Epidemiology, Diagnosis and Therapy of Thyroid Dysfunction in the Elderly and in Regions with Different Iodine Supply

Thesis

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**Introduction**

We performed a thyroid screening study on ethnographical homogenous groups living in an abundant iodine intake area and in a region with low iodine intake. Thyroid function parameters were evaluated and compared between different groups: young and old people, men and women, subjects in relatively good and relatively poor health.

In two previous studies, the efficiency of the blood spot versus sensitive serum TSH screening was investigated in elderly subjects. In contrast to the previous studies we screened healthy adults, nursing home residents and elderly subjects living at home in relatively good health and the screening was performed in a region of abundant iodine intake with an expected significant incidence of elevated TSH.

The safety of thyrostatic treatment in old age has not been investigated systematically so far. In our study we followed elderly patients with toxic nodular goitre on long term methimazole treatment and compared the efficacy of this therapy to the results of radioiodine treatment with different doses.

**Objectives**

A. We performed epidemiological investigations on people living in iodine deficient and iodine sufficient areas. We evaluated iodine excretion, thyroid dysfunction, thyroid volume, goitre prevalence and thyroid nodules and compared the results between young and old people, men and women, subjects in relatively good and relatively poor health.

B. We also investigated the efficiency of the blood spot versus sensitive serum TSH screening in elderly subjects living in a sufficient iodine intake area.

C. We compared the efficacy of long term thyrostatic versus radioiodine treatment with different doses in elderly patients with toxic nodular goitre.

**Patients and methods**

A. We performed a thyroid screening study in groups of elderly nursing home residents and healthy adults living in iodine rich (N=362, average iodine excretion: 256.1 µg/g creatinine) and in iodine deficient (N=331, average iodine excretion: 60.41 µg/g creatinine) areas. The parameters investigated were age, gender, weight, height, BMI, iodine excretion, TSH, FT4, anti-TPO, anti-Tg, and thyroid size and structure determined by ultrasound examination.
B. We investigated whether the blood spot thyrotropin (TSH) method was adequate for screening elderly subjects with abundant iodine intake for hypothyroidism. The groups investigated were: 97 healthy adults (group A), 210 nursing home residents (group B) and 265 elderly subjects living at home (group C). The sensitivity (Se), specificity (Sp), positive and negative predictive value (+PV, -PV) of various blood spot TSH cut off points to predict elevated sensitive TSH were calculated.

C. We performed a retrospective analysis of the therapeutical outcome in 66 patients over 60 years of age with toxic nodular goitre. The patients were divided into two groups. Group A consisted of 28 patients on methimazole treatment: starting dose 5-30, median (M) 10 mg, maintenance dose 2.5-15 (M) 5 mg, follow up 6 to 240 months (M=23.5 months). Group B included a total of 38 patients treated by either 100-300 MBq (N=14, subgroup B1) or 325-1000 MBq (N=24, subgroup B2) $^{131}$I, follow up 18 to 156 months (M=48 months). The efficacy of the different therapeutical approaches was compared by calculating the occurrence rate of persisting and relapsing thyroid dysfunction and associated side effects.

**Important results**

A. In the iodine rich region, iodine excretion was significantly higher in the elderly as compared to young adults ($F=3.86; P=6.7x10^{-6}$). No significant differences were found between the iodine excretion of elderly and young people, men and women, subjects in relatively good or relatively poor health in the iodine deficient area. No significant difference was found between the iodine excretion of cases with or without goitre in either region. In the iodine rich region, iodine excretion increases with age ($r=0.22; P=3.47x10^{-5}$). There is a positive correlation between iodine excretion and body mass index (BMI) in the iodine deficient region ($r=0.15; P=6x10^{-3}$).

In the region where iodine intake is abundant, subclinical thyroid dysfunction ($P=0.049$), hypothyroidism ($P=0.02$) and all thyroid dysfunction ($P=0.01$) were observed more frequently in elderly than in young people. Women living in iodine rich regions have high anti-TPO levels ($P=0.007$) more often than men. In the iodine deficient region subnormal TSH levels were observed more frequently in women than in men. There were no significant differences in thyroid dysfunction and autoantibody levels between subjects in relatively good and relatively poor health in the areas of different iodine supply.

Nodular goitre (in iodine rich region: $P=8.25x10^{-3}$; in iodine depleted area: $P=0.03$) and thyroid nodules (in iodine rich region: $P=2.62x10^{-3}$, in iodine depleted area: $P=0.01$) were
more frequent in old age than in young controls. In women, thyroid nodules (in iodine rich region: $P=0.04$, in iodine depleted area: $P=1.57\times10^{-3}$) were present more frequently than in men.

Thyroid volume increases with age in areas with abundant iodine intake ($r=0.13$, $P=0.01$). A positive correlation was found between thyroid volume and BMI in subjects living in iodine rich ($r=0.12$; $P=2\times10^{-4}$) and iodine depleted regions ($r=0.11$; $P=0.03$).

**B.** We compared the efficiency and cost benefit of spot TSH (cost 0.4 USD) with the serum TSH method (cost 1.2 USD). Cases with significantly elevated ($\geq10.0$ mU/l) serum TSH were detected at blood spot cut off points 10.0-4.0 mU/l with a sensitivity of 1.0 and without considerable loss of specificity. Elevated (>3.5 mU/l) serum TSH levels were detected with the required sensitivity of greater than 0.9 only if the cutoff point of the blood spot TSH was set as low as 2.5 mU/l, but this led to a considerable loss of specificity. At a cutoff point of 2.5 mU/l, the rate of positivity was 39% and the cost of blood spot screening/person increased to 0.88 USD, as positive cases have to be rechecked by serum TSH to exclude false positivity.

**C.** Numerous relapses occurred in group A in the follow up: 5 clinical and 13 subclinical hyperthyroidism. Poor patient compliance (9/28), or dose reduction by the physician (5/28) were the main causes of the relapses. Transient clinical (3 cases) or subclinical (6 cases) hypothyroidism also occurred. In 50% of the patients in group B1 hyperthyroidism persisted (versus 16.7% in group B2, $P=0.028$). In this same group methimazole treatment had to be continued in 64.3% of the patients (versus 20.8% in group B2, $P=0.074$), while radiotherapy had to be repeated in 35.7% of the patients (versus 20.8% in group B2, not significant).

**Main Conclusions**

1. This is the first thyroid screening study on ethnographical homogenous, numerous groups living in an iodine rich and in an iodine deficient area, where thyroid function parameters were evaluated and compared between different groups: young and old people, men and women, subjects in relatively good or relatively poor health.

2. Only in the iodine deficient region was iodine excretion positively correlated with BMI. The reason for this may be that in iodine depleted areas the main iodine source is iodinated salt and food with iodine content.

3. There is an increased prevalence of subnormal TSH values in iodine depleted region caused by thyroid autonomy, but non thyroidal illness cannot be the reason for this. At the same time,
there are no significant differences in thyroid dysfunction and antibody levels between subjects in relatively good and relatively poor health in the areas of different iodine supply.

4. In regions with abundant iodine intake thyroid dysfunction (subclinical dysfunction, all dysfunction and hypothyroidism) was met more frequently in elderly than in young people. There was no significant difference between high antibody levels in these groups. The explanation could be that high anti-TPO levels occur already at a younger age, but the hypothyroidism rate becomes significantly high only in old age.

5. There were no significant differences in thyroid dysfunction between men in areas of different iodine supply.

6. In the iodine depleted region there is an increased prevalence of subnormal TSH values in women as compared to men (14.8% versus 4.8%, P=0.04). This is probably caused by the increased incidence of goitre and thyroid autonomy in women.

7. In old age there was no difference between clinical status and goiter prevalence.

8. A stronger correlation was found between thyroid volume and BMI in subjects living in iodine rich than in iodine depleted regions. The reason for this is that thyroid volume is determined by the low iodine supply in the iodine depleted region.

9. Cases with significantly elevated (>10.0 mU/l) serum TSH were detected with adequate sensitivity and without considerable loss of specificity, so the blood spot method is suitable for the screening of clinical hypothyroidism.

10. Elevated (>3.5 mU/l) serum TSH levels were detected with the required sensitivity of greater than 0.9 only if the cut off point of the blood spot TSH was set as low as 2.5 mU/l, but this led to a considerable loss of specificity. At a cut off point of 2.5 mU/l, the rate of positivity was 39% and the cost of blood spot screening/person increased to 0.88 USD, as positive cases have to be rechecked by serum TSH to exclude false positivity. We conclude that blood spot TSH method is inadequate to detect subclinical hypothyroidism accurately and would, therefore, fail to detect most affected subjects.

11. We conclude that long term thyrostatic treatment is not safe in elderly patients with toxic nodular hyperthyroidism because of the increased prevalence of clinical (17.8%) and subclinical (46.4%) hyperthyroidism relapses. The patients need a longer time to become euthyroid and there are several cardiac symptoms associated with the relapses.

12. The main causes of the relapses are: poor compliance or dose reduction by the physician. There is an individual variability of the appropriate maintenance dose, so the patient should be seen more often (at least every three months and not only twice a year as is the practice in our country).
PUBLICATIONS REGARDING THE THESIS


ABSTRACTS AND PRESENTATIONS


BOOK CHAPTERS
