985) Paleolithic nutrition. N. Engl. J. Med. 312, 283-288.
18. Ebrahim S, Smith GD. Lowering blood pressure: a systematic review of sustained effects of non-pharmacological interventions. J Public Health Med. 1998 Dec; 20(4):441-8.
19. Elliott P, Stamler J, Nichols R et al. Intersalt revisited: further analyses of 24 h sodium excretion and blood pressure within and across populations. Intersalt Cooperative Research Group. BMJ 1996; 312: 1249–1253.
20. Elliott P, Walker LL, Little MP et al. Change in salt intake affects blood pressure of chimpanzees: implications for human populations. Circulation 2007;116:1563–1568.
21. ESC: Guidelines Committee. 2003 European Society of Hypertension - European Society of Cardiology guidelines for the management of arterial hypertension. J Hypertens. 2003;21:1011–1053.e24, e25
22. Frohlich ED. The salt conundrum: a hypothesis. Hypertension. 2007 Jul;50(1):161-6 .
23. Fung TT, Chiuve SE, McCullough ML, et al. Adhaerence to a DASH-style diet and risk of coronary heart disease and stroke in women. Arch Intern Med. 2008; 168:713–720.
24. Gaziano T. Harvard School of Medicine, Boston, MA, World Congress of Cardiology 2012.
25. He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens 2002;16:761–770.
26. He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. Cochrane Database Syst Rev 2004; 3: CD004937.
27. He J, Klag MJ, Whelton PK, Chen JY et al. Migration, blood pressure pattern, and hypertension: the Yi Migrant Study. Am J Epidemiol 1991;134:1085–1101.
28. He FJ, MacGregor GA. How far should salt intake be reduced? Hypertension2003; 42:1093-9.
29. He J et al. (1999) Dietary sodium intake and subsequent risk of cardiovascular disease in overweight adults. JAMA 282: 2027-2034.
30. Heer M, Baisch F, Kropp J, Gerzer R, Drummer C. High dietary sodium chloride consumption may not induce body fluid retention in humans. Am J Physiol Renal Physiol. 2000 Apr;278(4):F585-95.
31. Hunt SA. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure) J Am Coll Cardiol. 2005;46:e1–82.
32. James WP, Ralph A, Sanchez-Castillo CP. The dominance of salt in manufactured food in the sodium intake of affluent societies. *Lancet* 1987;1:426–y 429.
33. Kato S, Tsukamoto T, Mizoshita T et al. High salt diets dose-dependently promote gastric chemical carcinogenesis in Helicobacter pylori-infected Mongolian gerbils associated with a shift in mucin production from glandular to surface mucous cells. Int J Cancer. 2006;119:1558–1566.
34. Kayikcioglu M, Tumuklu M, Ozkahya M et al. The benefit of salt restriction in the treatment of end-stage renal disease by haemodialysis. Nephrol Dial Transplant 2009; 24: 956–962.
35. Kumanyika SK, Cook NR, Cutler JA, et al. Sodium reduction for hypertension prevention in overweight adults: further results from the Trials of Hypertension Prevention Phase II. J Hum Hypertens. 2005;19:33–45.
36. Kupari, M., Koskinen, P. and Virolainen, J. (1994) Correlates of left ventricular mass in a population sample aged 36 to 37 years: focus on lifestyle and salt intake. Circulation 89, 1041-1050.
37. MacGregor GA, Markandu ND, Singer DR et al. Moderate sodium restriction with angiotensin converting enzyme inhibitor in essential hypertension: a double blind study. Br Med J (Clin Res Ed) 1987; 294:531–534.
38. Maduell F, Navarro V. Assessment of salt intake in hemodialysis. Nefrologia 2001; 21: 71–77.
39. Mallamaci F, Lonardis D, Billizzi V et al. Does high salt intake cause hyperfiltration in patients with essential hypertension? J Hum Hypertens. 1996;10:157–161.
40. Mancilha-Carvalho JJ, de Oliveira R, Esposito RJ. Blood pressure and electrolyte excretion in the Yanomamo Indians, an isolated population. J Hum Hypertens 1989;3:309–314.
41. Michael B. Rothberg, Senthil K. Sivalingam. The New Heart Failure Diet: Less Salt Restriction, More Micronutrients. J Gen Intern Med. 2010 October; 25(10): 1136–1137.
42. Nagata C, Takatsuka N, Shimizu N et al. Sodium intake and risk of death from stroke in Japanese men and women. Stroke. 2004; 35:1543–1547.
43. Nakasato M, Strunk CM, Guimarães G et al. [Is the low-sodium diet actually indicated for all patients with stable heart failure?]. Arq Bras Cardiol. 2010 Jan;94(1):92-101.
44. Neaton JD, Grimm RH Jr, Prineas RJ, et al. Treatment of Mild Hypertension Study. Final results. J Am Med Assoc 1993;270:713-24.
45. Negri E, La Vecchia C, D'Avanzo B et al. Franceschi S. Salt preference and the risk of gastrointestinal cancers. Nutr Cancer. 1990;14:227–232.
46. Nordin BEC, Need AG, Morris HA et al. (1993) The nature and signficance of the relationship between urinary sodium

and urinary calcium in women. Journal of Nutrition 123:1615-1622.

47. Nozaki K, Shimizu N, Inada K et al. Synergistic promoting effects of Helicobacter pylori infection and high-salt diet on gastric carcinogenesis in Mongolian gerbils. Jpn J Cancer Res. 2002;93:1083–1089.
48. Ozkahya M, Ok E, Toz H et al. Long-term survival rates in haemodialysis patients treated with strict volume control. Nephrol Dial Transplant 2006; 21: 3506–3513.
49. Page LB, Vandevert DE, Nader K et al. Blood pressure of Qash'qai pastoral nomads in Iran in relation to culture, diet, and body form. Am J Clin Nutr 1981;34:527–538.
50. Pavan L, Casiglia E, Braga LM et al. Effects of a traditional lifestyle on the cardiovascular risk profile: the Amondava population of the Brazilian Amazon. Comparison with matched African, Italian and Polish populations. J Hypertens 1999;17:749–756.
51. Palar K, Sturm R. Potential societal savings from reduced sodium consumption in the U.S. adult population. Am J Health Promot. 2009 Sep-Oct; 24(1):49-57.
52. Paterna S, Gaspare P, Fasullo S et al. Normal-sodium diet compared with low-sodium diet in compensated congestive heart failure: is sodium an old enemy or a new friend? Clin Sci (Lond). 2008 Feb;114(3):221-30.
53. Poulter NR, Khaw KT, Hopwood BE et al. The Kenyan Luo migration study: observations on the initiation of a rise in blood pressure. BMJ 1990;300:967–972.
54. PSC: Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002; 360: 1903-1913.
55. Ribstein J, Mimran A. Dietary sodium and target organ damage in essential hypertension.Am J Hypertens. 2002;15:222–229.
56. Ritz E, Mehls O. Salt restriction in kidney disease—a missed therapeutic opportunity? Pediatr Nephrol. 2009 January; 24(1): 9–17.
57. Sacks FM et al. for the DASH-Sodium Collaborative Research Group (2001) Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. N Engl J Med 344: 3-10.
58. Schmieder RE, Messerli FH, Garavaglia GE, Nunez BD. Dietary salt intake: a determinant of cardiac involvement in essential hypertension. Circulation. 1988;78:951–961.
59. Scientific Advisory Committee on Nutrition (2003) Salt and Health. The Stationery Office, Londonhttp://www.sacn.gov.uk/ pdfs/sacn_salt_final.pdf.
60. Simpson FO. Sodium intake, body sodium, and sodium excretion. Lancet 1988; 2: 25–29.
61. Stamler J. The INTERSALT Study: background, methods, findings, and implications. Am J Clin Nutr. 1997;65(suppl):626–642.
62. Stamler R, Stamler J, Grimm R, et al. Nutritional therapy for high blood pressure. Final report of a four-year randomized controlled trial – The Hypertension Control Program. J Am Med Assoc 1987;257:1484-91.
63. Stolarz-Skrzypek K, Kuznwtsova T, Thijs L, et al; European Project on Genes in Hypertension (EPOGH) Investigators. Fatal and nonfatal outcomes, incidence of hypertension, and BP changes in relation to urinary sodium excretion. JAMA. 2011;305:1777-1785.
64. Strazzullo P, Lanfranco D'Elia, Ngianga-Bakwin Kandala et al. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. BMJ 2009;339:b4567.
65. Swift, P. A., Markandu, N. D., Sagnella, G. A. et al. (2005) Modest salt reduction reduces blood pressure and urine protein excretion in black hypertensives: a randomized control trial. Hypertension 46, 308-312.
66. Taylor RS, Ashton KE, Moxham Tet al. Reduced dietary salt for the prevention of cardiovascular disease: a meta-analysis of randomized controlled trials. Am J Hypertens. 2011 Aug;24(8):843-53.
67. Tuomilehto J, Jousilahti P, Rastenyte D et al. Urinary sodium excretion and cardiovascular mortality in Finland: a prospective study. Lancet 2001; 357: 848-851.
68. Uzodike VO. University of London; 1993. Epidemiological studies of arterial blood pressure and hypertension in relation to electrolyte excretion in three Igbo communities in Nigeria. Thesis (MD).
69. Whelton PK, Appel LJ, Espeland MA et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA 1998; 279:839–846.
70. WHO: http://www.who.int/cardiovascular_diseases/en/. Accessed August 5, 2013.
71. World Health Organization. Reducing salt intake in populations. Report of a WHO Forum. 2006.
72. World Health Report 2002: Reducing risks, promoting healthy life. Geneva, Switzerland: World Health Organisation; 2002. www.who.int/whr/2002.
73. Yamori Y, Nara Y, Mizumisha S, et al. Nutritional factors for stroke and major cardiovascular diseases: international epidemiological comparison of dietary prevention. Health Rep. 1994; 6:22–27.
74. Yu HCM, Burrell LM, Black MJ, et al. Salt induces myocardial and renal fibrosis in normotensive and hypertensive rats. Circulation. 1998; 98:2621–2628.