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The effect of age on Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn contents in intact human prostate investigated by neutron activation analysis

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ABSTRACT

The effect of age on trace element contents in intact prostate of 64 apparently healthy 13–60 years old men was investigated by neutron activation analysis. Mean values (M ± SEM) for content (mg/kg, dry weight basis) of trace elements were: Ag—0.057 ± 0.007, Co—0.036 ± 0.003, Cr—0.48 ± 0.06, Fe—96.9 ± 6.2, Hg—0.045 ± 0.006, Rb—12.5 ± 0.6, Sb—0.050 ± 0.005, Sc—0.020 ± 0.003, Se—0.63 ± 0.03, and Zn—548 ± 55, respectively. A tendency of age-related increase in Co, Fe, Hg, Sc, and Zn content was observed.

1. Introduction

Globally, prostate cancer is the sixth most common cancer, and the third most common cancer in males in Western industrialized countries (Kumar et al., 2004; Pischon et al., 2008). In North America, it is the most common cancer in males and, except for lung cancer, is the leading cause of death from cancer (Cohen, 2002; Jones et al., 2008; Van Patten et al., 2008). Although the etiology of prostate cancer is unknown, several risk factors including age and diet (calcium, zinc and some other nutrients) have been well identified (Yamada et al., 2000; Rebbeck, 2006). It is also reported that the risk of having prostate cancer drastically increase with age, being three orders of magnitude higher for the age group 40–79 years than in those younger than 39 years (Jemal et al., 2003; Rebbeck, 2006).

It is well known that zinc levels in the peripheral zone of dorsal and lateral lobes of the prostate are almost 10 times higher than in other soft tissues (Zaichick et al., 1997). The high content of zinc in the prostate suggests that zinc may play a role in prostate health. Therefore, in investigating the effect of diet on prostate cancer risk, much attention has been paid to dietary and supplemental zinc (Schrauzer et al., 1977; Whelan et al., 1983; Kolonel et al., 1988; West et al., 1991; Andersson et al., 1996; Key et al., 1997; Vlajinac et al., 1997; Kristal et al., 1999; Zaichick and Zaichick, 1999; Leitzmann et al., 2003), as well as consumption of red meat (Whittemore et al., 1995; Food, Nutrition and the Prevention of Cancer, 1997; Hayes et al., 1999; Kolonel, 2001; Michaud et al., 2001; Cross et al., 2004), as it is a major source of zinc from food for the residents of the continental countries (Platz and Helzlsouer, 2001). It should also be noted that zinc is more bioavailable in red meat and less bioavailable in vegetables (Groff and Gropper, 2000). Estimates of per capita zinc intake in many countries showed a positive correlation with mortality from prostatic cancer (Schrauzer et al., 1977; Whelan et al., 1983; Zaichick and Zaichick, 1999). A positive association with risk of prostate cancer was also observed in a population-based case-control study in the island of Oahu, Hawaii (Kolonel et al., 1988). Leitzmann et al. (2003) examined the association between supplemental zinc intake and prostate cancer risk among 46,974 U.S. men participating in the Health Professionals Follow-Up Study. It was shown that men who consumed more than 100 mg/day did have a relative risk of advanced prostate cancer of 2.29–2.37 greater than nonusers. Consumption of red meat has been proposed as a possible risk factor for prostate cancer (Food, Nutrition and the Prevention of Cancer, 1997). Many epidemiological studies that have presented results on this subject showed statistically significant increased risk with increasing meat consumption (Whittemore et al., 1995; Food, Nutrition and the Prevention of Cancer, 1997; Hayes et al., 1999; Kolonel, 2001; Michaud et al., 2001; Cross et al., 2004). On the contrary, modest to moderate inverse associations were observed in two case-control studies for dietary zinc (Key et al., 1997) and zinc supplement use (Kristal et al., 1999). Some case-control studies have not observed a cancer protective association for dietary or combined dietary and supplemental zinc intake (West et al., 1991; Andersson et al., 1996; Vlajinac et al., 1997).

The possibility that zinc adversely affects prostate cancer opposes its possible beneficial effect on the health of elderly individuals (Mocchegiani et al., 2000; Ekmekcioglu, 2001; High, 2001; Padro et al., 2002; Miyata, 2007). It is, therefore, important

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to clarify the role of dietary zinc and supplemental zinc on prostate cancer risk among older men.

At present there are two diametrically opposite points of view on this issue. Proponents of the position that high zinc intakes and, consequently, high intraprostatic zinc concentrations may be positively associated with prostate cancer risk use multiple arguments to support their theory (Leitzmann et al., 2003; Zaichick, 2004b). For example, zinc enhances the activity of telomerase (Nemoto et al., 2000), an enzyme thought to be responsible for unlimited proliferation tumor cells, the activity of which is increased in prostate cancer (Sommerfeld et al., 1996). Zinc has also been found to antagonize the potential inhibitory effect of bisphosphonates on prostate tumor cell invasion (Boissier et al., 2000). Excessive intake of zinc has undesirable metabolic effects, such as immune dysfunction (Chandra, 1984) and impaired antioxidant defense (Samman and Roberts, 1988) that are potentially related to prostate cancer. In humans, zinc intake is positively correlated with circulating levels of insulinlike growth factor-I (Holmes et al., 2002) and testosterone (Prasad et al., 1996) that are directly related to prostate carcinogenesis. Much data have been accumulated on both direct and indirect effect of zinc on the DNA, and to its vital role for prostatic cell division (Schwartz, 1975; Matusik et al., 1986; Blok et al., 1995). All these facts allow it to be assumed that excessive intracellular concentrations of zinc are probably one of the main factors acting at both initiation and promotion stages of prostate carcinogenesis. Thus, zinc supplementation could promote the development of prostate cancer.

Much of the interest in zinc as an agent for prostate cancer treatment and prevention (Costello et al., 2004; Costello et al., 2005; Costello and Franklin, 2006) is due to studies that have shown a marked reduction in prostate tissue zinc levels in prostate cancer cells versus normal prostate cells (Zaichick et al., 1997). Proponents of this theory think that high cellular zinc accumulation is detrimental to the malignant activities of prostate cancer cells. Due to lifestyle, eating and dietary habits, and physiological effects of aging, the elderly male population is normally predisposed to conditions of zinc deficiency (Mocchegiani et al., 2000; Ekmekcioglu, 2001; High, 2001; Padro et al., 2002; Vaquero, 2002), which can increase their susceptibility to prostate cancer. According to their hypothesis in the absence of zinc supplement cellular zinc uptake will be depressed and zinc levels in prostate normal cells will be reduced (Costello et al., 2005; Costello and Franklin, 2006). Moreover there is evidence that the complexity of interactions amongst multiple dietary factors affects the intestinal absorption and assimilation of zinc (King et al., 2000; Krebs, 2000; Lonnerdal, 2000). For example, the absorption of zinc could be inhibited by iron, calcium, and numerous other ingested nutrients.

To confirm or refute these hypotheses it is necessary to investigate the age-related dynamics of zinc in prostate tissue in combination with other chemical elements, which can be considered as potential antagonists of zinc. There are few studies regarding the effect of age on content of some chemical elements in prostate, using chemical techniques and instrumental methods (Hienzsch et al., 1970; Leissner et al., 1980; Tisell et al., 1982; Oldereid et al., 1993). However, majority of these data are based on non-intact tissue. In many studies tissue samples are ashed. In other cases, prostate samples are treated with solvents (distilled water, ethanol, etc.) and then are dried at high temperature for many hours. There is evidence that by these methods some amount of chemical elements is lost upon treatment (Zaichick, 2004a). Moreover, only one study used a quality control using certified reference materials for Zn, Cd, and Pb contents (Oldereid et al., 1993).

This work had three aims. The first one was to assess the Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, Zn contents and the Zn/Ag, Zn/Co, Zn/Cr, Zn/Fe, Zn/Hg, Zn/Rb, Zn/Sb, Zn/Sc, Zn/Se content ratios in intact prostate of healthy men using non-destructive instrumental neutron activation analysis. The second aim was to evaluate the quality of obtained results. The third aim was to compare the contents of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, Zn and the ratios of Zn/Ag, Zn/Co, Zn/Cr, Zn/Fe, Zn/Hg, Zn/Rb, Zn/Sb, Zn/Sc, Zn/Se contents in different age groups.

All studies were approved by the Institute of Forensic Medicine, Moscow, and the Medical Radiological Research Center, Obninsk, Ethical Committees.

2. Material and methods

2.1. Samples

Prostates were removed at necropsy from 64 men (mean age 36.5 years, range 13–60) who had died suddenly. The majority of deaths were due to traumas. Some of deaths were due to alcohol poisoning and acute illness (cardiac insufficiency, stroke, embolism of pulmonary artery) but without inpatient treatment. Information about chronic alcoholism or other diseases was not available from the medical reports of subjects. All cadavers had undergone routine autopsy at the Institute of Forensic Medicine, Moscow. Tissue samples were collected from the peripheral zone of prostate dorsal and lateral lobes within 2 days of death and then divided into two portions. One of them was used for morphological study while another was intended for chemical element analysis. A histological examination was used to control the age norm conformity as well as the absence of microadenomatosis and latent cancer.

2.2. Sample preparation

After the samples intended for chemical element analysis were weighed, they were transferred to $-20\ ^{\circ}C$ and stored until the day of transportation in the Medical Radiological Research Center of Russian Academy of Medical Sciences (MRRC RAMS), Obninsk. In the MRRC RAMS all samples were freeze-dried and homogenized. The pounded sample weighing about 50 mg was used for chemical element measurement by instrumental neutron activation analysis with high resolution spectrometry of long-lived radionuclides (INAA-LLR). The samples for INAA-LLR were wrapped separately in a high-purity aluminum foil washed with rectified alcohol beforehand and placed in a nitric acid-washed quartz ampoule.

2.3. Standards and certified reference materials

To determine contents of the elements by comparison with a known standard, biological synthetic standards (BSS) prepared from phenol–formaldehyde resins were used (Mosulishvili et al., 1975). Corrected certified values of BSS element contents were reported by us before (Zaichick, 1995). In addition to SSB, aliquots of commercial, chemically pure compounds were also used as standards. Ten certified reference material IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) sub-samples weighing about 50–100 mg were treated and analyzed in the same conditions as that of the prostate samples to estimate the precision and accuracy of results.

2.4. Instrumentation and methods

A vertical channel of nuclear reactor was applied to determine the content of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn by INAA-LLR. The quartz ampoule with prostate samples, standards, and certified reference materials was soldered, positioned in a transport aluminum container and exposed to a 24-h neutron irradiation in a vertical channel with a neutron flux of $1.3 \times 10^{13}\ n\ cm^{-2}\ s^{-1}$. Ten days after irradiation samples were reweighed and repacked.