Journal of Women's Health Care

Abdoli, J Women's Health Care 2016, 5:4
DOI: 10.4172/2167-0420.1000320

Short Communication Open Access

Salt and Pregnancy Complications: A Proposal for Future Research

Abdoli A*

Department of Parasitology, Tarbiat Modares University, Tehran, Iran

***Corresponding author:** Amir Abdoli, Faculty of Medical Sciences, Department of Parasitology, Tarbiat Modares University, Tehran, Iran, Tel: +98 82884861, +98 9127144223; E-mail: a.abdoli@modares.ac.ir

Rec date: June 30, 2016; **Acc date:** July 07, 2016; **Pub date:** July 25, 2016

Keywords: Inflammation; Pregnancy; Miscarriage; Pre-eclampsia; Salt; T-helper 17

Introduction

Salt (sodium chloride, NaCl) is a major mineral element that plays a pivotal role in health and disease [1]. According to the world hypertension league (WHL) and the international society of hypertension (ISH), the daily levels of dietary salt intake should be less than 5 g (sodium 2000 mg) for adults [2,3]. Excessive dietary salt intake is one of the important causes of cardiovascular diseases, hypertension and stroke [4,5].

Recently, different investigations demonstrated that excessive salt intake has a pivotal role in the development of inflammatory reactions [6-8]. On the other hand, different studies indicated the role of inflammation in the pathophysiology of pregnancy complications, such as miscarriage and preeclampsia [9,10]. Hence, an important question arises about this condition: may excessive dietary salt intake increases risk of pregnancy complications?

Immune Regulation during Normal Pregnancy

Pregnancy has a number of profound immunological and hormonal alterations [11]. Pregnancy hormones affect the immunological balance during the three trimesters of pregnancy [11]. It is very well documented that immunological shift toward anti-inflammatory responses are essential for a successful pregnancy [11-13].

Common examples of this phenomenon are:

1. Decrease the activities of inflammatory cells; including T-helper 1 cells (Th1) and T-helper 17 cells (Th17) associated with their inflammatory cytokines (e.g., interferon gamma (IFN-γ), Tumor necrosis factor alpha (TNF-α), interleukin-1 (IL-1), IL-6, IL-17 and IL-23).
2. Increase the activities of anti-inflammatory cells; including T helper cell type 2 (Th2) and regulatory T cells (Treg) associated with their anti-inflammatory cytokines (e.g., IL-4, IL-5, IL-9, IL-10, IL-13 and Transforming growth factor-β (TGF-β)) [11,12,14].

Inflammation and Pregnancy Complications

Numerous studies have been demonstrated the role of inflammatory reactions in the pathophysiology of pregnancy complications; including miscarriage and preeclampsia [9,10,15]. It is observed that increased concentration of IFN-γ and TNF-α can damage the fetoplacental tissues [13]. By contrast, increase an anti-inflammatory cytokine IL-10 can prevent fetoplacental damages and spontaneous abortions in murine models [16].

Different investigations indicated the roles of increased Th1/Th17 and decreased Th2/Treg patterns and their cytokines in recurrent miscarriages and preeclampsia [9,15,17,18]. For example, Wang et al. [19,20] reported an increased number of Th17 cells in placental tissues and a high level of IL-17 cytokine in peripheral blood of women with recurrent miscarriage.

Calleja-Agius et al. [17] found increased levels of TNF-α/IL-10 and IFNγ/IL-10 ratios in pregnant women who had a high risk of miscarriage. Inflammatory cytokines TNF-α and IL-6 also involve in the pathphysiology of hypertension during preeclampsia [21].

Salt-derived Inflammation

In 2013, two studies that published in Nature uncovered that excessive dietary salt intake induced severe inflammatory reactions through augmentation of Th17 cells and their highly inflammatory cytokines [6,7]. The results showed that a high salt treatment promotes the severity of experimental autoimmune encephalomyelitis (EAE) (a mouse model of multiple sclerosis) and increased inflammatory cytokines (IL-17, IL-23, TNF-α and IL-2) in murine model [6,7].

Conversely, a high salt treatment inhibits activities of regulatory T cells and anti-inflammatory cytokines IL-4 and IL-13 [22,23]. High salt treatment also decreases anti-inflammatory cytokines and increases inflammatory cytokines by mouse and human macrophages in vitro [24,25].

Yi et al. [26] found a higher number of monocytes in the blood of healthy individuals with high dietary salt intake (12 g/d) than the individuals with normal dietary salt intake. It is of interest that reducing salt intake led to increased production IL-10 and decreased production of IL-23 and IL-6 by lymphocytes [26].

Possible Role of High Salt Intake in the Pathophysiology of Pregnancy Complications

There are a few studies about the involvement of high salt intake and pregnancy complications. For example, it is reported that high dietary salt intake increased risk of gestational hypertension and preeclampsia [27-29]. Although, Abdoli [30] and Rakova et al. [31] proposed that high salt intake can involve in the pathophysiology of miscarriage and preeclampsia through involvement of Th17 cells and their associated inflammatory reactions.

Nevertheless, the link between high salt intake and pregnancy complications is seem to be logical, because high salt intake has a pivotal role in the induction of severe inflammatory reactions [6,7] and inflammatory reactions are involved in the pathophysiology of pregnancy complications [9,10] (Figure 1).

Figure 1: Possible role of high salt intake in the pathophysiology of pregnancy complications.

Therefore, an increase risk of pregnancy complications is plausible for pregnant women with high dietary salt intake. However, further researches should be conducted to elucidate the role of high salt intake in the pathophysiology of pregnancy complications.

References

1. Kotchen TA, Cowley Jr AW, Frohlich ED (2013) Salt in health and disease-a delicate balance. N Engl J Med 368: 1229-1237.
2. Campbell N, Lackland D, Chockalingam A, Lisheng L, Schiffrin EL, et al. (2014) The World Hypertension League and International Society of Hypertension call on governments, nongovernmental organizations, and the food industry to work to reduce dietary sodium. J Clin Hypertens (Greenwich) 16: 99-100.
3. Campbell NR, Correa-Rotter R, Cappuccio FP, Webster J, Lackland DT, et al. (2015) Proposed nomenclature for salt intake and for reductions in dietary salt. J Clin Hypertens (Greenwich) 17: 247-251.
4. Mozaffarian D, Fahimi S, Singh GM, Micha R, Khatibzadeh S, et al. (2014) Global sodium consumption and death from cardiovascular causes. N Engl J Med 371: 624-634.
5. Blaustein MP, Leenen FH, Chen L, Golovina VA, Hamlyn JM, et al. (2012) How NaCl raises blood pressure: a new paradigm for the pathogenesis of salt-dependent hypertension. Am J Physiol Heart Circ Physiol 302: H1031-H1049.
6. Kleinewietfeld M, Manzel A, Titze J, Kvakan H, Yosef N, et al. (2013) Sodium chloride drives autoimmune disease by the induction of pathogenic TH17 cells. Nature 496: 518-522.
7. Wu C, Yosef N, Thalhamer T, Zhu C, Xiao S, et al. (2013) Induction of pathogenic TH17 cells by inducible salt-sensing kinase SGK1. Nature 496: 513-517.
8. Van der Meer JW, Netea MG (2013) A salty taste to autoimmunity. N Engl J Med 368: 2520-2521.
9. Saini V, Arora S, Yadav A, Bhattacharjee J (2011) Cytokines in recurrent pregnancy loss. Clin Chim Acta 412: 702-708.
10. Christiansen OB, Nielsen HS, Kolte AM (2006) Inflammation and miscarriage. Semin Fetal Neonatal Med 11: 302-308.
11. Robinson DP, Klein SL (2012) Pregnancy and pregnancy-associated hormones alter immune responses and disease pathogenesis. Horm Behav 62: 263-271.
12. Challis JR, Lockwood CJ, Myatt L, Norman JE, Strauss JF 3rd, et al. (2009) Inflammation and pregnancy. Reprod Sci 16: 206-215.
13. Raghupathy R (1997) Th1-type immunity is incompatible with successful pregnancy. Immunol Today 18: 478-482.
14. Saito S (2010) Th17 cells and regulatory T cells: new light on pathophysiology of preeclampsia. Immunol Cell Biol 88: 615-617.
15. Lee SK, Kim JY, Lee M, Gilman-Sachs A, Kwak-Kim J (2012) Th17 and regulatory T cells in women with recurrent pregnancy loss. Am J Reprod Immunol 67: 311-318.
16. Chaouat G, Meliani AA, Martal J, Raghupathy R, Elliott J, et al. (1995) IL-10 prevents naturally occurring fetal loss in the CBA x DBA/2 mating combination, and local defect in IL-10 production in this abortion-prone combination is corrected by in vivo injection of IFN-tau. J Immunol 154: 4261-4268.
17. Calleja-Agius J, Muttukrishna S, Pizzey AR, Jauniaux E (2011) Pro- and anti-inflammatory cytokines in threatened miscarriages. Am J Obstet Gynecol 205: 83.
18. Wu L, Luo LH, Zhang YX, Li Q, Xu B, et al. (2014) Alteration of Th17 and Treg cells in patients with unexplained recurrent spontaneous abortion before and after lymphocyte immunization therapy. Reprod Biol Endocrinol 12: 74.
19. Wang WJ, Hao CF, Qu QL, Wang X, Qiu LH, et al. (2010) The deregulation of regulatory T cells on interleukin-17-producing T helper cells in patients with unexplained early recurrent miscarriage. Hum Reprod 25: 2591-2596.
20. Wang WJ, Liu FJ, Qu HM, Hao CF, Qu QL, et al. (2013) Regulation of the expression of Th17 cells and regulatory T cells by IL-27 in patients with unexplained early recurrent miscarriage. J Reprod Immunol 99: 39-45.
21. Gilbert JS, Ryan MJ, LaMarca BB, Sedeek M, Murphy SR, et al. (2008) Pathophysiology of hypertension during preeclampsia: linking placental ischemia with endothelial dysfunction. Am J Physiol Heart Circ Physiol 294: H541-H550.
22. Hernandez AL, Kitz A, Wu C, Lowther DE, Rodriguez DM, et al. (2015) Sodium chloride inhibits the suppressive function of FOXP3+ regulatory T cells. J Clin Invest 125: 4212-4222.
23. Binger KJ, Gebhardt M, Heinig M, Rintisch C, Schroeder A, et al. (2015) High salt reduces the activation of IL-4- and IL-13-stimulated macrophages. J Clin Invest 125: 4223-4238.
24. Zhang WC, Zheng XJ, Du LJ, Sun JY, Shen ZX, et al. (2015) High salt primes a specific activation state of macrophages, M(Na). Cell Res 25: 893-910.
25. Hucke S, Eschborn M, Liebmann M, Herold M, Freise N, et al. (2016) Sodium chloride promotes pro-inflammatory macrophage polarization thereby aggravating CNS autoimmunity. J Autoimmun 67: 90-101.
26. Yi B, Titze J, Rykova M, Feuerecker M, Vassilieva G, et al. (2015) Effects of dietary salt levels on monocytic cells and immune responses in healthy human subjects: a longitudinal study. Transl Res 166: 103-110.
27. Martillotti G, Ditisheim A, Burnier M, Wagner G, Boulvain M, et al. (2013) Increased salt sensitivity of ambulatory blood pressure in women with a history of severe preeclampsia. Hypertension 62: 802-808.
28. Khan AE, Scheelbeek PF, Shilpi AB, Chan Q, Mojumder SK, et al. (2014) Salinity in drinking water and the risk of (pre)eclampsia and gestational hypertension in coastal Bangladesh: a case-control study. PLoS One 9: e108715.
29. Scheelbeek PF, Khan AE, Mojumder S, Elliott P, Vineis P (2016) Drinking Water Sodium and Elevated Blood Pressure of Healthy Pregnant Women in Salinity-Affected Coastal Areas. Hypertension.
30. Abdoli A (2016) Salt and miscarriage: Is there a link? Med Hypotheses 89: 58-62.
31. Rakova N, Muller DN, Staff AC, Luft FC, Dechend R (2014) Novel ideas about salt, blood pressure, and pregnancy. J Reprod Immunol 101-102: 135-139.