Endocrine Abstracts

September 2020 Volume 70
ISSN 1479-6848 (online)

22nd European Congress of Endocrinology

5-9 September 2020, European Society of Endocrinology

eECE 2020
22nd European Congress of Endocrinology

published by
bioscientifica

Online version available at
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Volume 70
September 2020

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For statistical analysis, we used IBM SPSS v.21 and MaxStat v.3.6. We applied non-parametric tests and defined $P<0.5$ as significant.
Results
Of 12 703 samples, 430 (3.4%) met the inclusion criteria. Of these, 398 had available serum for precipitation with PEG. Patients with initial TSH < 15 mU/l were younger than those with TSH 15 mU/l or above ($P=0.03$). The group with recovered TSH percentage of up to 24% ($n=106$) had a lower initial TSH value when compared with 25% or higher ($n=292$) ($P=0.01$). Older age (50 and older, $n=200$) was associated with a higher level of monomeric TSH ($P=0.003$). The initial TSH values of 7.77 mU/l or above had tendency towards higher value of monomeric TSH ($P=0.066$).
Conclusions
Our results suggest there could be a potential role for monomeric TSH determination prior to treatment initiation for subclinical hypothyroidism, mainly in young patients. The main strong point of our study is its real-world setting. The limitations are that we did not take into account the patients' background and treatment; we also did not have a possibility to use gel filtration chromatography which is considered a gold standard for monomeric TSH determination. At the next stage, we are planning to compare these results with a group of patients who have normal TSH values.

DOI: 10.1530/endoabs.70.AEP918

AEP919

The effects of naringenin on NRF2 and antioxidant enzymes expressions in the thyroids of the old-aged Wistar rats

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Citrus flavanone naringenin (NAR) is a potent antioxidant with ability to change pituitary-thyroid function. NAR increases concentration of thyroid-stimulating hormone (TSH) in serum by increasing Sirtuin1 expression in the pituitary thyrotrophs and improves thyroid hormonogenesis capacity in old-aged rats. Thyroid hormone production is followed by generation of large quantities of reactive oxygen species (ROS) which are essential for iodine organification. A master regulator of redox status, NRF2 protein, together with antioxidant enzymes (AOE), is responsible for maintenance of redox/antioxidant balance in the cell. Considering that NRF2 expression can be affected by NAR, besides TSH, the study aim is to analyze gene and protein expressions of NRF2 and AOE in the thyroids of 24-month-old male Wistar rats. NAR was suspended in sunflower oil (vehicle) and administrated directly to the oral cavity, at a dose of 15 mg/kg b.m., during 4 weeks. Control group received vehicle only. We performed qPCR and immunoblot analyses for gene and protein expressions, respectively. Obtained results showed that NAR treatment lowered ($P<0.05$) mRNA levels of Nrf2, superoxide dismutase 1 and 2 (Sod1, Sod2) and catalase (Cat) for 42%, 32%, 45% and 35%, respectively, while it only increased ($P<0.05$) expression of glutathione peroxidase (Gpx) for 54%, all in comparison with the controls. Gene expression of glutathione reductase (Gr) remained unchanged. Also, NAR up-regulated ($P<0.05$) protein expression of NRF2 and SOD2 for 58% and 50%, respectively, and down-regulated ($P<0.05$) SOD1 expression for 48%, all when compared to the adequate control values. CAT, GR and GPx protein expressions didn't change after NAR treatment. It can be concluded that NAR changes gene and protein expression of NRF2 in old-aged rat model. Down-regulation in Nrf2 gene expression, and some AOE, is in line with previously observed TSH stimulation after NAR. Antioxidant protection in thyroid needs to be lowered in order to ensure sufficient ROS for adequate thyroid hormones production. However, due to NAR prooxidant properties, redox status in thyroid upon its application was changed, inducing accumulation of NRF2 protein in the thyrocytes. This led to increment of Gpx gene and SOD2 protein expression, helping in maintenance of fundamental antioxidant protection and disposal of excessive ROS in the thyroid gland of old-aged rats.

DOI: 10.1530/endoabs.70.AEP919

AEP920

Retrospective analysis of low risk thyroid cancers. Total thyroidectomy or lobectomy is the optimal approach for follow up?

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Background
Differentiated thyroid cancer (DTC) <1 cm without risk factors require only lobectomy, and there is no need for radioiodine remnant ablation (RRA). The approach for surgery and RRA after surgery is less clearly defined for tumours measuring 1–4 cm.
Objectives
We aimed to evaluate the surgical approaches of DTC in stages pT1–2 in a moderate iodine deficient area. We compared our data to the current European Thyroid Association (ETA,2006) and American Thyroid Association (ATA,2015) clinical practice guidelines.
Methods
Data of 111 DTC patients treated between 2013–2018 at Flór Ferenc Hospital, Kistarcsa were retrospectively analyzed. The therapeutical response could be evaluated in 96 DTC patients.
Results
81 patients were classified with DTC in stages pT1–2. 64 patients were found in stages pT1, 17 patients were detected in stages pT2. The histological distribution of DTC was 65/81 (80.2%) papillary thyroid cancer (PTC) and 16/81 (19.8%) follicular thyroid cancer (FTC). Lymph node metastases were present in 21.5% of PTC and 0% of FTC. No distant metastases were detected. 25% of pT1 DTC was multifocal (9% limited to one lobe, 16% involved both lobes/isthmus), and 11.7% of pT2 DTC was multifocal (5.8% limited to one lobe, 5.8% involved both lobes). Thus pT1–2 multifocal DTC located in both lobes/isthmus were found in 11 patients (13.5%), all PTC, whereby 4/37 (10.8%) were in stage pT1a, 5/27 (18.5%) were in stage pT1b, 2/17 (11.8%) were in stage pT2. All of them underwent total thyreoidectomy, and in 10 of 11 were done postsurgical RRA. The tumour size in the contralateral lobe was <5 mm in 5 cases, was >5 mm in 3 cases (mean 9.6 mm) and there were no exact data in 3 cases.
Conclusions
In 13.5% of pT1–2 patients (11/81) the tumour involved both lobes, which changes the staging of the disease. The size of the tumour in the contralateral lobe is small in most cases (mean 1.4 mm), this fact makes almost impossible to detect and follow up them by ultrasound. Therefore we suggest total thyreoidectomy in moderate or low iodine supplied areas in T1b–T2 cases to improve the risk stratification, to determine the necessity of RRA and the long-term follow up, which are almost impossible if only lobectomy is being done.

DOI: 10.1530/endoabs.70.AEP920

AEP921

Early diagnosis of medullary thyroid cancer in case of low serum calcitonin: Role of calcitonin measurement in fine-needle aspiration washout fluid

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Background
Screening serum calcitonin (sCT) measurement in patients with thyroid nodules is still debated. Moreover, sCt cutoffs for medullary thyroid carcinoma (MTC) are not univocally defined. Also, sensitivity of cytology by fine needle aspiration biopsy (FNAb) has been demonstrated to detect approximately half of MTCs. Ct measurement in fine-needle aspiration washout fluid (Ct-FNAb) has high sensitivity and specificity and is helpful in case of non-diagnostic cytology[1]. Recently, a series oflow sCt MTC has been collected[2].
Aim
The objectives of this retrospective observational study were to define Ct-FNAb levels in subjects with low sCt (below cutoffs diagnostic for MTC) and to evaluate their clinical, ultrasonographic (US), cytological and histological characteristics.

Methods
We selected subjects with sCt above local normal ranges but below one of the diagnostic cutoff proposed for MTC (26 pg/ml in females and 68 pg/ml in males), subjected to FNAb with Ct-FNAb measurement and then thyroidectomized.
Results
Surprisingly, 50% (8/16) had MTC at histology, 19% cellular C hyperplasia (CCH) and only 31% neither MTC nor CCH. Ct-FNAb was significantly higher in MTC compared to both no MTC no CCH (2001 vs 25.32±55.72 pg/ml; *P=0.013*) and to CCH (2001 vs 195.56±286.09 pg/ml; *P=0.008*). Even if below the diagnostic cutoff, also sCt was higher in MTC compared to no CCH and no MTC group (19±7 vs 9±4 pg/ml; *P=0.019*) but was not able to discriminate MTC from CCH. US failed to identify suspicious nodules, since MTC differed only for being solid and not haloed. At cytology nearly 90% of MTC lesions were non-diagnostic or, mainly, indeterminate. At histology, 7/8 were low risk micro MTCs.
Conclusion
HighCt-FNAb despite sCt only slightly elevated suggests: i) early detection of MTC before the onset of high secretion of Ct, ii) a peculiar variant of MTC, able to produce Ct but not to secrete it in bloodstream because of intracellular secretory pathway alteration, iii) possible methodological interferences in the dosage of sCt. In conclusion, this study demonstrates the importance of Ct-FNAb to discover early stages of MTC with sCt below diagnostic cutoffs.
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DOI: 10.1530/endoabs.70.AEP921

AEP922

Impact ofhypothyroidism on early preneoplastic changes at the transcriptomic level in mammalian cells

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Introduction
Studies suggest that disturbed thyroid hormones (TH) homeostasis may lead to increased cancer risk. However, the exact role of TH in cancerogenesis is unknown. We have previously identified 15 genes linked with TH signaling in 7 cancer types and 10.967 cancer patients. Here, we investigated the influence of hypothyroidism on the expression of these 15 genes in rat tissues/organs from which the previously identified, TH-related cancer types originate.
Material and methods
Female Wistar-Kyoto rats were divided into 3 groups: i) treated with methimazole (MMI) (17 mg/kg daily for 8 weeks); ii)thyroidectomized;iii) control rats. $n=3$ rats per group. Gene expression was analyzed (qPCR) in: mammary glands, renal cortex, lungs, thyroid gland, endometrium, liver, ovary, and colon epithelium. Statistical analysis: Student's unpaired t-test, *P*-values <0.05 were considered significantly different. PanCancer analysis of co-expression of genes encoding mesenchymal stem cells (MSC) markers and genes linked to TH signaling was performed using publically available TCGA data from 10.967 cancer patients. The study was approved by the local ethics committee (Second Warsaw Local Ethics Committee for Animal Experimentation) no. *WAW2/022/2018.*
Results
The induction of hypothyroidism in rats was confirmed by serum evaluation of T4 (avg. 0.60 µg/dl) and TSH (avg. 20.23 ng/ml). In mammary and thyroid glands of MMI treated rats, strong induction of analyzed genes expression was observed, including *ARNT, THRA, THRB, SLC16A2, SLC2A1, CTNNB1, NCOA1, HDAC1, CMYC, HIF1A* upregulated in both tissues, and *VIM, CDH1 and TPO*upregulated only in thyroid glands. In the residual MMI-treated tissue types the only significant expression changes were: *HDAC1*downregulation in renal cortex and lungs, *DIO2* downregulation in endometrium, and *THRA* upregulation in colon epithelium. Expression profile in mammary glands ofthyroidectomized rats did not confirm induction of gene expression observed in MMI treated rats. Results of PanCancer TCGA data analysis revealed associations between expressions of genes linked with TH signaling and MSC functioning, including THY1/RCAN2 and ENG/RCAN2 which occurred in 11 cancer types.
Discussion
The study suggests that observed expression changes in mammary and thyroid glands are caused not only by hypothyroidism but also by MMI influence on these tissues. Elucidation of the observed expression changes requires further research. Since MMI, apart from TPO, can interact with other peroxidases like MPO, EPO and LPO,this interaction may lead to decreased selectivity of MMI inhibition and cause broader impact on gene expression.
Supported by grants: 501-1-25-01-19 and 2018/29/B/NZ5/01 211 (National Science Center, Poland).

DOI: 10.1530/endoabs.70.AEP922

AEP923

Adverse effects of tyrosine kinase inhibitors in advanced thyroid carcinoma – a summary of 10-year experience

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Introduction
To date, only four tyrosine kinase inhibitors (TKIs) have demonstrated beneficial effect on progression free survival in advanced medullary thyroid cancer (MTC; vandetanib and cabozantinib) andradioiodine-refractory differentiated thyroid cancer (RR-DTC; sorafenib and lenvatinib). However, there is still lack of unequivocal proofs of their significant impact on overall survival. Therefore, treatment-related side effects and their potential impact on quality of life has been recently widely discussed.
Aim
We conducted a retrospective analysis to evaluate TKIs toxicity in advanced thyroid cancer. The comparison of particular drugs was not aimed.
Material and methods
The study group involved 72 patients at mean age at treatment start of 51 ± 14 years. RR-DTC was diagnosed in 32 patients, whereas MTC in 40 subjects. All side effects were evaluated according to CTCAE (*Common Terminology Criteria for Adverse Events*), V 4.03. The median treatment time was 20.6 months (range: 0.5 months–142.8 months).
Results
In total, 74 treatment courses were assessed: 27 with lenvatinib, 9 with sorafenib, 22 with vandetanib, 9 with cabozantinib, 4 with motesanib, and 3 with axitinib. Treatment-related side effects were present in 97.3% courses. The most common were skin reactions – 68.9% courses, diarrhea – 67.6% courses, hypertension – 59.5% courses, weight loss – 56.8% courses, mucositis – 48.6% courses, abdominal pain– 29.7% courses, fatigue – 29.7% courses, and nausea in 18.9% courses. Skin changes were more frequent in MTC than in RR-DTC patients ($P=0.0128$). Similarly, fatigue was reported more commonly by MTC patients than by RR-DTC patients ($P=0.0387$). Fatigue also occurred more frequently in patients ≥55 years old at treatment onset comparing to younger ones <55 years. This difference was statistically significant ($P=0.0108$). No other significant differences in the frequency of the most common TKI-related side effects were noticed regrading tumor histopathology, age of treatment start, sex, and comorbidities. Due to poor tolerability drug interruption was necessary in 70.3% treatment courses, dose reduction in 62.2% courses, whereas permanent drug withdrawal was required in 25.7% courses.
Conclusions
TKI-related side effects were present in nearly all patients treated due to advanced thyroid cancer. Early diagnosis of adverse effects as well as a supportive management and dose modifications, if necessary, allowed avoiding serious complications and making possible to keep the patient on treatment as long as it was beneficial.
The study was supported by MILESTONE – STRATEGMED 2/26 7398/4/NCBR/2015.

DOI: 10.1530/endoabs.70.AEP923

AEP924

Octreotide and pasireotide effects on medullary thyroid carcinoma (MTC) cells growth, migration and invasion

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