doi:10.4149/endo_2014_03_120

Boron and antioxidants complex: a new concept for the treatment of kidney stones without rigorous pain

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Objective. Stone disease is an increasingly common form of renal disease. Diet plays an important role in expression of the tendency to stone formation. Renal epithelial cell injury by reactive oxygen species is a pre-requisite step and the administration of natural antioxidants has been used to protect against nephrolithiasis. Considering the nutrients, boron as an ultra-trace element is revealing to enhance the antioxidant defense mechanism and along vitamin status seems to have an impact on the stone removal.

Methods. A male patient with urolithiasis received daily boron plus antioxidants supplement and asked to consume enough of the dairy serving products plus adequate liquids.

Result. Ultrasonography assessment revealed continuous stone removal or disposal without hydronephrosis with significant pain alleviation and reduction in hematuria. The lithiasic residues were collected. The 9*20 mm size of the one eliminated stone is of noteworthy.

Conclusion. Successful and comfortable kidney stone repulsion with a minor pain and bleeding indicates that this impact of boron plus antioxidants deserves further study and clarification.

Key words: boron, antioxidants, urolithiasis, male, stone removal

Urolithiasis is a multifactorial disorder influenced by both intrinsic and environmental factors. Among the studied factors, male sex with a three times higher incidence than female sex is considered as a risk factor, mainly occurring in the third and fourth decades of life (Curhan 2007; Travison et al. 2009).

To reduce the incidence of renal lithiasis, an important number of etiologic factors can be adequately modified through diet, since it must be considered that the urine composition is directly related to diet. In fact, the change of inappropriate habitual diet patterns should be the main measure to prevent kidney stones (Grases et al. 2006). Considering the nutrients, the biological, medical and environmental roles of trace elements have attracted considerable attention over the years in prevention of chronic or acute diseases, such as renal diseases. Recently, boron has attracted a lot of attentions with a widespread role in biochemistry and nutrition. To initiate a link between boron and urolithiasis, two decades ago, a male individual (age=27 years) who voluntarily had participated in the study reported to discard and collected a 2.0 mm urinary stone, after consuming 10.0 mg boron for three days. Later, this finding was reported by some other patients who consumed boron.

Recently, fourteen volunteer patients whose urolithiasis was confirmed by ultrasonography method and admitted to receive 10 mg boron supplement per day were free from stones and mostly reported that there was no discard and apparently the stone(s) has been dissolved (Naghii et al. 2012). Consequently, we have

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increased the number of successful treatment cases to 30 patients, by now.

A female patient with a 10.0 mm stone in lower pole underwent extracorporeal shock wave lithotripsy (ESWL) received 10 mg boron supplement/day for two weeks revealed complete stone removal or disposal without hydronephrosis, with significant pain alleviation and a significant reduction in hematuria (Naghii 2013).

Although, a complete picture of the pathophysiological mechanisms involved is still unclear, but there is increasing evidence that reactive oxygen species (ROS) and development of oxidative stress (OS) are produced during idiopathic calcium oxalate (CaOx) nephrolithiasis (Khan 2012).

As experimental and clinical studies have demonstrated, the most frequently studied natural antioxidants with free radical scavengers to provide superior renal protection are vitamins A and carotenoids, E, C, B6 and antioxidant trace elements, selenium and zinc (Santhosh Kumar and Selvan 2003; Thamilselvan and Menon 2005; Bardaoui et al. 2010; Holoch and Tracy 2011; Oyewole 2011; Ortiz-Alvarado et al. 2011) that can be easily and safely increased in tissues by supplementation. Medical treatment of stone-forming patients using pyridoxine is considered as an effective first-line therapy to decrease hyperoxaluria in patients who form stones (Ortiz-Alvarado et al. 2011) and zinc is believed to have inhibitory effect on calcium oxalate stone formation (Atakan et al. 2007).

In this report, the effect of boron supplementation plus antioxidants on removal of kidney stones in a male subject is presented.

Methods

A 46 years old industrial machinery salesman patient whose first renal calculi was diagnosed 4 years ago had a recurrence episode 1.5 year ago, recently developed renal lithiasis and refused to undergo extracorporeal shock wave lithotripsy (ESWL) prior to this study. He was referred 8 month ago.

Initially, two ultrasonography reports confirmed the presence of several renal calculi and consequently he accepted to be treated after giving informed consent.

The ultrasonography reports revealing the status of kidney stones and their descriptions during treatment course are presented in Table 1.

During treatment period, he received 20 mg boron supplement (2*10 mg capsule) per day. The capsules were formulated and provided by a pharmacist colleague, using sodium tetraborate (Merck- Germany) as the source of boron. In addition, One EuRho vital Selen plus capsule (Euro OTC Pharma GmbH) containing food supplement with 125 mg Vitamin C, 50 μg Selenium, 8 mg Zinc, 40 mg Vitamin E and 400 μg

Table 1

The status and the descriptions of kidney stones during treatment course

Date	Right kidney	Left kidney	Comment
26 Dec 2012	LC: 17*11 mm, 10 mm	LC: 10 mm	3 stones: 3, 10 & 4 mm discarded within a week
7 Jan 2013	kidney size: 117*57 mm LC: 18 mm	kidney size: 121*63 mm all calyxes: 4.5, 5, 10.5 & 13 mm	---
17 Feb 2013	LC: 17 mm, 8 mm M-LC: 10 mm	MC & LC: a few stones: 5-6 mm	6 stones were discarded within 10 weeks
6 May 2013	kidney size: 118*58 mm LC: 18 mm, 11 mm	kidney size: 119*63 mm MC: a few stones: max. 9.5 mm	2 stones were discarded within 1 week
24 July 2013	kidney size: 129*60 mm LC: 11 mm MC: 6 mm	kidney size: 118*65 mm MC: a few stones: max. 7.5 mm	10 stones were discarded within 3 weeks; the largest size were: 8*10 mm & 9*20 mm
28 Aug 2013	kidney size: 118*54 mm LC: 4 mm MC: 4 mm	kidney size: 115*59 mm MC: 9 mm MC & UC: a few stones: max. 6 mm	---

In all reports, both kidneys had normal shape, cortical thickness and corticomedullary echogenicity. LC - Lower Calyx; MC - Middle Calyx; UC - Upper Calyx; M-LC - Middle-Lower Calyx

Fig. 1. Stones discarded and collected during treatment period by patient.

Vitamin A; a 400 IU softgel capsule of Vitamin E as dl-Alpha Tocopheryl Acetate (Zahravi Pharm. Co., Tabriz, Iran); and a 40.0 mg tablet of Pyridoxine HCL (Vitamin B6) (Ramopharmin Pharmaceutical Lab., Tehran, Iran) was administered daily.

The patient was asked to consume enough dairy serving products plus adequate liquids and 50 ml of lemon juice per day as the source of citrate, to avoid foods high in oxalate concentration, and allowed to withdraw any time he wished. He was instructed to collect the stone residuals and asked to perform ultrasonography diagnosis several times.

Results

The description of the stones are derived from the reports and presented in Table 1. The patient has cooperated and completed the course of treatment and performed the pre and post ultrasonography assessments in the same center. He reported pain alleviation and cease of hematuria within hours to 2-3 days after consumption, and mostly at the time of discarding his stones. No side effects were reported for supplements intake and expressed a sense of satisfaction.

In the first week, stone removal was initiated and within three weeks after 24 July 2013, ten stones were discarded. The largest sizes were: 8*10 mm & 9*20 mm, removed with intermittent and severe pain episodes only at the time of penile expulsion. Stones are shown in the attached picture.

The patient is now continuing the treatment protocol with no pain or complaints.

Discussion

The aim of this preliminary investigation was to evaluate the effect of boron and antioxidants supplementation on removal of kidney stones. The reports of the ultrasonography assessment revealed partial treatment and clearance of the disintegrated calculi within six months. No side effects were reported for supplements intake and the patient expressed a sense of satisfaction and had a proper daily life functioning.

Moreover, more placebo-controlled randomized clinical trials are needed to establish the usefulness of boron plus antioxidants in the adjunctive treatment of urolithiasis.

Renal lithiasis is a multifactorial disease. An important number of etiologic factors can be adequately modified trough diet, since it must be considered that the urine composition is directly related to diet. In fact, the change of inappropriate habitual diet patterns should be the main measure to prevent kidney stones.

Boron has been recognized as essential for plants, and there is evidence that it may be required by human and animals. Foods particularly rich in boron include avocado, peanuts, pecans, grapes, raisins, and wine. Legumes, nuts, and avocados contain 1.0-4.5 mg boron/100 g, while fruits and vegetables provide 0.1-0.6 mg boron/100 g. Meat and dairy products are poor sources, providing <0.6 mg boron/100 g (Gropper et al. 2004). Boron in foods, and the compounds sodium borate and boric acid are rapidly absorbed and excreted largely in the urine. Absorption appears to be virtually complete (95% in humans and rats), and boron appears rapidly in the blood and body tissues of several mammalian species following ingestion (Nielsen 1988; Naghii and Samman 1997).

The Food and Nutrition Board of the Institute of Medicine (2004) has recently established the Tolerable Upper Intake Level of boron for adults over 18 years old as 20 mg/day. Recent findings reported that boron workers (n=75) with a mean daily boron intake of 31.3 mg boron/day, and a subset of 16 of these men, employed at a plant with heavy boron contamination of water supply, having an estimated mean daily intake of 125 mg boron/day (Scialli et al. 2010); and a population with average 42 mg boron/ day (Robbins et al. 2008)

showed no clear evidence of male reproductive adverse effects and adverse semen parameters due to high and chronic boron exposure.

Recent findings also indicate that boron and borates have attracted scientific attention due to recent reports indicating that they may possess anti-carcinogenic properties (Cui et al. 2004). It is also reported that boric acid inhibits human prostate cancer cell proliferation (Barranco and Eckhert 2004) and ingestion of boron in drinking water decreases the incidence of cervical cancer-related histopathological findings (Korkmaz et al. 2007). Results of the chemical and morphological effects of boric acid on human skin melanoma cells suggest that high concentrations have an anti-proliferative effect and show signs consistent with apoptosis (Acerbo and Miller 2009). In a study on the joint effects of boron intake and HRT use on lung cancer risk, it was reported for the first time that boron intake was inversely associated with lung cancer in women (Mahabir et al. 2008). Also, evidence exists that boron may have antioxidants and anti-inflammatory properties (Nielsen 2000; Armstrong and Spears 2003).

Furthermore, in a recent study, one week boron supplementation resulted in a significant decrease in plasma TNF-α concentration (12.32 vs. 9.97 pg/ml) and a remarkable decrease (about 50%) in plasma concentration of hsCRP (1460 vs. 795 ng/ml) and IL-6 (1.55 vs. 0.87 pg/ml) in healthy male subjects, respectively (Naghii et al. 2011).

The results provided a scientific rational for treatment roles of antioxidant nutrient complex in human kidney stone disease.

There is increasing evidence that reactive oxygen species and development of oxidative stress are produced during idiopathic calcium oxalate nephrolithiasis. It is reported that oxidative stress, renal epithelial injury and inflammation are also engaged in idiopathic stone formation which is indicated by the urinary excretion of reactive oxygen species, products of lipid peroxidation, enzymes indicative of renal epithelial injury as well as many markers of chronic kidney disease and suggested that stone formation can lead to hypertension, diabetes, chronic kidneys disease and myocardial infarction (Khan 2012).

Moreover, the administration of antioxidants has been used to protect against nephrotoxicity in human and experimental animals. In the kidney, these treatments are reported to diminish the increase in malondialdehyde (MDA) and the decrease in protective enzyme activity that are induced by chemical and pharmacological agents (Naziroglu et al. 2004).

It is realized that stones less than 5 mm in diameter will usually pass spontaneously, although it may require several weeks of conservative management, while about 50% of stones larger than 5 mm require urologic intervention for removal, and those above 10 mm are very unlikely to pass unaided (Coll et al. 2002). Initial management of stones less than 5 mm in patients without anatomic abnormalities of the urinary tract is watchful waiting, to allow time for stone passage (Holdgate and Pollock 2004).

Our patient reported having a sensation of renal colic or ureteral spasm after boron supplementation and reasonable pain alleviation.

Overall, the current study data indicated that administration of a combination of natural antioxidants, showed beneficial effects on elimination of renal calculi. It seems that the effect of the selected nutrients on prevention and disruption of the kidney stones may be, at least, in part due to its antioxidant effects.

Acknowledgement

Author would like to express his warm thanks to the subject who voluntarily participated in this study.

References

Acerbo AS, Miller LM: Assessment of the chemical changes induced in human melanoma cells by boric acid treatment using infrared imaging. Analyst 134, 1669-1674, 2009. http://dx.doi.org/10.1039/b823234b

Armstrong TA, Spears JW: Effect of boron supplementation of pig diets on the production of tumor necrosis factor-alpha and interferon-gamma. J Anim Sci 81, 2552-2561, 2003.

Atakan IH, Kaplan M, Seren G, Aktoz T, Gul H, Inci O: Serum, urinary and stone zinc, iron, magnesium and copper levels in idiopathic calcium oxalate stone patients. Int Urol Nephrol 39, 351-356, 2007. http://dx.doi.org/10.1007/s11255-006-9050-4

Bardaoui M, Sakly R, Neffat F, Najjar MF, El Hani A: Effect of vitamin A supplemented diet on calcium oxalate renal stone formation in rats. Exp Toxicol Patho 62, 573-576, 2010. http://dx.doi.org/10.1016/j.etp.2009.08.005

Barranco WT, Eckhert CD: Boric acid inhibits human prostate cancer cell proliferation. Cancer Lett 216, 21-29, 2004. http://dx.doi.org/10.1016/j.canlet.2004.06.001

Coll DM, Varanelli MJ, Smith RC: Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. AJR Am J Roentgenol 178, 101-103, 2002. http://dx.doi.org/10.2214/ajr.178.1.1780101

Cui Y, Winton MI, Zhang ZF, Rainey C, Marshall J, De Kernion JB, Eckhert CD: Dietary boron intake and prostate cancer risk. Oncol Rep 11, 887-892, 2004.

Curhan GC: Epidemiology of stone disease. Urol Clin North Am 34, 287-293, 2007. http://dx.doi.org/10.1016/j.ucl.2007.04.003

Food and Nutrition Board, Institute of Medicine. Dietary reference intakes for vitamin A, vitamin K, arsenic, boron, chromium, copper, iodine, iron, manganese, molybdenum, nickel, silicon, vanadium, and zinc. Washington, DC: National Academy press; 2004.

Grases F, Costa-Bauza A, Prieto RF: Renal lithiasis and nutrition. Nutr J 5, 23, 2006. http://dx.doi.org/10.1186/1475-2891-5-23

Gropper SS, Smith JL, Groff JL: Advanced Nutrition and Human Metabolism. 4th ed. Belmont, CA: Thomson Wadsworth, pp. 492-493, 2004.

Holdgate A, Pollock T: Systematic review of the relative efficacy of non-steroidal anti-infllammatory drugs and opioids in the treatment of acute renal colic. BMJ 328, 1401, 2004. http://dx.doi.org/10.1136/bmj.38119.581991.55

Holoch PA, Tracy CR: Antioxidants and self-reported history of kidney stones: the National Health and Nutrition Examination Survey. J Endourol 25, 1903-1908, 2011. http://dx.doi.org/10.1089/end.2011.0130

Khan SR: Is oxidative stress, a link between nephrolithiasis and obesity, hypertension, diabetes, chronic kidney disease, metabolic syndrome? Urol Res 40, 95-112, 2012. http://dx.doi.org/10.1007/s00240-011-0448-9

Korkmaz M, Uzgoren E, Bakirdere S, Aydin F, Ataman OY: Effects of dietary boron on cervical cytopathology and on micronucleus frequency in exfoliated buccal cells. Environ Toxicol 22, 17-25, 2007. http://dx.doi.org/10.1002/tox.20229

Mahabir S, Spitz MR, Barrera SL, Dong YQ, Eastham C, Forman MR: Dietary boron and hormone replacement therapy as risk factors for lung cancer in women. Am J Epidemiol 167, 1070-1080, 2008. http://dx.doi.org/10.1093/aje/kwn021

Naghii MR, Samman S: The effect of boron supplementation on its urinary excretion and selected cardiovascular risk factors in healthy male subjects. Biol Trace Elem Res 56, 273-286, 1997. http://dx.doi.org/10.1007/BF02785299

Naghii MR, Mofid M, Asgari AR, Hedayati M, Daneshpour MS: Comparative effects of daily and weekly boron supplementation on plasma steroid hormones and proinflammatory cytokines. J Trace Elem Med Biol 25, 54-58, 2011. http://dx.doi.org/10.1016/j.jtemb.2010.10.001

Naghii MR, Einollahi B, Rostami Z: Preliminary evidence hints at a protective role for boron in urolithiasis. J Altern Complement Med 18, 207-209, 2012. http://dx.doi.org/10.1089/acm.2011.0865

Naghii MR: Significant pain alleviation, cease of hematuria, and renal stone removal after extracorporeal shock wave lithotripsy with adjuvant boron therapy - case report. Endocr Regul 47,101-104, 2013. http://dx.doi.org/10.4149/endo_2013_02_101

Naziroglu M, Karaoglu A, Aksoy AO: Selenium and high dose vitamin E administration protects cisplatin-induced oxidative damage to renal, liver and lens tissues in rats. Toxicology 195, 221-230, 2004. http://dx.doi.org/10.1016/j.tox.2003.10.012

Nielsen FH: The ultra trace elements. In: Smith KT (ed.) Trace minerals in foods. Marcel Dekker, New York, pp. 357-428, 1988.

Nielsen FH: The emergence of boron as nutritionally important throughout the life cycle. Nutrition 16, 512-514, 2000. http://dx.doi.org/10.1016/S0899-9007(00)00324-5

Ortiz-Alvarado O, Miyaoka R, Kriedberg C, Moeding A, Stessman M, Monga M: Pyridoxine and dietary counseling for the management of idiopathic hyperoxaluria in stone-forming patients. Urology 77, 1054-1058, 2011. http://dx.doi.org/10.1016/j.urology.2010.08.002

Oyewole OI: Chemopreventive role of vitamin C and E on potassium bromate induced renal oxidative damage in rat. J Med Med Sci 2, 1189-1192, 2011.

Robbins WA, Wei F, Elashoff DA, Wu G, Xun L, Jia J: Y:X sperm ratio in boron-exposed men. J Androl 29, 115-121, 2008. http://dx.doi.org/10.2164/jandrol.107.003541

Santhosh Kumar M, Selvam R: Supplementation of vitamin E and selenium prevents hyperoxaluria in experimental urolithic rats. J Nutr Biochem 14, 306-313, 2003. http://dx.doi.org/10.1016/S0955-2863(03)00033-0

Scialli AR, Bonde JP, Bruske-Hohlfeld I, Culver BD, Li Y, Sullivan FM: An overview of male reproductive studies of boron with an emphasis on studies of highly exposed Chinese workers. Reprod Toxicol 29, 10-24, 2010. http://dx.doi.org/10.1016/j.reprotox.2009.10.006

Thamilselvan S, Menon M: Vitamin E therapy prevents hyperoxaluria-induced calcium oxalate crystal deposition in the kidney by improving renal tissue antioxidant status. BJU Int 96, 117-126, 2005. http://dx.doi.org/10.1111/j.1464-410X.2005.05579.x

Travison TG, Araujo AB, Hall SA, McKinlay JB: Temporal trends in testosterone levels and treatment in older men. Curr Opin Endocrinol Diabetes Obes 16, 211-217, 2009. http://dx.doi.org/10.1097/MED.0b013e32832b6348