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The Effectiveness of a 40-year Long Iodine Prophylaxis in Endemic Goitre Region of Grobnik, Croatia

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A B S T R A C T

The region of Grobnik, in the north west of Croatia, 15 km away from the Adriatic coast and 400 meters above the sea level, used to be known as a centre of endemic goitre. Iodine prophylaxis of 10 mg KJ added per kilo salt started in Croatia during the year 1953 and it was increased to 25 mg KJ per kilo in 1996. During 1961, the prevalence of goitre among Grobnik school children was 63%, while in the adult population it was 34%. In 1981, 18% of goitrous school children and 11% of goitrous adults were found in the same region, which shows the fall in goitre prevalence in the twenty-year period, from a severe to a mild one. The aim of this study was to estimate the effectiveness of iodine prophylaxis in goitre eradication and to compare the obtained results to those found in the same region 20 and 40 years ago, namely, in 1961 and 1981. The research was conducted in 2001. We examined 472 Grobnik inhabitants, 378 children (196 girls and 182 boys, aged 7–15 years) and 94 adults. Regarding their size thyroid glands were graded according to WHO and PAHO classification. Data regarding lifestyles and health conditions were collected by individual and family questionnaires. The prevalence of goitre in 2001 was 6.6% in school children and 6.4% in adults. In relation to 1981, we found a statistically significant fall of goitre in school children at the level of $p<0.01$ ($\chi^2=23.65$), but the prevalence change was not statistically significant in adults ($p>0.01$, $\chi^2=1.419$). The frequency of thyroid gland hereditary diseases in native inhabitants was high, 11.7%. There were no statistically significant differences in the prevalence of goitre or thyroid hereditary diseases between groups of native and newcomers' children. According to our results, in the year 2001 the area of Grobnik was still was a region of a mildly expressed endemic goitre. This study presents final results of a 40-year long follow up of endemic goitre eradication, demonstrating the long-term effectiveness of iodine prophylaxis.

Key words: *goitre, endemic, epidemiology, iodine prophylaxis, Grobnik, Croatia*

Introduction

Iodine is essential for the normal thyroid function. The majority of individuals tolerate a wide range of iodine dietary levels. Responding to iodine depletion, the thyroid gland maintains the thyroid hormone's production by increasing the gland's mass. The enlargement of the thyroid, or goitre, is the most common clinical manifestation of the nutritional deficiency of iodine. If present in more than 10% of population or more than 5% of school children in one geographic area, goitre is defined as endemic[1]. Goitre is an adaptive disease induced by the persistent stimulation of the thyroid gland as a consequence of the increased thyrotropin (TSH) secretion due to iodine deficiency. If iodine deficiency is severe or persistent, other clinical manifestations of the Iodine Deficiency Disorders (IDD) could be observed, such as hypofertility, abortion, stillbirth, higher infant mortality, neonatal chemical hypothyroidism, congenital anomalies, retarded growth, mental retardation, deafness and dumbness, endemic cretinism, hypothyroidism, early aging, hyperplasia or even carcinoma. A higher prevalence of IDD in females is usually found in endemic areas. The most vulnerable population are females in the age to procreate. Iodine deficiency during pregnancy is the main cause of cretinism[2,3].

Endemic goitre is a multifactorial disease in which the major factor would be environmental or iodine defi-

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ciency, with a lesser role played by genetic factors. Etiologic factors other than iodine deficiency, such as dietary goitrogens, have been suggested[4,5]. The best example is the island of Krk in the northern Adriatic Sea, where the goitre prevalence is 33% among school children despite the adequate iodine intake[6]. Vegetables belonging to the Brassica genus of the Cruciferae family, such as cabbage, turnip and Brussels sprouts, are rich with sulphur-containing thionamids that interfere with the synthesis and the secretion of the thyroid hormones.

Besides the iodine intake and environmental influences, genetic factors are probably also involved in the IDD development. In heterozygots, mutations of the genes involved in thyroid hormogenesis could lead to a less effective metabolic pathway in the iodine transport or hormogenesis. Multiple genes are likely to be involved. At the present time, only hypotheses could be made[7]. A higher prevalence of goitre is found in children of goitrous parents than in those who are not. Consanguinity was found to play a very minor role, while the concordance rate was higher among monozygotic than dizygotic twins.

The iodine deficiency is relatively neglected by those who are responsible for the Public Health Care, particularly so in the developing countries. The eradication is easy and cheap, but it requires rigorous protocols and the control of results. It is estimated that in 1990 about 1 billion and 570 million of people, or 28% of the entire world population in 118 countries were exposed to iodine deficiency. About 665 million were goitreous, with 11.2 million endemic cretins and 43 million mentally retarded people. Consequently, the importance of additional iodine supplementation in endemic regions is more than obvious[8,9.] The choice of iodine supplementation methods, all of which are very easy and cheap, in most examples did not depend on practical considerations or WHO suggestions, but on political and economic demands.

There are three methods of continuous and effective additional iodine supplementation: permanent diffusion of iodine in water by a silicone cartridge, with a high effectiveness in areas where the water supply is based on soil wells[10]. The second method is iodised oil, which is sometimes very useful because of the »lateness effect« of iodine liberation. The last method is iodised salt, recognized as the best method in the fight against endemic goitre in most of the world regions. The iodine losses appearing until the iodised salt becomes used are included in the iodination doses count, for example, 50% of iodine may be lost in salt that is stored in bad conditions, in the period of nine months[10]. However, in non-salt consumer areas and in regions where endemic cretinism is found, iodised oil is the best way of iodine supply[11,12,13,14].

Mandatory iodine prophylaxis by iodination of all salt for human and animal use was introduced in Croatia in 1953, representing one of the first of such programs in Europe. The level of iodination was 10–15 mg potassium iodide (KI) per kilo of salt. The organization and the control of iodination posed many financial and technical problems. The programme has been carried out in several steps over the years, and the complete iodine prophylaxis was achieved by 1956. Ten years later, the prevalence of goitre was halved and endemic cretinism disappeared[15]. In 1961, five years after the beginning of iodine prophylaxis, the Grobnik region was still the area of severe endemic goitre. The prevalence of goitre among school children was 63% and among adults it was 34%. There was no endemic cretinism[16]. Since 1981, the prevalence of goitre decreased to 18% among school children and 11% in adults, fulfilling thus the criteria for moderate to mild goitre[17]. In the beginning of the 90's of the last century, endemic goitre was considered to be eradicated and did not make part of the list of Croatian public health problems[18]. But, soon afterwards, the new nationwide goitre study showed that a mild iodine deficiency still persisted, with the goitre prevalence among schoolchildren between 8 and 35%[19]. In 1996, being aware of this result, the Croatian Ministry of Health adopted a new regulation, requiring obligatory iodination of 25 mg KJ per kg of all salt for human and animal use[20].

The aim of this study was to estimate the effectiveness of iodine prophylaxis in the goitre endemic Grobnik area five years after the iodination rate was raised. Our aim was also to compare our results with those found twenty and forty years ago in the same region.

Patients and Methods

The research was conducted in March and April of 2001 in the Grobnik region. We examined 378 children, representing 92% of the entire school children population, all attending Drazice School. There were 196 girls and 182 boys aged 7–15 years. We also included 146 inhabitants above the age of 15 years, from 61 families living in Lukezi village. They represented 80% of all adult inhabitants, 94 of them being natives.

Data on patients' lifestyles and health conditions were collected by individual and family questionnaires. They included general data on family members, their roots, economic status, social and hygienic conditions, food quality, water supply and housing conditions. Individual questionnaires made enquiries about the data on the place and time of birth, education, employment and previous diseases. Questionnaires used in this research were designed according to those used in previous endemic goitre studies conducted in the same region.

Physical examinations of thyroid glands were performed with all participants[21]. Regarding their size, they were graded according to WHO (World Health Organization) and PAHO (Pan-American Health Organization) classification as: stage 0: no goitre, IA: goitre detectable only by palpation and not visible even when the neck is fully extended, IB: goitre palpable and visible only when the neck is fully extended, II: goitre visible with the neck in normal position, palpation not needed for diagnosis, III: very large goitre, recognized at a considerable distance[22].

Results

Prevalence of goitre in school children of Grobnik region

The region of Grobnik is situated between the coastal and mountainous region, some 15 km on the northwest of the City of Rijeka, at 400 m above the sea level. About twenty villages of this region are situated in the Grobnicko Polje Valley and by the river Rjecina. They are organized in two municipalities, of Cavle and Jelenje. Studies were made in the municipality of Jelenje, where the increase in population of 8.2% was noticed during the last 40 years. In the same period there was a decrease of 46% in the number of school children, indicating the trend of aging. More than half of the population was still native, 64% of adults and 61% of school children.

The research conducted in 1961 by Kopajtic B. et al., showed the prevalence of goitre in school children of 63%, while in adults it was 34%. There were no endemic cretins. According to these results from 1961, endemic goitre in the region was still severe eight years after the iodine prophylaxis had begun[16]. Twenty years later, in 1981, Crncevic Z. proved the significant fall of goitre in Lukezi village, with the prevalence of 18.3% in school population and of 10.9% among adults[17]. These results indicated the analysed region as a mild endemic for goitre in 1981. In the present research from 2001, goitre was found in 25 or 6,6 % of children (Figure 1). By physical examination, in 21 (5.5%) children goitre was graded as stage IA, and in 4 of them (1.1%) as stage IB. Prevalence according to the age is shown on picture 2. In relation to 1981, the decrease of goitre was statistically significant at the level of $p<0.01$ ($\chi^2=23.65$, Table 1).

In our study, we found goitre in 14 out of 232 native children (6%). A family history of the thyroid gland disease was found in 22 children (5.8% of all included children), while only 3 of them (13.6%) had goitre. According to these results, no statistically significant difference in goitre prevalence between native and newcomers' children was found (χ^2 =0.128, p>0.01), just as it was the case with hereditary diseases of the thyroid gland (χ^2= 0.853, p>0.01). The results are shown in Table 2.

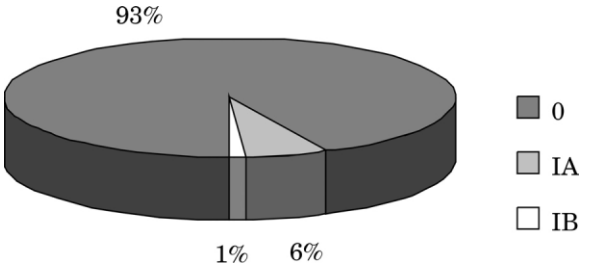

Fig. 1. Goitre prevalence among school children in Grobnik, 2001. Goitre classification: O – no goitre, IA – goitre not visible, detectable only by palpation, IB – goitre visible when the neck is extended.

Prevalence of goitre in adult inhabitants of Lukeži village

The village of Lukezi belongs to Jelenje municipality. We chose the population of this village as the representative sample because they had the highest prevalence of goitre in earlier researches. Our study included all the inhabitants of Lukezi in the age above 15 years. There were 182 of them, representing 3.7% of all the municipality population. In comparison with the previous research, there was a decrease of 24% in the number of inhabitants in the municipality in the last twenty years.

The social status was evaluated according to the number of employed members in each family, the quality of nutrition, the respondent's statement and the examiner's impression, classified as good (45 or 74% of households), average (11 families or 18%) and bad (5 households or 8%). Nutrition varied. Fruit, vegetables, meet, milk and cereals were taken almost daily, and fish once a week. Vegetables were grown by almost half of the households, and 10% of them had cattle and poultry.

TABLE 1
ENDEMIC GOITRE IN GROBNIK IN 1981 AND 2001

	1981			2001			Significancy
	N	Goitres	%	N	Goitres	%	
Adults	147	16	10.9	94	6	6.4	ns (χ^2=0,914, p>0.01)
Children	437	80	18.3	378	25	6.6	s (χ^2=23.65, p<0.01)

TABLE 2
GOITRE PREVALENCE BETWEEN NATIVE CHILDREN AND IN THOSE WITH HEREDITARY THYROID GLAND DISEASE

	N	Native	%	Hereditary disease	%
Goitre	25	14	56	3	
No goitre	353	218	62	19	5
Total	378	232	ns (χ^2=0.853, p>0.01)	22	s (χ^2=0.128, p>0.01)

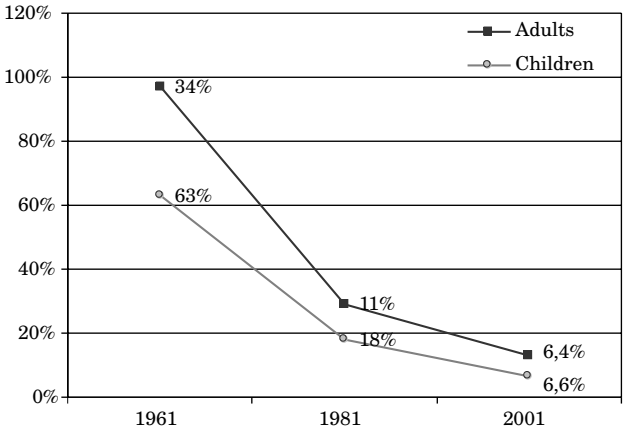

Fig. 2. Decrease of goitre in Grobnik during 40 years.

In all of the households salt iodinated according to Croatian regulations was used, while in 95% of households we found sea salt from the biggest Croatian salt-works, situated on the island of Pag. Extra salted food was consumed in 10% of included families, while 5% of households cooked their food by adding minimal or no salt. Twenty years ago only 14% of households had water supply, others used water from soil wells or from the river. In this study, only 3 households (5%) used the water from soil wells.

Cardiovascular diseases, hypertension, injuries, rheumatic, skin and mental diseases were the most common morbidities in Lukezi inhabitants. We also found thyroid gland, respiratory tract and gastrointestinal system diseases. Thyroid gland diseases were more common in middle aged and older females. A total of nine inhabitants (9.6%), all women, had thyroid gland disturbances or were with goitre, two of them had hereditary thyroid gland diseases and they were all with facial hair. In six women the thyroid gland disturbance was diagnosed earlier in life, while three of them had goitre.

The prevalence of goitre among adults in 1961 was 34%, in 1981 it was 11%, and twenty years later, in 2001, 6.4 % (Figure 2). The last verified decrease of goitre prevalence in adult population was not at a statistically significant level $p<0.01$ ($\chi^2=0.914$).

Discussion

There was an increase of 8.2% in the population of Grobnik region during the last 40 years, but the population was becoming older. In 1961, there were 17% of school children among all inhabitants, and only 8.4% in 2001. During our research, the majority of inhabitants were still native, 64% of adults and 61% of school children.

The prevalence of goitre in 2001 was 6.6 % in school children aged 7–15 years and 6.4% in the analysed sample of adults. Goitres found in children were small, of IA or IB (in proportion IA:IB = 21:4), more common in girls than boys (in proportion girls:boys = 16:9). Among adults, goitre was found only in women, which is in accordance with the previous knowledge that endemic areas have much higher goitre prevalence in females. The incidence of goitre in boys under 15 years of age was found to be 25%, with an increasing trend from childhood to puberty and decreasing in the post puberty period. In females, the goitre incidence increased after puberty.

In this study, we demonstrated the success of iodine prophylaxis in practice. Salt iodinated according Croatian regulations was used in almost all the households. The incidence of goitre among school children and adults was equal, demonstrating a better iodine supply. Our results showed the decrease of goitre prevalence in relation to the 90's of the last century, when it was 8–35% in school children in Croatia.

The incidence of goitre in Grobnik, in accordance with the changes in salt iodination, can be compared with the results from other Croatian regions[23,24] and European countries. When the salt iodination in Italy used to be on voluntary basis, iodised salt was produced in the proportion of only 3% of all salt production. In those times the prevalence of goitre was 8–13%[25]. In the middle of the 80's of the last century, Croatia was one of the countries in which goitre emerged after the transitory eradication period. The increase of iodination from 10 to 25 mg KJ per kilo of salt in 1996 improved the iodine deficit in population, leading to the results from 2001 that are discussed in this paper. As it was the case in Croatia, iodination was increased in other countries, such as Switzerland[26] and Austria[27]. Next to Sweden, Norway and Finland, these countries have successfully eradicated goitre. Another proof of the importance of iodine prophylaxis in goitre eradication and the maintenance of results was dramatically demonstrated in the goitre comeback in Russia and Poland during the period of 5 to 7 years after the iodine prophylaxis had been abandoned[28].

In 2001, Grobnik was still a region with a mildly expressed endemic goitre despite the iodine prophylaxis and the satisfactory iodine intake. The reason for the persistence may be found in the influence of dietary goitrogens. A contribution to this hypothesis could be found in the fact that the residents of Lukezi grow vegetables for their own nutrition and some of them even cattle and poultry. Earlier studies underlined the difference in goitre prevalence between villages situated by the river Rjecina's lake of Lukezi and other villages of the Grobnicko Polje Valley. The prevalence of goitre in the Lukezi area was 40%, while it was 29% in the villages in the Grobnicko Polje Valley. This disproportion was explained by the difference in the structure of soil.

In comparison to 18% of goitrous school children in 1981, this research showed a statistically significant fall of goitre to the level of 6.6% until the year 2001 ($\chi^2=23.65$, $p<0.01$). Despite the statistically significant fall, goitre was still not lower than 5%, which is the objective of IDD eradication according to WHO[10]. What are the reasons for this incomplete effect of the iodine prophylaxis in this endemic region? It can be influenced by local

dietary goitrogens discussed above, or by genetic aberrations. The frequency of hereditary diseases of the thyroid gland in native inhabitants was found high, 11.7%, but there were no statistically significant differences in the goitre prevalence between native and newcomers' children, as well as in children with hereditary diseases of the thyroid gland (χ^2=0.128, p>0.01, χ^2=0.853, p<0.01).

In this paper we demonstrated the effectiveness of a 40-year long iodine prophylaxis in the eradication of goitre in the region with a long history of a severe endemic goitre. Despite these satisfying results, a mildly endemic goitre still persists, pointing out the need for a further investigation of its causes.

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UČINCI 40 GODINA PROFILAKSE JODOM NA ENDEMSKU GUŠAVOST REGIJE GROBNIK, HRVATSKA

SAŽETAK

Hrvatska sjeverozapadna regija Grobnik, 15 km udaljena od Jadranskog mora, na 400 metara nadmorske visine, u prošlosti je bila poznata kao područje endemske gušavosti. Profilaksa jodom započeta je u Hrvatskoj 1953. dozom od 10 mg KJ po kilogramu soli, da bi 1996. bila povećana na 25 mg KJ po kilogramu. Godine 1961., na navedenom je području utvrđena prevalencija gušavosti od 63% u školske djece i 34% među odraslima. Tijekom 1981., u istoj je regiji detektirano 18% gušave školske djece i 11% odraslih, što je bio pad prevalencije gušavosti sa stupnja teške na blagu. Cilj ove studije je praćenje endemske gušavosti u ispitivanoj populaciji i procjena učinaka jodne profilakse u njenoj eradikaciji. Istraživanje je provedeno 2001., uključeno je 472 stanovnika Grobnika, 378 djece (196 djevojčica i 182 dječaka, raspona dobi od 7 do 15 godina), te 94 odraslih. Dobiveni su rezultati uspoređeni s podacima za isto područje 20 i 40 godina ranije. Temeljem veličine štitne žlijezde, stupanj gušavosti je određen prema WHO i PAHO klasifikaciji. Podaci o životnim navikama i zdravstvenim uvjetima, dobiveni su osobnim i obiteljskim upitnicima. Prema rezultatima, prevalencija gušavosti u 2001. je bila 6,6% među školskom djecom i 6,4% među odraslima. U odnosu na 1981., navedeno predstavlja statistički značajan pad u skupini školske djece na razini p<0.01 (χ^2=23,65), dok statističke značajnosti nema u grupi odraslih, p>0.01 (χ^2=1.419). Istraživanjem određena učestalost nasljednih bolesti štitnjače u starosjedilaca iznosi 11,7%. Razlike u prevalenciji gušavosti i nasljednih bolesti štitnjače u grupama djece starosjedilaca i doseljenika nemaju statističke značajnosti. Grobnik je 2001. bio regija s blagom endemskom gušavošću. Konačni rezultati 40-godišnje jodne profilakse endemske gušavosti potvrđuju njenu uspješnost, učinkovitost i dugoročnu opravdanost.