THE EFFECT OF AGE ON THE LITHIUM CONTENT IN PROSTATE OF HEALTHY MEN

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Introduction

In the last decades there is a growing fear of environmental diseases in the population of many countries and an increasing awareness of health and wellness. Chemical elementosis, considered as environmental diseases, is caused by low (deficiency) or high (excess) intake of chemical elements. Therefore there is an increasing interest in monitoring chemical element contests in humans, not only in cases of known high special burden, but also for individuals of the so-called "normal population" [1]. Information on chemical elements of human tissues and of their body burdens may be useful for assessing nutrition and for prevention and control of various disease states caused by mineral or trace element imbalance.

The results of lifelong lithium-poor nutrition of animals show that lithium is essential to the fauna, and thus, to humans as well [2-7]. It was shown that lithium-poor nutrition has a negative influence on feed intake, organism growth, skin properties, reproduction performance, milk production, mortality, and on some enzyme activity, mainly the enzymes of the citrate cycle, glycolysis, and of nitrogen metabolism [8]. On the other hand, lithium is widely used in medicine as an antidepressant drug. Moreover, lithium is also effective in the treatment of herpes virus infection and of seborrheic dermatitis in humans [9]. Prophylactic treatment of HIV patients with lithium was shown to prevent the onset/progression of the HIV-associated cognitive impairments [10].

The lithium intake by adult humans with mixed diets was systematically investigated in 10 test populations from different regions of Germany [11]. It was shown that men consume 24% more lithium than women. Adults of both genders with mixed diets consumed significantly more lithium with increasing age. On average, seniors consumed 30-46% more lithium.

The content of Na in the tissue of the prostate gland of older men is 1.5 times higher than in children [12]. Hence we hypothesize that the level of Li in the prostate gland, alkaline element of the same group of the periodic table, is increases with age. Since Li affects the function of the reproductive organs, excessive accumulation of this element in the prostate tissue may have a negative impact on the prostate condition and function. Therefore we

performed the following study with two objectives. The first objective was to determine the normal levels of Li in the prostate gland of healthy men. The second objective was to check age-related changes of Li contents in prostate tissue.

Experimental

Samples of the normal human prostate were obtained from 83 cadavers (age range: from newborn to 72 years) with intact bodies at post-mortems within 24 hours of death. Every child aged below 10 (n=10) died of asphyxia or pneumonia. The death of teenager aged 11 to 20 (n=10) was mainly caused by traumas. The majority of deaths among men aged 21 to 72 (n=63) was due to traumas, alcohol poisoning, and acute illness (cardiac insufficiency, stroke, embolism of pulmonary artery). Samples were taken from the prostate lateral lobe and then divided into two portions. One of them was used for morphological study while another was intended for Li determination. A histological study was used to control the age norm conformity as well as the unavailability of microadenomatosis and latent cancer. Samples intended for Li determination were weighed, freeze-dried, then repeatedly weighed again and homogenised. The homogenised tissue was used to select specimens weighing about 100 mg for LI determination by Inductively Coupled Plasma Mass Spectrometry (ICP-MS). A tool made of titanium and plastic was used for sampling and sample preparation.

Prostate samples were placed in one-chamber autoclaves (Ancon-AT2, Ltd., Russia) to which 1.5 mL of concentrated HNO_3 *(Nitric acid 65%, max. 0.0000005% Hg, GR, ISO, Merck)* and 0.3 mL of H_2O_2 (*pure for analysis*) were added and then heated for 3 h at 160 – 200°C for the samples to decompose. Then the autoclaves were cooled to room temperature. The solutions from the autoclaves were diluted with deionized water to 20 mL and transferred to plastic measuring bottles. Simultaneously the same procedure was performed in autoclaves without samples and the resultant solutions were used as control samples.

The contents of Li in the obtained solutions were determined by ICP-MS using the Spectrometer X-7 ICP-MS (Thermo Electron, USA). The measurements were made at the following spectrometer parameters: RF generator power - 1250 W, nebulizer – PolyCon, spray chamber - cooling 3^{o}C, plasma gas flow rate - 12 L/min, auxiliary flow rate - 0.9 L/min, nebuliser flow rate - 0.9 L/min, sample update - 0.8 mL/min, resolution - 0.8M.

The main parameters of mass-spectrum measurements were: detector mode – double (pulse counting and analogous) and scanning mode - Survey Scan and Peak Jumping. The setting for the Survey Scan was: the number of runs - 10, dwell time - 0.6 ms, channels per mass - 10, acquisition duration - 13.2 s. The setting for the Peak Jumping was: sweeps - 25, dwell time - 10 ms, channels per mass - 1, acquisition duration - 34 s.

The Li contents in aqueous solutions were determined by the quantitative method using calibration solutions (*High Purity Standards, USA*) with 5, 10, and 100 μkg/L. Indium was used as an internal standard in all measurements.

The detection limit (DL) was calculated as:

$$DL = C_{Li} + 3 \cdot SD$$

where C_{Li} – is a mean value of the Li content for measurements in control samples and SD – is a standard deviation of C_{Li} determination in control samples.

Uncertainties of Li determination in prostate samples by ICP-MS expressed as mean relative standard deviation (±RSD) in repeatability study did not exceed 10%.

Three sub-samples of the Institute of Nuclear Chemistry and Technology (Poland) certified reference material CTA-OTL-1 Oriental Tobacco Leaves were analyzed simultaneously with prostate samples to estimate the precision and accuracy of results. The samples of certified reference material were treated in the same way as the prostate samples.

All prostate samples were prepared in duplicate and mean value of Li was used in final calculation. Using standard programs, the summary of statistics, arithmetic mean, standard deviation, standard error of mean, minimum and maximum values, median, and percentiles with 0.025 and 0.975 levels were calculated for Li content. The reliability of difference in the results between the age groups was evaluated by Student's *t*-test.

Results and discussion

Table 1 depicts our data for Li mass fractions in samples of certified reference material and the certified values of these materials. The detected mean for the Li content (M ± SD) in the certified reference material CTA-OTL-1 Oriental Tobacco Leaves obtained in this work was in good agreement with the mean of certified value (Table 1). This indicates an acceptable accuracy of the results on the Li content in the intact prostate samples.

Table 1. ICP-MS data of Li content (M±SD) in Certified Reference Material CTA-OTL-1 Oriental Tobacco Leaves (mg/kg on dry weight basis)

Certified Reference Material	Certificate	This work result
CTA-OTL-1 Oriental Tobacco Leaves	23.0±1.8	23.5±1.1

M - arithmetic mean; SD – standard deviation

Fig.1 shows individual data for the Li mass fraction in the prostate tissue for all samples and lines of trend with age.

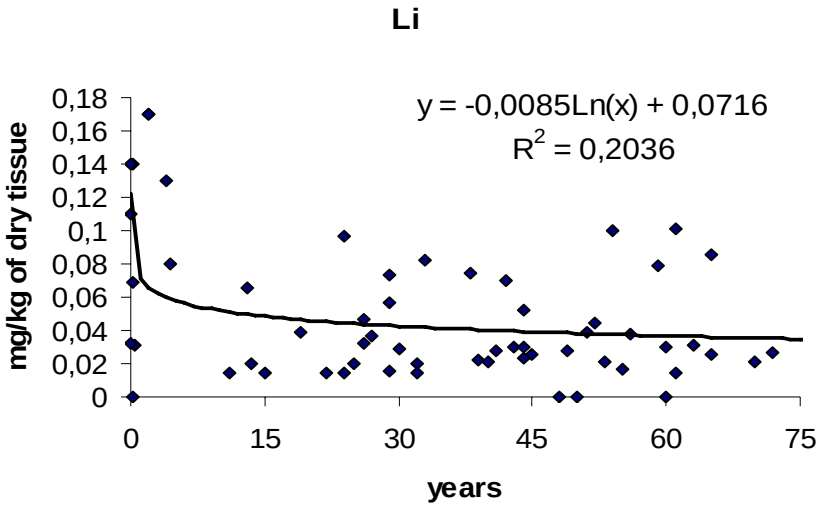

Fig.1. Individual data of the Li content in the prostate tissue and line of trend with age.

In order to estimate the effect of age on the investigated parameter we used five age groups: 1) newborn-10 years (M =1.4 year), 2) 11-20 years (M =15.8 year), 3) 21-40 years (M =30.4 year), 4) 41-60 year (M =49.6 year), and 5) 61-72 years (M =65.3 year). Table 2 represents certain statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels) of the Li content in prostate tissue of every age group. The results for adults from 21 to 72 years (A) and all age groups (Σ), taken together, are shown in Table 2 too.

Table 2. Some statistical parameters of Li content (mg/kg on dry weight basis) in the prostate tissue of healthy men

Age group	M	SD	SEM	Min	Max	Med	P0.025	P0.975
1 (M=1.4 y, n=10)	0.107	0.052	0.016	0.031	0.170	0.120	0.031	0.170
2 (M=15.8 y, n=10)	0.031	0.022	0.007	0.015	0.066	0.020	0.015	0.063
3 (M=30.4 y, n=28)	0.039	0.027	0.005	0.015	0.097	0.029	0.015	0.091
4 (M=49.6 y, n=27)	0.041	0.024	0.005	0.017	0.100	0.030	0.019	0.092
5 (M=65.3 y, n=8)	0.044	0.035	0.013	0.015	0.101	0.027	0.016	0.099
A (M=43 y, n=63)	0.040	0.025	0.003	0.015	0.100	0.030	0.015	0.098
Σ (M=31 y, n=83)	0.052	0.041	0.006	0.015	0.170	0.032	0.015	0.160

y- years, M - arithmetic mean; SD – standard deviation; SEM – standard error of mean; min – minimum value; max – maximum value; P0.025 – percentile with 0.025 level; P0.975 – percentile with 0.975 level

Statistically significant ($p \leq 0.01$, *t*- test) an age-related decrease in Li content was observed. As shown in Figure 1 and the data in Table 2, the average content of Li in the prostate gland in children under 3 years is about 3 times higher than in the adult prostate. With age, Li content in children decreases rapidly, stabilizes after puberty, and remains at a constant level until old age.

In the literature available to us, we did not find data on the content of Li in the prostate.

The study reported here is only concerned with samples obtained from subjects who have not been exposed to lithium except that derived from the natural environment. All the deceased were citizens of Moscow. None of those who died a sudden death had suffered from any systematic or chronic disorders before. Thus, our data for Li mass fractions in the human prostate may serve as indicative normal value for men.

Conclusions

The inductively coupled plasma mass spectrometry allows the determination of the contents of Li in prostate tissue of healthy adults with uncertainties under 10%. Mean values (M ± SEM) for the mass fraction of Li in prostate of all subjects taken together was 0.052±0.006 milligram per kilogram of dry tissue. Mean values (M ± SEM) for the mass fraction of Li in five age groups: newborn-10 years (1), 11-20 years (2), 21-40 years (3), 41-60 year (4), and 61-87 years (5) were 0.107±0.016, 0.031±0.010, 0.039±0.007, 0.041±0.006,

and 0.043±0.013 milligram per kilogram of dry tissue, respectively. Statistically significant ($p \leq 0.01$, *t*- test) an age-related decrease in Li content was observed. The results obtained may serve as indicative normal values for the lithium content in human prostate.

Acknowledgments

The authors acknowledge the support of the ICP-MS determination in the framewok of the RAS Presidium program for basic research “Creation and improvement of metods of chemical analysis and investigation of substances and materials structure"

References

1. Drasch G., Wanghofer E., Roider G. Are Blood, Urine, Hair and Muscle Valid Bio-Monitors for the Internal Burden of Men with the Heavy Metals Mercury, Lead and Cadmium? An Investigation on 150 Deceased. Trace Elem. Electrolytes, 1997, **14**, 116-123.
2. Anke M., Grün M., Groppel B., Kronemann H. The biological importance of lithium. Mengen- und Spurenelemente, 1981, **1**, 217-239.
3. Anke M., Arnhold W., Groppel B., Krause U. The biological importance of lithium. In: Lithium in Biology and Medicine (Eds.: Schrauzer G.N. and Klippel G.H.). VHC, Weinheim, 1991, pp. 149-167.
4. Ono T., Wada O., Yamamoto M. Study on the essentiality of lithium. Biomed. Res. Trace Elements, 1992, **3**, 41-47.
5. Schäfer U. Essentiality and toxicity of lithium. J. Trace Microprobe Techn., 1997, **15**, 341-349.
6. Birch N.J. Inorganic pharmacology of lithium. Chem. Rev., 1999, **99**, 2659-2682.
7. Schrauzer G.N. Lithium: occurrence, dietary intakes, nutritional essentiality. J. Amer. Coll. Nutrition, 2002, **21**, 14-21.
8. Anke M., Arnhold W., Schäfer U., Müller R. Recent progress in exploring the essentiality of the ultratrace element lithium to the nutrition of animals and man. Biomed. Res. Trace Elements, 2005, **16**, 3, 169-176.
9. Horrobin D.F. Lithium effects on fatty acid metabolism and their role in therapy of seborrhoeic dermatitis and herpes infections. In: Lithium in Biology and Medicine (Eds.: Schrauzer G.N. and Klippel G.H.). VHC, Weinheim, 1991, pp. 67-72.
10. Everall I.P., Bell C., Mallory M., Langford D., Adame A., Rockestein E., Masliah E. Lithium Ameliorates HIV-gp120-Mediated Neurotoxicity. Molecular and Cellular Neuroscience, 2002, **21**, 493–501.
11. Anke M., Arnhold W., Groppel B., Kräuter U. Die biologische Bedeutung des Lithiums als Spurenelement. Erfahrungsheilkunde, 1991, **10**, 656-664.
12. Hienzsch E., Schneider H.-J., Anke M. Vergleichende Untersuchungen zum Mengen- und Spurenelementgehalt der normalen Prostata, des prostataadenoms und des Prostatakarzinoms. Zeitschrift für Urologie und Nephrologie, 1970, **63**, 7, 543-546.