Enfermedades cardiovasculares, hipertensión arterial y consumo de sodio: una relación controversial

Cardiovascular diseases, high blood pressure and sodium intake: a controversial relationship

Doenças cardiovasculares, hipertensão e ingestão de sódio: a relação controversa

Guadalupe Ruiz Vivanco
Universidad Autónoma de Tlaxcala, Doctorado en Ciencias Biológicas
Facultad de Medicina, Benemérita Universidad Autónoma de Puebla
Laboratorio de Investigación en Fisiopatología de Enfermedades Crónicas, Centro de Investigación Biomédica de Oriente, IMSS, México
grv47@hotmail.com

Jorge Rodríguez Antolín
Centro Tlaxcala de Biología de la Conducta, Universidad Autónoma de Tlaxcala, México
antolin26@gmail.com

Enrique Torres Rasgado
Facultad de Medicina, Benemérita Universidad Autónoma de Puebla, México
entora30@yahoo.com

Margarita Martínez Gómez
Departamento de Biología Celular y Fisiología. Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México. Centro Tlaxcala de Biología de la Conducta, Universidad Autónoma de Tlaxcala, México
marmag@biomedicas.unam.mx

Martha Elba Gonzalez Mejia
Facultad de Medicina, Benemérita Universidad Autónoma de Puebla, México
elba.gonzalezmejia@gmail.com

Ricardo Pérez Fuentes
Facultad de Medicina, Benemérita Universidad Autónoma de Puebla
Laboratorio de Investigación en Fisiopatología de Enfermedades Crónicas, Centro de Investigación Biomédica de Oriente, IMSS, México
rycardoperez@hotmail.com

Resumen

Las enfermedades cardiovasculares (ECV) son la principal causa de muerte en el mundo. El alto consumo de sal es uno de los principales factores de riesgo que se asocian al desarrollo de CVD. Las guías clínicas recomiendan restricciones de consumo de sal en pacientes con hipertensión arterial e insuficiencia cardíaca; Sin embargo, los ensayos clínicos han reportado resultados contradictorios. Las dietas de restricción de sodio se asocian con un mayor desarrollo de la aterosclerosis, que actúa a través de la activación del sistema renina-angiotensina-aldosterona, lo que lleva al desarrollo de las enfermedades cardiovasculares.

El objetivo de la investigación es aportar evidencias científicas pertinentes que alerten y faculten al profesional de la salud en la toma de decisiones objetivas sobre el control de la ingesta de sal en la dieta, particularmente en pacientes con riesgo de desarrollar enfermedades cardiovasculares.

Palabras clave: sodio, enfermedad cardiovascular, HAS.

Abstract

Cardiovascular Diseases (CVD) are the leading cause of death in the world. High consumption of salt is one of the main risk factors associated with the development of CVD. Clinical guidelines recommend restrictions on salt consumption in patients with arterial hypertension and heart failure; however, clinical trials have reported conflicting results. The sodium restricted diets are associated with a greater development of atherosclerosis, which acts through the activation of the renin-angiotensin-aldosterone system, which leads to the development of cardiovascular disease.

El objetivo de la investigación es aportar evidencias científicas pertinentes que alerten y faculten al profesional de la salud en la toma de decisiones objetivas sobre el control de la ingesta de sal en la dieta, particularmente en pacientes con riesgo de desarrollar enfermedades cardiovasculares.

Key words: sodium, cardiovascular disease, Hypertension (HTN).

Resumo

As doenças cardiovasculares (DCV) são a principal causa de morte no mundo. A ingestão de elevado teor de sal é um dos principais factores de risco associados ao desenvolvimento de doenças cardiovasculares. Diretrizes clínicas recomendam restrições à ingestão de sal em pacientes com hipertensão e insuficiência cardíaca; No entanto, os ensaios clínicos têm relatado resultados conflitantes. As dietas restritas sódio estão associados com o aumento do desenvolvimento de aterosclerose, que actua através da activação do sistema renina-angiotensina, conduzindo ao desenvolvimento de doenças cardiovasculares.

O objetivo da pesquisa é fornecer evidências científicas relevantes para alertar e capacitar o profissional de saúde na tomada de decisões objetivas sobre o controle da ingestão de sal na dieta, particularmente em pacientes com risco de desenvolver doença cardiovascular.

Palavras-chave: sódio, doença cardiovascular, TEM.

Fecha recepción: Enero 2016 **Fecha aceptación:** Junio 2016

Introduction

Cardiovascular diseases (CVD), including disorders of the heart and blood vessels, including coronary heart disease, stroke, heart, rheumatic and other conditions (WHO, 2016), represent the leading cause of death worldwide. It is estimated that in 2012 they died for this cause 17.5 million people, 31% of all deaths worldwide. In addition, more than 75% of deaths from CVD are produced in middle and low income countries (WHO, 2015), including Mexico, a developing country with income media where the proportional mortality from EVC is 24% (WHO, 2014). In 2011, the mortality rate from heart disease was 96.8 per 100 000 inhabitants, with 783 720 life years potentially lost; as cerebrovascular disease mortality rate was of 28.6 per 100 000 inhabitants (Ministry of Health, 2015. Secretaría de Salud by it name in Spanish).

The factors of cardiovascular risk as smoking, Dyslipidemia, obesity, diabetes, sedentary lifestyle, age and gender (Ministry of Health, 2010), include Hypertension (HTN), which contributes to at least 40% of all diseases of the heart and Cerebrovascular Accident (CVA) (PAHO, s. f.), which is considered the main risk factor for CVD (PAHO, 2013).

In addition, a high intake of dietary sodium has been considered as an development risk factor of CVD (He F.J. and MacGregor, G.A., 2002) (Strazzullo P., D'Elia L., Kandala N.B. and Cappuccio F.P., 2009) (Aburto N.J., Ziolkovska A, Hooper L, Elliott P., Cappuccio F.P. and Meerpohl J.J., 2013.)

In accordance with He, Li J. and MacGregor (2009), studies in experimental models made in rats, dogs, chickens, rabbits, baboons and chimpanzees have shown that sodium plays an important role in the regulation of the Blood Pressure (BP), and in all forms of experimental hypertension, regardless of the animal model, demonstrating that a high consumption of this mineral is essential for the increase of the BP.

The main source of sodium in the diet is salt (Gaitán, D., Chamorro, R., Cediel, G., Lozano, G. and Da Silva-Gomes, F. (2015); the relationship between the consumption of salt with BP has been established through population, epidemiological, migration and in experimental intervention studies (Strazzulo et al., 2009) studies. See table 1.

Therefore, it has been proposed that a moderate reduction in salt intake of the population could contribute to an important public health worldwide improvement (He F. J. et. Al., 2009).

In fact, today the restriction in sodium intake recommendation is the most common self-care in patients with SAH and heart failure (HF) diet (He FJ et al., 2013), (Gupta, D., Georgiopoulou , VV, Kalogeropoulos, AP, Dunbar, SB, Reilly, CM and Sands, JM et. al. 2012)

This recommendation is based on the premise that the reduction in salt intake has been associated with decreased BP, and keep it under control cardiovascular risk (CVR) (Heb F. J. et al., 2013) would be reduced.

It has also been argued that reducing salt intake is a cost-effective strategy on the burden of heart disease in the long term (Shoaibi, A., Ghandour, R., Khatib, R. et. Al., 2013) , reducing the high costs of care, so it is considered one of the best investments in public health (Wang D. G. and Labarthe, 2011).

WHO recommends less than 2 grams per day (g / d) of sodium (5 g / d of salt) in adult intake as a measure to reduce the PA, CVR, strokes and coronary heart disease (WHO, 2012 and 2013).

Participation sodium in regulating the PA has authorized the health policy recommends dietary restriction based on the premise that with the reduction, or control of the PA, cardiovascular risk would be reduced (RCV) (He, FJ et al., 2013). See Table 1, section A. It has also been argued that reducing salt intake is a cost-effective strategy on the burden of heart disease in the long term (Shoaibi, A., Ghandour, R., Khatib, R. et. al., 2013) which reduces the high costs of care, so it is considered one of the best investments in public health (Wang, G. y Labarthe, D., 2011) (S. B., Reilly, C. M. y Sands, J. M. et. al. 2012).

Table 1. Studies sodium and cardiovascular health

Modelo	Sodio	Resultados	Fuente
Evidencia a favor de la disminución de Na			
Humanos (n=10079) multicéntrico (52)	En 42 centros incremento de Na.	Asociado a incremento de la PA con la edad, pero no a la PA media o a la prevalencia de HAS.	INTERSALT (1988)
Chimpancés (98.8 % de homología genética con el hombre)	Aumento gradual consumo de sal 0.5 g/ d (200 mg Na)	Aumento progresivo de la PA	Denton D. et al. (1995)
Humanos (n=10074)	Excreción >100 mmol/d (2300 mg Na)	En mediana edad 55 vs 25 años, incremento de PA de 10-11/6 mmHg	Elliot P. et al. (1996)
Meta-análisis humanos 17 ensayos (n=734 HAS) seguimiento por 3 semanas 11 ensayos (n=220 normo tensos) seguimiento por 4 semanas	Mediana de reducción: 78 mmol/d (4.6 g de sal) 74 mmol/d (4.4 g de sal) Ingesta de 3 g sal (1200 mg Na)	< 5 mmHg PAS/2.7 mmHg PAD < 2 mmHg PAS/1 mmHg PAD Reduciría PAS 5.6/PAD 3.2 mmHg en HAS y 3.5/1.8 TA normotensos.	He F.J. y MacGregor GA. (2003)
Chimpancés (n=127) En Gabón, Franceville (n=17) seguimiento > 3 años Dieta isocalórica, Na cambios 75, 35 y 120 mmol En Bastrop, Texas (n=110) seguimiento 2 años Grupo A: Dieta estándar, Na 250 mmol/d Grupo B: se redujo Na 50 %	Reducción Na 100 a 120 mmol/d (2300 – 2720 mg)	< PA en alrededor de 6 a 13 mm Hg	Elliott P. et al. (2007)
Humanos TOPH I (n=744) 18 meses TOPHII (n=2382) 36-48 meses	Reducción Na 44 mmol/d (1012 mg) 33 mmol/d (759 mg)	< PA y el riesgo a largo plazo de eventos CV	Cook N.R. et al. (2007)
Meta-análisis 13 estudios (n=1777025) 3.5 a 19 años	Ingesta superior Diferencia promedio 86 mmol/d (5 g sal/d)	> Riesgo de ACV, ECV	Strazzullo P. et al. (2009)

Meta-análisis humanos 34 estudios ≥ 4 semanas (N=3230)	Reducción de la excreción de 100 mmol/d (6 g sal/d)	Reduce PAS 5.8 mm Hg. Hipertensos: < PAS 5.39 mmHg/2.82 mmHg PAD. Normotensos: < 2.42 mmHg PAS/1.00 mmHg PAD. Aumento actividad Renina-Aldosterona, noradrenalina No significativos en lípidos.	He, F.J. et al. (2013)
Humanos Meta-análisis 36 estudios	Na < 2 g/d Alta ingesta de Na Disminución de la ingesta de sodio	< PAS 3.47/PAD 1.81 mmHg. > riesgo de ACV y mortalidad por enfermedad coronaria. No efectos adversos significativos sobre función renal, lípidos sanguíneos o catecolaminas.	Aburto, N.J. et al. (2013)
Meta-análisis humanos 169 estudios	Ingesta de 2 g de sodio/ día. Alto consumo de Na	Reduce la PA y el efecto antihiper-tensivo, reduce el riesgo de ECV y derrame cerebral. Induce efectos adversos además de elevar la PA.	Mozaffarian, D. et al. (2014)
Evidencias que no soportan la disminución de Na			
Humanos (n=20729) NHANES I Observacional seguimiento 20 años	Disminución de ingesta de Na	Asociado inversamente a mortalidad por todas las causas y CV. No justifica el incremento o disminución de consumo de sal en la dieta.	Alderman M.H. et al. (1998).
Meta-análisis humanos Ensayos clínicos (6 meses a 7 años): 3 estudios PA normal (n=2326), 5 estudios hipertensos no tratados (n=387) 3 estudios hipertensos tratados (n=801)	Disminución de ingesta de Na	< disminuye 1 mmHg PAS/< disminución de la PAD. Muy difícil mantener dieta baja en sal. La reducción de la PA > personas con PA más alta. En la suspensión del Tx antihipertensivo, la reducción de sal ayuda a mantener la PA baja.	Hooper, L. et al. (2004)
Humanos Cohorte (2000 – 2005) n=232 pacientes con ICC compensada. Reingresos por ICC 180 días	< excreción de Na 80 mmol UNaE 24 hr (2606.66 mg de Ingesta) Consumo normal de Na 120 mmol UNaE 24 hr (4778.88	Niveles de aldosterona y actividad de renina significativamente altos < incidencia de re-hospitalización, disminución significativa de péptido	Paterna, S. et al. (2008)

Excreción basal de 120 mmol/d	mg de Ingesta)	natriurético, aldosterona y actividad de renina plasmáticos.	
Humanos (n=3681) Cohorte seguimiento promedio 7.9 años	< excreción de Na 1 tercil: 107 mmol UNaE 24 hr (2934.44 mg de Ingesta)	> mortalidad ECV, solo modificación de PAS con cambios en la excreción de Na, sin > riesgo de HAS o ECV.	Stolarz-Skrzypek, K. et al. (2011)
Humanos (n=638) Cohorte (2000 – 2010) Pacientes con DT2	< excreción de Na 1 tercil: 150 mmol UNaE 24 hr (3833.33 mg de Ingesta)	> riesgo de mortalidad por todas las causas y mortalidad CV.	Ekinci, E.I. et al. (2011)
Humanos (n = 2807) Estudio epidemiológico (1998 a 2002) Pacientes con DT1	< excreción de Na 102 mmol UNaE 24 hr (2606.66 mg de Ingesta) Consumo alto de sal 187 mmol UNaE 24 hr (4778.88 mg de Ingesta)	> riesgo de mortalidad por todas las causas y enfermedad renal terminal. > riesgo de mortalidad general	Thomas, MC. et al. (2011)
Humanos (n=288809 Análisis 2 cohortes pacientes con ECV o DT 2001 a 2008 Excreción basal de 4 a 5,99 g por día (Ingesta 4444.44 a 6655.55 mg/d)	< excreción de Na 3g UNaE 24 hr (3333.33 mg de Ingesta) >excreción de Na 7g UNaE 24 hr (7777.77 mg de Ingesta)	> riesgo de la mortalidad cardiovascular y hospitalizaciones por ICC. > riesgo de todos los eventos CV, La asociación entre la excreción de sodio y los eventos CV tuvo forma de J.	O´Donnell, M.J. et al. (2011)
Humanos (n=360000) 23 studios observacionales	Ingesta de Na < 2.5g y > 6.0 g/d	Asocia a incremento de riesgo CV Identifica una relación en forma de J, que no soporta la reducción de Na universalmente.	Alderman, M.H. y Cohen, H.W. (2012)
Meta-análisis humanos 167 estudios ; 2 grupos: 1. HAS con ingesta elevada de Na 5008.88 mg, se redujo a 1814.44mg por 28 días en promedio. 2. PA normal con alta ingesta de Na (5136.66 mg) y se disminuyó a 1277.77 mg por 7 días en promedio.	Reducción media de sodio 3194.44 mg (125 mmol UNaE 24 hr) 3731.11 mg (146 mmol UNaE 24 hr)	Disminución de 1 % en la PA en normotensos, del 3.5 % en HAS. Aumento significativo ($p<0.001$) en Renina, Aldosterona, Adrenalina y Noradrenalina plasmáticas. > Colesterol de 2.5 % y 7 % en TGC. Efectos estables en los estudios ≥ 2 semanas.	Graudal, N.A. et al. (2012)
Ratones (n=160) *Diabéticos apo E* KO Dietas isocalóricas	Baja en sal (0.05 % Na) Baja en sal + IECA (2mg/Kg/d)	> Acumulación de placa, asociada a la activación del SRAA, Aterogénesis suprimida asociada con	Tikellis, C. et al. (2013)

6 semanas	Alta en sal (3.1% Na)	Supresión del SRAA. Aterogénesis suprimida, eficacia comparable a la inhibición de la ECA.	
Humanos (n=2648) FinnDiane study DT1 sin antecedentes de ECV o Enfermedad Renal Crónica terminal (ERC)	Baja ingesta de sodio Alta ingesta de sodio La relación en forma de J nudo: 102 mmol UNaE 24 hr (2606.66 mg ingesta) - mortalidad y 141 mmol UNaE 24 hr (3603.33 mg ingesta) - desarrollo de ECV.	> riesgo de mortalidad por todas las causas y nuevos eventos CV Asociación con resultados adversos, La disminución de la PA es un objetivo importante en la DT1, sin embargo, la activación del SRAA puede contribuir al desarrollo de las complicaciones CV en pacientes DT1 con bajo consumo de Na.	
Humanos (n=296) DT2	Pacientes sin ECV Ingesta 3155 mg Na/d Pacientes con ECV 2913 mg Na/d	La ingesta de Na no se asocia con ERC. Los pacientes con ECV disminuyen ingesta de Na.	Ferreira, PL. et al. (2014).
Meta-análisis humanos (n=247683). 25 estudios	Baja ingesta de sodio < 115mmol (2645 mg Na, 6.6 g sal) Alta ingesta de sodio 4945mg Na,12.4g sal	Relación en forma de U: la ingesta baja y alta de sodio se asocia con mayor CV y mortalidad por todas las causas.	Graudal N, et al. (2014)
Humanos (n=2642) Cohorte 10 años adultos mayores	Ingesta > 2300 mg Na/d con FC.	No asociación con mortalidad, ECV falla cardiaca, HAS, independientemente del grupo racial.	Kalogeropoulos, AP. et al. (2015)
Humanos Meta-análisis: 4 estudios n=133 118 63559 con HAS 69559 sin HAS (Desenlace: muerte y eventos ECV mayores seguimiento 4.2 años)	Alta ingesta de sodio, (excreción> 6g Na/día) Baja ingesta de sodio, (excreción <3g Na/día) (La reducción de la ingesta, solo aplicada a pacientes con HAS y dieta alta en Na).	> riesgo de eventos CV y muerte en HAS (No se asoció en PA normal) > riesgo de eventos CV y muerte sujetos con o sin HAS.	Mente, A. et al. (2016)

However, several studies have shown that not all individuals consuming high salt is associated with hypertension (Young, C. H. et al., 2015), nor all subjects respond equally to reducing sodium intake. It has been suggested that a diet low in sodium (3 g salt Na / d) could be more effective in reducing BP in women and the elderly (He, FJ et al., 2009) and in subjects black or Asian race compared with Caucasian (Graudal NA, 2012).

The underlying mechanisms that promote this variability are complex, ranging from genetics to environmental influences (Young, C. H., 2015).

It has been proposed that the decrease in BP due to sodium restriction, can have transient effects and may even be "paradoxical" increases in BP in some people (DiNicolantonio, J. J., 2013). Therefore, it has recently emerged a major debate on sodium consumption from the perspective of health, although some authors have shown evidence that sodium reduction lowers BP and antihypertensive effect reduces heart disease and stroke with a sodium intake of at least 2 g / d (Mozaffarian, D. et al., 2014), while others have suggested that a restriction in sodium intake is associated with overall mortality and CV (Kyu, HS, 2014).

A model of diabetic rats found that a low-salt diet was a potent inducer of atherosclerosis more diabetes alone, probably due to activation associated RAAS salt restriction. And in adults with DT 1 low sodium intake it was associated with an increased risk of all-cause mortality and development of cardiovascular events. This suggests that the association between intake of Na and cardiovascular outcomes in diabetes is more complicated than simply raising the PA (Tikellis C., 2013).

Some authors have stated that there is no conclusive evidence that a low-sodium diet reduces cardiovascular events in normotensive and hypertensive and even pre-hypertensive patients; on the contrary, there is evidence that a diet low in sodium leads to a worse cardiovascular prognosis in patients with CHF and DT1 and 2 (DiNicolantonio, J. J.).

It has been proposed that even if there was a reduction of 1 to 2 mm Hg in the PA per 75-100 mmol of decreased intake of Na, we should consider the risk-benefit of reducing intake across the population, because the modification can bring adverse effects (Alderman, MH, 2000).

Because of the relatively small effects and antagonistic nature of the effects (decrease in BP, increased hormones and lipids), these results do not support that sodium reduction has net beneficial effects, for example, in Caucasians (Graudal, NA , et al, 2012), seniors (Kalogeropoulos, A. P, 2015) or in diabetic patients (Thomas MC, 2011), who may not require restriction greater than the current recommendation for the general adult population sodium.

In the case of heart failure, Na restriction is a standard measure in the treatment. However, many health professionals are not aware of the controversy about the degree of restriction of sodium intake, since a severe restriction can lead to worse forecasts (Weiss, B. D., 2014).

Some researchers (Penner, S. B. et al, 2007 and Farquhar, W. B. et al, 2015), have stated that these studies may have methodological shortcomings.

Meanwhile, C. Y. Wang et al., 2015 and Huang, L. et al. 2015, show that only studies using a urine sample UNAE 24 hr, provide reliable information on sodium intake. Recently, Graudal et al., 2015 described in a meta-analysis of 15 studies, the effect of reducing Na exists in people with PA in "Borderline" and hypertensive, and is most effective in just one week and remains stable, while in normotensive effects are observed only with a very large decrease in intake (> 248 mmol / d, 5,600 mg Na / d).

The above results suggest that more studies to objective conclusions about the benefits or harm of a reduction of sodium (eg below 1.5 or 1.0 g / d), either in general populations or subgroups of patients at high required risk (Mozaffarian D., 2014).

In this regard, the committee that evaluates the consequences of sodium reduction in populations of the United States, has ruled that it is necessary to conduct more controlled clinical trials to determine the effect of sodium on health, considering the evidence with lower intakes to 2300 or 1500 mg / d, which are the guidelines recommended by health in this country, is still insufficient. Therefore propose the design of controlled studies to evaluate the effects of varying levels of sodium intake and thereby estimate the reduction goal of the ideal intake and determine the risk of developing cardiovascular disease, stroke and association with overall mortality trials and CV (IOM, 2013). It has also been proposed to determine the effect of sodium reduction <1.2 g / day on BP and adverse effects (changes in blood lipids and catecholamine levels) in adults and

children (WHO, 2012); and highlights the need to collect high-quality evidence on the risks and benefits of reducing sodium (Oparil, S., 2014).

However, despite the existence of such a discussion at international level and have opted for the need to obtain reliable information -on which to estimate the guidelines for the restriction or sodium intake, by region, race, health status , age and genre, the current clinical practice guidelines still recommend sodium restriction as a treatment regimen must respect the non-pharmacological treatment in certain pathologies and as a general measure at the population level. See Table 2.

Table 2. Current recommendations for sodium intake in the adult population.

Población	Referencia	País	Año	Recomendación de restricción de sodio
General	OMS	-I	2012	< 2000 mg/d
General	HHS	EUA	2015	< 2300 mg/d
HAS	USDA		2015	< 1500 mg/d
IC	ADA		2016	< 2000 mg/d
Diabetes	ADA		2015	< 2300 mg/ d
ECV.	AHA		2012	< 1500 mg/d
Diabetes	ALAD	LA	2013	< 1600 mg/d
HAS en DT2 y SM	Consenso LA		2013	< 32000 mg/d
General	OPS		2011	< 2000 mg/d
General	ILSI		2011	< 2000 mg/d
General (sana)	Bourges	MEX	2005	500 mg (Requerimientos mínimos)
HAS	GPC HAS		2014	< 1500 mg/día (< 50 años) < 1300 mg/d (51 – 71 años) < 1200 mg/d (> 70 años)
DT2 + HAS	GPC DT		2014	< 2400 mg/d
DISLIPIDEMIAS	GPC D		2012	< 5 g de sal /d
HAS	GPC RCV		2010	< 5 g de sal /d
DT2 + HAS	NOM-015		2010	< 2000 mg/d
HAS	NOM-030		2009	< 2400 mg/d

There is no unification on the criteria of the recommendation of sodium intake in the diet, and even in the GPC HAS most recently in Mexico is a major constraint as age increases, which could be counterproductive. Thus, it calls for responsible for designing public policies to review and, if necessary, reconsider the recommendations, taking into account recent evidence, such as proposed by WHO and IOM.

Conclusion

This review sought to provide relevant scientific evidence entitling the health professional to make objective decisions on the control of salt intake in the diet. Clinical and experimental evidence shows the existence of a controversy over the degree of restriction of sodium intake, specifically in patients with CVD, since sodium restriction can lead to increased mortality.

Bibliography

Aburto, N. J., Ziolkovska, A., Hooper, L., Elliot, T. P., Cappuccio, F. P. & Meerpohl J. J. (2013). Effect of lower sodium intake on health: systematic review and meta-analyses. BMJ, 346, f1326. doi: http://dx.doi.org/10.1136/bmj.f1326

Alderman, M. H. & Cohen H. W. (2012). Dietary Sodium Intake and Cardiovascular Mortality: Controversy Resolved? Am J Hypertens, 25 (7), 727-734. doi: 10.1038/ajh.2012.52

American Dietetic Association (ADA) citado por Hummel, S. L. & Konerman, M.C. (2016). Dietary sodium restriction in heart failure: a recommendation worth its salt? JCHF, 4(1), 36-38. doi:10.1016/j.jchf.2015.10.003

Asociación Latinoamericana de Diabetes (ALAD) (2013). Guías ALAD sobre diagnóstico, control y tratamiento de la diabetes mellitus tipo 2 con medicina basada en evidencia. *Revista de la ALAD*, 52-63.

Alderman, M. H. (2000). Salt, Blood Pressure, and Human Health. *Hypertension,* 36, 890-893.

Alderman, M. H., Cohen, H. & Madhavan, S. (1998). Dietary sodium intake and mortality: the National Health and Nutrition Examination Survey (NHANES I) *Lancet*; 351, 781–85.

American Diabetes Association (2015). Foundations of Care: Education, nutrition, physical activity, smoking cessation, psychosocial care, and immunization. *Diabetes Care*; 38, Suppl. 1:S20-S30.

Bourges, H., Casanueva, E. y Rosado, J. L. (2005). Recomendaciones dietéticas diarias de vitaminas y nutrimentos inorgánicos. Recomendaciones de ingestión de nutrimentos para la población mexicana. Ed. Médica Panamericana, México.

Cook, N. R., Cutler, J. A., Obarzanek, E., Buring, J. E., Rexrode, K. M., Kumanyika, S. K., et al. (2007). Long term effects of dietary sodium restriction on cardiovascular disease outcomes: observacional follow-up of the trials of hypertension prevention (THOP). BMJ, 334, 885-8. doi: 10.1136/bmj.39147.604896.55

Denton, D., Weisinger, R., Mundy, N. I., Wickings, E. J., Dixson, A., Moisson, P., et. al. (1995). The effect of increased salt intake on blood pressure of chimpanzees. *Nat Med;* 1, 1009–1016.

DiNicolantonio, J. J., Pharm, D., Niazi, A. K., Sadaf, R., O' Keefe, J. H., Lucan, S. C. et al. (2013). Dietary Sodium Restriction: Take It with a Grain of Salt. *The American Journal of Medicine,* 126, 951-955.

Elliot, P., Stamler, J., Nichols, R., Dyer, A. R., Stamler, R., Kesteloot, H. et al. (1996). Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. *BMJ*, 312, 1249-53.

Ekinci, E. I., Clarke, S., Thomas, M. C., Moran, J. L., Cheong, K., MacIsaac, R. J. et al. (2011). Dietary salt intake and mortality in patients with type 2 diabetes. Diabetes Care, 34, 703–709. doi: 10.2337/dc10-1723.

Elliott, P., Walker, L. L., Little, M. P., Blair-West, J. R., Shade, R. E., Lee, D. R. et al. (2007). Change in salt intake affects blood pressure of chimpanzees: implications for human populations. Circulation, 116, 1563-1568. doi:10.1161/CIRCULATIONAHA.106.675579

Farquhar, W. B., Edwards, D. G., Jurkovitz, C. T., Weintraub, W. S. (2015). Dietary Sodium and Health More Than Just Blood Pressure. Journal of the American College of Cardiology. 65 (10), 1042-1050. doi: http://dx.doi.org/10.1016/j.jacc.2014.12.039

Ferreira, P. L., Stark, S., Steenkiste, A., Piraino, B. & Sevick, M. A. (2014). Dietary Sodium Intake in Type 2 Diabetes. *Clinical Diabetes, 32(3), 106-112.*

Gaitán, D., Chamorro, R., Cediel, G., Lozano, G. & Da Silva-Gomes F. (2015). Sodio y enfermedad cardiovascular: contexto Latinoamérica. *Archivos Latinoamericanos de Nutrición*, 65(4), 206-215.

Graudal, N., Hubeck-Graudal, T., Jürgens, G. & McCarron, D. A. (2015). The significance of duration and amount of sodium reduction intervention in normotensive and hypertensive individuals: A Meta-Analysis. *Adv Nutr,* 6, 169-177.

Graudal, N. A., Hubeck-Graudal, T. & Jurgens, G. (2012). Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride. Am J Hypertens, 25(1), 1-15. doi: 10.1038/ajh.2011.210

Graudal, N., Jürgens, G., Baslund, B. & Alderman M. H. (2014). Compared with usual sodium intake, low and excessive sodium diets are associated with increased mortality: a meta-analysis. American Journal of Hypertension: 27(9),1129-37. doi: 10.1093/ajh/hpu028

Gupta, D, Georgiopoulou, V. V., Kalogeropoulos, A. P., Dunbar, S. B., Reilly, C. M. & Sands, J. M. et. al. Dietary sodium intake in heart failure. Circulation. 2012; 126: 479-485. doi: 10.1161/CIRCULATIONAHA.111.062430

He, F. J. & MacGregor, G. A. (2002). Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. J Hum Hypertens, 16(11), 761-70. doi: 10.1038/sj.jhh.1001459

He, F.J. & MacGregor, G. A. (2003). How Far Should Salt Intake Be Reduced? Hypertension, 42, 1093-1099. doi: 10.1161/01.HYP.0000102864.05174.E8

He, F.J. & MacGregor, G.A. (2009). A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. Journal of Human Hypertension, 23, 363–384. doi: 10.1038/jhh.2008.144.

He, F.J., Li, J. & MacGregor, G. A. (2013). Effect of longer-term modest salt reduction on blood pressure. Cochrane Database of Systematic Reviews, 4(CD004937). doi: 10.1002/14651858.CD004937.pub2.

Hooper, L., Bartlett, C., Davey, S. G. & Ebrahim, S. (2004). Advice to reduce dietary salt for prevention of cardiovascular disease. Cochrane Database of Systematic Reviews, 1 (CD003656). doi: 10.1002/14651858.CD003656.pub2

Huang, L., Crino, M., Wu, J. H. Y., Woodward, M., Barzi, F., Land, M. A. et al (2015). Mean population salt intake estimated from 24-h urine samples and spot urine samples: a systematic review and meta-analysis. International Journal of Epidemiology, 1–12. doi: 10.1093/ije/dyv313

He, J., Gu, D., Chen, J., et al (2009). Gender difference in blood pressure responses to dietary sodium intervention in the GenSalt study. *J Hypertens,* 27, 48-54.

Instituto Mexicano del Seguro Social (2014). Diagnóstico y tratamiento de la hipertensión arterial en el primer nivel de atención, México.

Instituto Mexicano del Seguro Social (2014). Tratamiento de la diabetes mellitus tipo 2 en el primer nivel de atención, México.

INTERSALT (1988). An international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *BMJ* 297, 319-328.

Institute of Medicine (2013). Sodium Intake in Populations Assessment of Evidence. *National Academy of Sciences.*

López-Jaramillo, P., Sánchez, R. A., Díaz, M., Cobos, L., Bryce, A., Parra-Carrillo, J. Z. et al. (2013). Consenso latinoamericano de hipertensión en pacientes con diabetes tipo 2 y síndrome metabólico. *Acta Med Colomb*, 38, 154-172.

Kalogeropoulos, A. P., Georgiopoulou, V. V., Murphy, R. A., Newman, A. B., Bauer, D. C. et al. (2015). Dietary sodium content, mortality, and risk for cardiovascular events in older adults. The Health, Aging, and Body Composition (Health ABC) Study. JAMA Intern Med, 175(3), 410-419. doi:10.1001/jamainternmed.2014.6278

Kyu, H. S. (2014). Dietary salt intake and hypertension. Electrolyte Blood Press, 12, 7-18, doi: http://dx.doi.org/10.5049/EBP.2014.12.1

Mozaffarian, D., Singh, G. M. & Powles, J. (2014). Sodium and Cardiovasvcular Disease. Correspondence. *N ENGL J MED,* 371(22), 2134-2139.

Mozaffarian, D., Fahimi, S., Singh, G. M., Micha, R., Khatibzadeh, S., Engell, R. E. et al. (2014). Global sodium consumption and death from cardiovascular causes. N Engl J Med, 4 (371), 624-34. doi: 10.1056/NEJMoa1304127

O´Donnell, M. J., Yusuf, S., Mente, A., Gao, P., Mann, J. F., Teo, K. et al. (2011). Urinary Sodium and Potassium Excretion and Risk of Cardiovascular Events. JAMA, 306(20), 2229-2238. doi: 10.1001/jama.2011.1729.

Organización Mundial de la Salud Guideline: Sodium intake for adults and children, 2012. Geneva, World Health Organization. Recuperado de: http://www.who.int/nutrition/publications/guidelines/sodium_intake/en/

Organización Mundial de la Salud (2016). Cardiovascular diseases. WHO. Recuperado de: http://www.who.int/cardiovascular_diseases/en/

Organización Mundial de la Salud (2015). Enfermedades cardiovasculares, OMS. Recuperado de: http://www.who.int/mediacentre/factsheets/fs317/es/

Organización Mundial de la Salud (2014). Noncommunicable Diseases (NCD) Country Profiles. WHO. Recuperado de: http://www.who.int/nmh/countries/mex_en.pdf

Organización Panamericana de la Salud (2013). La reducción de la sal en las Américas: una guía para la acción en los países. Washington, D.C. Recuperado de: http://www.paho.org/hq/index.php?option=com_docman&task=cat_view&gid=5395&Itemid=3482&lang=es

Organización Panamericana de la Salud. Programa de la OPS/OMS: Reducción de la sal (s. f.). Washington, D.C. Recuperado de: http://www.paho.org/hq/index.php?option=com_topics&view=article&id=352&Itemid=40940&lang=es

Oparil S. (2014). Low Sodium Intake - Cardiovascular Health Benefit or Risk? *N Engl J Med*, 371(7), 677-679.

Organización Mundial de la Salud (2012). Guideline: Sodium intake for adults and children. Geneva, WHO.

Organización Mundial de la Salud (2013). Global action plan for the prevention and control of non comunicable diseases 2013-2020.

Organización Panamericana de la Salud (2011). Grupo de expertos de la OMS/OPS sobre la prevención de las enfermedades cardiovasculares mediante la reducción de la ingesta de sal alimentaria de toda la población.

Paterna, S., Parrinello, G., Fasullo, S., Sarullo, F. M. & DiPasquale P. (2008). Normal-sodium diet compared with low-sodium diet in compensated congestive heart failure: is sodium an old enemy or a new friend? *Clinical Science*, 114, 221–230.

Penner, S. B., Campbell, N., Chockalingam, A., Zarne, K. &, Van, V. B. (2007). Dietary sodium and cardiovascular outcomes: a rational approach. *Can J Cardiol*., 23(7), 567-572.

Secretaría de Salud (2010). Detección y estratificación de factores de riesgo cardiovascular. CENETEC México. Recuperado de: http://www.cenetec.salud.gob.mx/descargas/gpc/CatalogoMaestro/421IMSS_421_11_Factores_riesgo_cardiovascular/IMSS_421_11_RIESGOCARDIOVASCULAR.pdf

Secretaría de Salud (2015). SINAVE/DGE/SALUD/Panorama Epidemiológico y Estadístico de la Mortalidad en México 2011, México. Recuperado de: http://www.epidemiologia.salud.gob.mx/doctos/infoepid/publicaciones/mortalidad/PEE Mortalidad_VE2011.pdf

Shoaibi, A., Ghandour, R., Khatib, R., Mason, H., O´Flaherty, M., Capewell S. et. al. (2013). Salt reduction as a population-based intervention for the prevention of coronary heart diseases: an economic assessment. Lancet, 382(S33). doi: http://dx.doi.org/10.1016/S0140-6736(13)62605-7

Stolarz-Skrzypek, K., Kuznetsova, T., Thijs, L., Tikhonoff, V., Seidlerová, J., Richart, T. et al. (2011). Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. JAMA, 305(17), 1777-1785. doi: 10.1001/jama.2011.5740.

Strazzullo, P., D'Elia, L., Kandala, N. B. & Cappuccio, F. P. (2009). Salt intake, stroke, and cardiovascular disease: metaanalysis of prospective studies. BMJ, 339, b4567. doi: 10.1136/bmj.b4567

Secretaría de Salud (2009). Norma Oficial Mexicana NOM-030-SSA2-2009. Para la prevención, detección, diagnóstico, tratamiento y control de la hipertensión arterial sistémica, México.

Secretaría de Salud (2010). Norma Oficial Mexicana NOM-015-SSA2-2010. Para la prevención, tratamiento y control de la diabetes mellitus, México.

Secretaría de Salud (2010). Detección y estratificación de factores de riesgo cardiovascular, México.

Secretaría de Salud. Diagnóstico y tratamiento de dislipidemias (2012), México.

Thomas, M. C., Moran, J., Forsblom, C., Hartjutsalo, V., Thorn, L., Ahola, A. et al. (2011). The association between dietary sodium intake, ESRD, and all-cause mortality in patients with type 1 diabetes. Diabetes Care, 34, 861–866. doi: 10.2337/dc10-1722.

Tikellis, C., Pickering, R. J., Tsorotes, D., Harjutsalo, V., Thorn, L., Ahola, A. et al. (2013). Association of dietary sodium intake with atherogenesis in experimental diabetes and with cardiovascular disease in patients with Type 1 diabetes. Clinical Science 124, 617–626 doi: 10.1042/CS20120352

U.S. Departments of Agriculture and Health and Human Services (2015 - 2020). Dietary Guidelines for Americans. 8th ed. Recuperado en: http://health.gov/dietaryguidelines/2015/guidelines/

Vannucchi, H., Weingarten, B. M., Masson, L., Cortés, Y., Sifontes, Y. & Bourges H. (2011). Propuesta de armonización de los valores de referencia para etiquetado nutricional en Latinoamérica (VRN-LA). *ALAN*, 61(4), 347-352.

Wang, C. Y., Carriquiry, A. L., Chen, T. C., Loria, C. M., Pfeiffer, C. M., Liu, K. et al. (2015). Estimating the Population Distribution of Usual 24-Hour Sodium Excretion from Timed Urine Void Specimens Using a Statistical Approach Accounting for Correlated Measurement Errors. J Nutr, 145(5), 1017-24. doi: 10.3945/jn.114.206250.

Wang, G. & Labarthe D. (2011). The cost-effectiveness of interventions designed to reduce sodium intake. J Hypertens; 29(9), 1693–1699. doi:10.1097/HJH.0b013e328349ba18.

Weiss, B. D., (2014). Sodium restriction in heart failure: how low should you go? *American Family Physician*, 89(7), 509 -510.

Whelton, P. K., Appel, L. J., Sacco, R. L. Anderson, C. A., Antman E. M., Campbell, N. et al. (2012). Sodium, blood pressure, and cardiovascular disease: further evidence supporting the American Heart Association (AHA) sodium reduction recommendations. Circulation, 126(24), 2880-9. doi: 10.1161/CIR.0b013e318279acbf

Young, C. H., Cheon, P. H. & Kyu, H. S. (2015). Salt Sensitivity and Hypertension: A Paradigm Shift from Kidney Malfunction to Vascular Endothelial Dysfunction. Electrolyte Blood Press, 13, 7-16. http://dx.doi.org/10.5049/EBP.2015.13.1.7