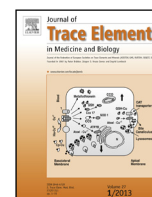
Journal of Trace Elements in Medicine and Biology 39 (2017) 30–35

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb



Biological effects of tolerable level chronic boron intake on transcription factors

Seda Orenay Boyacioglu [a], Mehmet Korkmaz [b,*], Erkan Kahraman [b], Hatice Yildirim [b], Selin Bora [c], Osman Yavuz Ataman [c]

[a] Department of Medical Genetics, Faculty of Medicine, Adnan Menderes University, Aydın 09010, Turkey
[b] Department of Medical Biology, Faculty of Medicine, Celal Bayar University, Manisa 45030, Turkey
[c] Department of Chemistry, Faculty of Arts and Sciences, Middle East Technical University, Ankara 06800, Turkey

ARTICLE INFO

Article history:
Received 18 April 2016
Received in revised form 10 June 2016
Accepted 27 June 2016

Keywords:
Boron
Biological effect of boron
Daily boron intake
Transcription factors
RNA synthesis
Gene expression

ABSTRACT

The mechanism of boron effect on human transcription and translation has not been fully understood. In the current study it was aimed to reveal the role of boron on the expression of certain transcription factors that play key roles in many cellular pathways on human subjects chronically exposed to low amounts of boron. The boron concentrations in drinking water samples were 1.57 ± 0.06 mg/l for boron group while the corresponding value for the control group was 0.016 ± 0.002 mg/l. RNA isolation was performed using *PAX gene RNA kit* on the blood samples from the subjects. The RNA was then reverse transcribed into cDNA and analyzed using the *Human Transcription Factors RT^2 Profiler*^{TM} PCR Arrays. While the boron amount in urine was detected as 3.56 ± 1.47 mg/day in the boron group, it was 0.72 ± 0.30 mg/day in the control group. Daily boron intake of the boron and control groups were calculated to be 6.98 ± 3.39 and 1.18 ± 0.41 mg/day, respectively. The expression levels of the transcription factor genes were compared between the boron and control groups and no statistically significant difference was detected ($P > 0.05$). The data suggest that boron intake at 6.98 ± 3.39 mg/day, which is the dose at which beneficial effects might be seen, does not result in toxicity at molecular level since the expression levels of transcription factors are not changed. Although boron intake over this level will seem to increase RNA synthesis, further examination of the topic is needed using new molecular epidemiological data.
© 2016 Elsevier GmbH. All rights reserved.

1. Introduction

Boron was classified as a trace element by the World Health Organization (WHO) in 1980 [1]. Recently, there is a strong need to re-classify boron as an essential element with the newly discovered positive effects on human health when consumed at Tolerable Chronic Intake (TCI) Level [2]. A TCI of 0.4 mg/kg body weight/d was recommended for humans, which is equal to about 28 mg boron/d for a 70 kg adult [3,4]. Boron plays an important role in mineral and hormonal metabolisms, cell membrane functions, and enzyme reactions. Boron also affects osteoporosis, brain functions, heart trouble, paralysis, diabetes, senility and kidney stone treatment [5,6]. The positive effects of daily boron intake (8.41 mg/day) on cervical cancer was pointed out, and it was emphasized that boron and its compounds may serve as therapeutic agents in the treatment process of prostate and several other cancer types [7–10].

Boron effect on transcription and translation has generally been identified in plant, animal, and yeast studies as human studies are limited [11–14]. Boron may affect the biological cell activities in both transcriptional and translational levels, in vitro. As previously reported, 10 mM boric acid increases in vitro RNA synthesis more than 10 times [12]. In another research, it has been found that 5 mM boric acid increases the level of RNA splicing [13]. Further, boron treatment in yeast activated transcription of *ATR1* through a transcription factor Gcn4, suggesting the role of boron in controlling the transcription factors [14].

As the impact mechanism for the start of general transcription, boron may play a role with the bridges formed by the *cis*-diol groups [15]. It was reported that low consumption of boron helps heal wounds via increasing RNA synthesis of transforming growth factor β (TGF-β), vascular endothelial growth factor (VEGF), and tumor necrosis factor α (TNF-α) [12,15]. Other in vitro studies examining boron and RNA relationship states that 10 mM boron increases total RNA in placenta core by 6.4 times, and 100 ng/ml boric acid application for 4 and 7 days increases mRNA expression of bone morphogenetic protein-7 (BMP-7) by 1.5 and 5.5 fold,

* Corresponding author.
E-mail address: mehmet.korkmaz@cbu.edu.tr (M. Korkmaz).

http://dx.doi.org/10.1016/j.jtemb.2016.06.009
0946-672X/© 2016 Elsevier GmbH. All rights reserved.

respectively [16]. Further, quantitative RT-PCR results have shown that boron treatment regulated Collagen type I (COL I), Osteopontin (OPN), Bone Sialoprotein (BSP), Osteocalcin (OCN), and RunX2 mRNA expressions in favor of osteoblastic function. Boron levels as low as 0.1 ng/ml increased BMP-4, −6 and −7 protein levels [17].

Although the studies defined the effect of boron on the metabolic and cellular processes, it was not revealed exactly which genes or proteins are interacting in the cellular pathways. In this study, it was aimed to clarify which cellular pathways boron plays a role in by examining the expression levels of transcription factors in several cellular pathways in people chronically exposed to boron, and in this context to determine the recommended daily intake of boron in diet.

2. Material and methods

No glassware was used in order to keep the boron levels low in blank solutions. All the containers and volumetric equipment were made of either PTFE or high density polymers. Deionized water from Millipore Milli-Q Water Purification System was used throughout the experiments with the quality of 18 MΩ cm. The analytical grade 65% (w/w) HNO_3 (Merck) was distilled using the Berghof Acid Distillation System for further purification.

2.1. Location of study

The study subjects were selected among residents who were born in Iskele town of Bigadic in the city of Balikesir where the water supplies for drinking and daily use are rich in boron. The levels of boron exposure of boron subjects were compared to those of controls selected among the residents of Manisa city center. Water samples from Iskele, Balikesir and Manisa were analyzed prior to selection of Manisa as the control region. Manisa is located about 130 km away from Iskele, Balikesir. Previous studies have shown that the underground and tap water samples in Iskele, Balikesir area contain 1 mg/l or higher levels of boron [18,8]. The groups were classified according to the boron levels in their water samples; higher than 1 mg/l in Iskele, Balikesir (boron group), and between 0.01 and 0.1 mg/l in Manisa (control group).

2.2. Ethics

This study was conducted in accordance with the good clinical practice and applicable regulatory requirements by the Declaration of Helsinki. The study was approved by the Celal Bayar University Institutional Review Board on February 25th, 2009 (#0051). An informed consent form was obtained from each subject prior to any study-related procedure.

2.3. Determination of boron in drinking water by ICP-MS

For the determination of boron in water samples, inductively coupled plasma–mass spectrometry (ICP-MS) was used. In analyses, a Thermo X Series instrument (Waltham, MA) was employed. ICP-MS conditions were optimized in order to improve the sensitivity. In the optimization procedure, one parameter was optimized while the others were kept constant. The optimum values for forward power, the argon flow rate in nebulizer, and the horizontal and vertical positions of the torch were 1400 W, 0.83 l/min, 63, and 619, respectively. Both of the boron isotopes, ^{10}B and ^{11}B, were monitored for consistency, the results were based on the calibration plot using the signals from the ^{11}B isotope cation formed in the argon plasma. The uncertainty obtained in boron determinations was 5.0% or lower as relative standard deviation. Limit of detection (LOQ) and limit of quantitation (LOQ) were found to be 3.8 and 13 μg/l. The accuracy of the results was validated and continuously monitored by using the certified reference materials, NIST 1573a Tomato Leaves (33.3 ± 0.7 mg/kg boron, certified

Table 1
The list of 84 genes in Human Transcription Factors RT^2 Profiler^{TM} PCR Array (Cat# PAHS-075Z) (SABiosciences, Frederick, MD).

Androgen Receptor Signaling: AR, CTNNB1, RB1.

Insulin Signaling: ELK1, FOS, FOXO1, JUN.

G-Protein-Coupled Receptor Signaling: CREB1, ELK1, FOS, JUN, NFATC1.

Growth Factor Signaling:
EGF Signaling: ELK1, FOS, JUN, STAT1, STAT3, STAT5A.
IGF-1 Signaling: ELK1, FOS, JUN.
PDGF Signaling: ELK1, FOS, JUN, STAT1, STAT3, STAT5A.
VEGF Signaling: ARNT, HIF1A, NFAT5, NFATC1, NFATC2, NFATC3, NFATC4.

JAK/STAT Signaling: CREBBP, MYC, STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, STAT6.

Notch Signaling: CREBBP, HDAC1.

TGFß/BMP Signaling: CREBBP, ID1, MYC, SMAD1, SMAD4, SMAD5, SMAD9, SP1.

Wnt Signaling: CREBBP, CTNNB1, HNF4A, JUN, MYC, NFAT5, NFATC1, NFATC2, NFATC3, NFATC4 (NFAT3), SMAD4, TCF7L2, TP53.

Immune Signaling:
NF-kappaB Signaling: NFKB1, NR3C1 (GRL), REL, RELA, RELB, STAT1.
Toll-like Receptor Signaling: ELK1, FOS, IRF1, JUN, NFKB1, PPARA, RELA, STAT1.
T-Cell & B-Cell Receptor Signaling: ELK1, FOS, JUN, NFAT5, NFATC1, NFATC2, NFATC3, NFATC4, NFKB1.
Cytokine and Chemokine-mediated Signaling: CEBPA, RELA, STAT3, STAT4, STAT5A, STAT5B.

EPO Signaling: ELK1, FOS, JUN, STAT5A.

TPO Signaling: FOS, JUN, STAT1, STAT3, STAT5A.

MAPK Signaling:
Erk1/Erk2 Signaling: ELK1, MYC, STAT3.
JNK Signaling: ATF2 (CREB2), ELK1, JUN, MEF2A.
p38 Signaling: ATF2 (CREB2), CREB1, ELK1, MAX, MEF2A, MYC, STAT1.
Other TFs involved in the MAPK Signaling: ATF4, CEBPA, FOS, JUN, JUND, MEF2C, NFATC2, NFATC4 (NFAT3), NFKB1, SP1, STAT1, TP53.

Other Transcription Factors: ATF1, ATF3, CEBPB, CEBPG, DR1, E2F1, E2F6, EGR1, ESR1 (ERa), ETS1, ETS2, FOXA2 (HNF3B), FOXG1, GATA1, GATA2, GATA3, GTF2B, GTF2F1, HAND1, HAND2, HOXA5, HSF1 (TCF5), JUNB, MYB, MYF5, MYOD1, NFYB, PAX6, POU2AF1, PPARG, SP3, TBP, HNF1A, TFAP2A, TGIF1, YY1.

Download English Version:

https://daneshyari.com/en/article/1226328

Download Persian Version:

https://daneshyari.com/article/1226328

Daneshyari.com