Nephrolithiasis: nutrition as cause or therapeutic tool

Irene Brenna1*, Elena Dogliotti1,2, Annalisa Terranegra1, Benedetta Raspini1 and Laura Soldati1*

Abstract

Nephrolithiasis is a very common disease with an increasing prevalence among industrialized populations. Kidney stone formation is a complex phenomenon, involving genetic and metabolic patterns, and nutrition can play an important role in this match both as a promoter or as a protective factor. To promote a deeper knowledge of such a challenging disease, clinicians and researchers have met in Rome, Italy, last March 2013, at the International Congress “Nephrolithiasis: a systemic disorder” to discuss patho-physiology and possible treatment of kidney stones. During the meeting, a whole session was dedicated to nutrition, seen both as a cause or a therapeutic tool for nephrolithiasis. Due to its etiopathogenesis, nephrolithiasis is also an ideal model for a nutrigenetics and nutrigenomics approach. Nutrigenomics and nutrigenetic respectively study the effects of a dietary treatment on gene expression and, on the other hand, the impact of an inherited trait on the response to a specific dietary treatment.

Introduction

Nephrolithiasis is a very common disease in countries with a high socio-economic level as other chronic diseases such as obesity, hypertension, atherosclerosis, cardiovascular disease and type 2 diabetes. In these countries, the prevalence of nephrolithiasis is about 10% [1] and in Italy it is one of the three main causes of hospitalization for nephro-urological reasons, together with renal failure and prostatic hyperplasia [2].

The etiopathogenesis of nephrolithiasis has not yet been fully clarified, although some predisposing factors significantly increase the probability of stones formation such as sex, age, ethnicity, genetics, climate, low water intake, low or high urinary pH, unbalanced diet, overweight or obesity [3]. Starting from epidemiology, in the last thirty years, several large cohort studies have examined the association between diet and stone disease [4,5].

Discussion

Several studies suggested that the typical industrialized countries diet, which is rich in salt and animal proteins, sugar-sweetened drinks and fructose, leads to high urinary excretion of calcium, uric acid, oxalate and phosphorus, and decreases urinary citrate and pH, thus promoting stone formation [6-8]. On the other hand, a higher consumption of fruit and vegetables seems to be a protective factor for stones, leading to an adequate intake of anti-lithogenic factors such as potassium, magnesium, citrate and phytate and reducing dietary salt intake [4,9,10]. The role of dietary calcium is more controversial. As a matter of fact, a low calcium intake was formerly thought to be protective against the onset of kidney stones, but nowadays it is considered useless, since it promotes the intestinal absorption of oxalate and it has been suggested that it could encourage the onset of bad dietary habits (such as a higher animal protein intake).

An example of nutrigenomics is given by the interaction between two candidate genes for nephrolithiasis, calcium sensing receptor (CaSR) and the tight junction protein claudin 14 with calcium diet intake. One of the most important functions of CaSR is the regulation of renal calcium excretion. The polymorphism R990G of CaSR gene gives a gain of function to CaSR protein [11-13]. This more activated receptor, in comparison to the wild type, leads to hypercalcuria by inhibiting PTH secretion in parathyroid cells as well as by inhibiting calcium transport in thick ascending limb of the loop of Henle (TALH) and collecting duct renal cells. In TALH cells, CaSR modulates the activity of some tight junction proteins. When activated by interstitial calcium, it...
inhibits claudin 16 translation to tight junctions to form, together with claudin 19, a paracellular calcium channel. At the same time, it promotes the translocation of claudin 14 that blocks this paracellular calcium channel. The expression of protein claudin 14 was modulated by calcium intake in mice experiments. Under normal dietary condition, equal to 0.61% in calcium, claudin 14 was suppressed by two microRNA molecules, but this effect was reversed with 5% of calcium in the diet [14]. These gene effects, in conjunction with calcium intake levels, may emphasize the predisposition to nephrolithiasis in kidney stone formers.

Beyond the mere association between dietary habits and kidney stones onset, something new about the pathogenesis of nephrolithiasis is emerging, especially about uric acid nephrolithiasis. This particular kind of stones originates from the combination of low urinary volume, hyperuricosuria and low urinary pH, resulting in titration of the soluble urate to the highly insoluble uric acid [15]. Uric acid stone formers, which are often obese, have an increased acid load to the kidney due to both an excessive dietary intake and an increased endogenous acid generation. This is still poorly understood, but seems to involve acquired insulin resistance and the intestinal bacterial flora [16]. Moreover, these kinds of patients are unable to properly utilize ammonia to buffer urinary protons. This defect seems to be caused by fat infiltration of the kidney, a sort of renal steatosis, due to the high levels of circulating free fatty acids typical of obese patients. This fat infiltration causes tubular lipotoxicity and alters tubular functions. As a result, the kidney uses alternative buffers to carry urinary protons, such as urate, which when titrated precipitates and forms stones. Uric acid nephrolithiasis is therefore a good model to understand how crucial is the interaction between nutrition and metabolic patterns in promoting the development of a complex pathology.

Even though the relationship between dietary habits and nephrolithiasis are being increasingly clear, it could be interesting to study the direct influence of dietary factors on genome, through epigenetic regulation of gene expression. This new kind of approach could lead to a deeper knowledge of nutrition potentiality and to a really personalized diet therapy for kidney stone formers.

Author details
1Department of Health Sciences, Università degli Studi di Milano, via A. Di Rudini 8, 20142, Milano, Italy. 2Fondazione Umberto Veronesi, p.zza Velasca 5, 20142, Milano, Italy.

Received: 5 June 2013 Accepted: 24 July 2013
Published: 26 July 2013

References
1. Bartoletti R, Cai T, Mondaini N, Melone F, Travaglini F, Carlini M, Rizzo M: Epidemiology and risk factors in urolithiasis. Urol Int 2007, 79:3–7.
2. Arcidiacono T, Terranegra A, Biasion R, Soldati L, Vezzoli G: Calcium kidney stones: diagnostic and preventive prospects. Ital Urol Nefrol 2007, 24(6):535–546.
3. Trinchieri A: Epidemiology of urolithiasis: an update. Clin Cases Miner Bone Metab 2008, 5(2):101–106.
4. Curhan GC, Willett WC, Knight EL, Stampfer MJ: Dietary factors and the risk of incident kidney stones in younger women (Nurses’ Health Study II). Arch Intern Med 2004, 164:885–891.
5. West B, Luke A, Durazo-Arvizu RA, Cao G, Shoham D, Kramer H: Metabolic syndrome and self-reported history of kidney stones: the National Health and Nutrition Examination Survey (NHANES III) 1988–1994. Am J Kidney Dis 2008, 51:741–747.
6. Robertson WG, Heyburn PJ, Peacock M, Hanes FA, Swaminathan R: The effect of high animal protein intake on the risk of calcium-stone formation in the urinary tract. Clin Sci 1979, 57:285–288.
7. Taylor EN, Stampfer MJ, Curhan GC: Dietary factors and the risk of incident kidney stones in men: new insights after 14 years of follow up. J Am Soc Nephrol 2004, 15(12):3225–3232.
8. Taylor EN, Curhan GC: Fructose consumption and the risk of kidney stones. Kidney Int 2008, 73(2):207–212.
9. Meschi T, Maggiore U, Fiacchioni E, Schianchi T, Bosi S, Adorni G, Riddolo E, Guerra A, Allegri F: The effect of fruits and vegetables on urinary stone risk factors. Kidney Int 2004, 66:2402–2410.
10. Nouvenne A, Meschi T, Prati B, Guerra A, Allegri F, Vezzoli G, Soldati L, Gambardella M, Maggiore U, Borghi L: Effects of a low-salt diet on idiopathic hypercalciuria in calcium-oxalate stone formers: a 3-mo randomized controlled trial. Am J Clin Nutr 2010, 91(3):565–570.
11. Vezzoli G, Terranegra A, Soldati L: Calcium-sensing receptor gene polymorphisms in patients with calcium nephrolithiasis. Curr Opin Nephrol Hypertens 2012, 21(4):355–361.
12. Falchetti A, Gazzini A, Terranegra A, Soldati L, Vezzoli G, Leoncini G, Giusti F, Franceschelli F, Mari L, Tanini A, Cavalli L, Brandi ML: A novel germ line inactivating mutation in the CASR gene in an Italian kindred affected by familial hypocalciuric hypercalcaemia. Eur J Endocrinol 2012, 166(5):933–940.
13. Vezzoli G, Terranegra A, Arcidiacono T, Biasion R, Coviello D, Syren ML, Paloschi V, Giannini S, Mignogna G, Rubinacci A, Ferrarietto A, Cusi D, Bianchi G, Soldati L: R990G polymorphism of calcium-sensing receptor gene does produce a gain-of-function and predispose to primary hypercalciuria. Kidney Int 2007, 71(11):1155–1162.
14. Gong Y, Renigunta V, Himmerkus N, Zhang J, Renigunta A, Bleich M, Hou J: Claudin-14 regulates renal Ca2+ transport in response to CaSR signalling via a novel microRNA pathway. EMBO J 2012, 31(8):1999–2012.
15. Moe OW: Uric acid nephrolithiasis: proton titration of an essential molecule? Curr Opin Nephrol Hypertens 2006, 15(4):366–373.
16. Maalouf NM, Cameron MA, Moe OW, Sakhaee K: Metabolic basis for low urine pH in type 2 diabetes. Clin J Am Soc Nephrol 2010, 5(7):1277–1281.

doi:10.1186/1479-5876-11-178
Cite this article as: Brenna et al.: Nephrolithiasis: nutrition as cause or therapeutic tool. Journal of Translational Medicine 2013 11:178.