

Safety of iodinated contrast media in patients with no risk factors for thyroid gland disease: thyroid function assessment after computer tomography with the use of iodine contrast media

Bezpieczeństwo jodowych środków kontrastowych u pacjentów bez czynników ryzyka chorób tarczycy: ocena funkcji tarczycy po tomografii komputerowej wykonywanej z użyciem jodowych środków kontrastowych

Grażyna Orlicz-Szczęsna, Andrzej Biłan, Jolanta Zdanowska

Department of Internal Medicine, Medical University, Lublin

Abstract

Purpose: A prospective study was performed to assess the influence of single, large iodine dose given intravenously to patients undergoing computer tomography living in areas with sufficient iodine supplementation with table salt.

Materials and methods: Thirty one patients with no personal familiar history of thyroid diseases in ages between 22 and 80 years old, were individually given 18.5-55.5 grams of iodine intravenously during computer tomography. Dose of iodine contrast media ranged from 50-150 ml. Evaluated patients had no contact with iodine during the last years. We included patients with no change in thyroid morphology in ultrasound taken by 10 MHz Siemens before trial. In all patients, levels of TSH and FT4 were measured before CT and after 1 and 3 months respectively.

Results: Thyroid hormone levels assessed after one and three months were in normal laboratory ranges. Large, single dose of iodine in contrast media caused no disturbances in assessed thyroid hormone levels.

Conclusions: In adult patients with no morphologic thyroid gland changes and no disturbances of hormonal function, single large dose of iodine is safe.

Keywords: Computer tomography, iodine contrast media, thyroid function

Streszczenie

Celem badania była ocena funkcji tarczycy u pacjentów, którym w trakcie badania tomografii komputerowej podano jodowy środek kontrastowy.

Grupę badaną stanowiło 31 pacjentów w wieku od 22 do 80 lat, bez chorób tarczycy w wywiadzie oraz z prawidłową morfologią gruczołu w badaniu ultrasonograficznym, którym w trakcie badania tomografii komputerowej podano od 50 do 150ml jodowego środka kontrastowego. Ocenę hormonów tarczycy i TSH wykonano przed badaniem oraz po upływie 1 miesiąca i 3 miesięcy.

Wyniki: Nie stwierdzono istotnych zaburzeń funkcji tarczycy w badanej grupie chorych.

Wnioski: Tomografia komputerowa z jednorazowym podaniem dużej ilości jodu w jodowym środku kontrastowym jest badaniem bezpiecznym.

Słowa kluczowe: tomografia komputerowa, jodowe środki kontrastowe, funkcja tarczycy

Introduction

In medicine there are widely used medias with large, overphysiologic doses of iodine both for diagnosis and treatment. It was interesting to investigate influence on hormonal thyroid balance and feedback with hypophysis in healthy adults with no previous history of any thyroid insufficiency. Patients from Lublin neighborhood were enrolled to our study. This East-Southern Poland region was assumed under iodine successful obligatory supplementation in 1997. Before it was successfully started, the area had been considered as moderate iodine deficient district. Supplementation with potassium iodide

at level $30\text{mg} \pm 10\text{mg}$ per kg table salt eliminated Iodine Deficiency Diseases in Poland and did not increase hyperthyroidism occurrence. In radiology, preferable applied contrast medias contain amounts of several dozens grams of iodine. It is mostly bounded with benzene ring and dose of free, released microelement is not more than one promille from used dose [1-3]. We aimed at assessment of thyroid gland state before application iodine contrast and after one and three months respectively. Such evaluation was also considered as Wolff-Chaikoff mechanism and escape phenomenon determinants considered as defending mechanism against colossal iodine overdose.

Material and methods

Study Protocol

All patients were informed about the aim of the study and consent was obtained. Patients filled up the questionnaire, where they answered to particular questions about prior personal and familiar history connected with thyroid disturbances. Qualified patients did not take any drugs or vitamins with iodine content. They also did not undergo any procedures with this element for the last 12 months. Three times collecting blood samples for hormonal assessment were performed. Clinical examination and ultrasonography of the thyroid gland was performed with 10 MHz sound of Siemens Sonoline G50. We excluded subjects with any single changes in thyroid morphology such as cyst, nodules, enlarged volume and echogenicity. Enlarged thyroid gland was defined as a volume exceeding 18ml for women and 25ml in men [4]. Patients qualified to study underwent head, thorax and abdomen computed tomography. These examinations were recommended by physicians because of suspected digestive system cancers, cephalic aorta aneurysm, pleura or uterus diseases.

Population Studied

In the study participated thirty-one adults, nineteen men and twelve women. The mean (\pm standard deviation) age of the study group was 57.2 ± 13.1 , ranged from 22 to 80n years, there was no age limit in inclusion criteria.

Iodine contrast media amounts

All patients were applied Ultravist 370 ((iopromide - the nonionic, monomeric group, Schering A.G. Germany) in computed tomography with Somatom Emotion 2004, Siemens Medical System in individual amount 50 to 150 ml intravenously upon body weight, one ml per one kg. Once given dose oscillate between 18.5 to 55.5 grams of iodine. Blood samples were taken three times before examination in the day of procedure, after one and three months respectively. Serum TSH and FT4 concentrations were analyzed with automated quantitative enzyme immunoassay using the ELFA technique (Enzyme Linked Fluorescent Assay), Bio-Merieux Company Lyon, France. Normal values range 0.25–5mIU/ml for basal TSH and 9–20pmol/l for FT4. Data for TSH and FT4 were expressed as mean \pm standard deviations for variables [4].

Statistical analysis

The collected data was submitted to a statistical study. The character of the data distribution was examined using Kolmogorow-Smirnow test. Student's t-test and Pearson linear correlation were analyzed. $p < 0.05$ was considered to

indicate a statistically significant difference. Statistical computations were performed with Statistica 6.0 PL.

Results

All median and particular assessed values were in normal laboratory range (table 1). None of the subject participated in the study developed any clinical or hormonal thyroid abnormalities.

Table 1 Average hormone levels - TSH and FT4 (mean \pm standard deviation SD)

Results		Average hormones concentration	SD
TSH (μ U/ml)	measurement 1	1.26	0.769
	measurement 2	1.12	0.760
	measurement 3	1.35	1.264
FT4 (pmol/l)	measurement 1	12.97	2.327
	measurement 2	11.93	2.373
	measurement 3	12.15	2.126

There were no significant difference between mean TSH and FT4 levels except significant difference observed between initial TSH level and second measurement after one month of observation (measurement 1-2). It decreased significantly ($p = 0.023$). Linear correlation coefficient of hormone levels after one month ($p = +0.112$), and after three months ($p = -0.138$) were not significantly important (table 2). All median FT4 changes were not statistically significant.

There were no significant interdependence in Pearson's linear correlation coefficient between TSH and FT4 median levels in particular measurements also after one month ($p = 0.112$), just like after 3 months ($p = -0.138$).

Discussion

Results of our study demonstrate that use of iodine contrast media at low-risk thyroid disease patients is safe and does not make any deficiency of thyroid hormonal stability connected with hypophysis feedback. Although many articles on contrast media exist, but a prospective study such as ours, with selected patients group from region just several years after introduction of sufficient iodine supplementation and moderate lack before, has not been published yet. We create homogenous group with no either morphologic or thyroid hormonal alterations. We assessed the influence of Ultravist 370 used in computed tomography on thyroid stimulating hormone and free thyroxin levels. Individually given doses were quantity of several dozen iodine grams what makes several hundred thousand times larger portion than 150 μ g daily recommended and established by World Health Organization. But nevertheless any of patients who participated in study did not developed either hormonal or

Table 2 Average differences of TSH and FT4 comparison in particular measurements before (1), after one (2) and three months (3) after use iodinated contrast medium

Analyzed data		Variance between two means			t-value	Statistical significance (p)
		Mean difference	S.	Standard error (S.E)		
TSH	Measurement 1- 2	0.23	0.551	0.097	2.395	0.023
	Measurement 1- 3	-0.15	0.839	0.151	-1.015	0.318
	Measurement 2- 3	-0.34	1.048	0.214	-1.578	0.128
FT4	Measurement 1- 2	0.86	3.374	0.596	1.441	0.160
	Measurement 1- 3	0.93	2.979	0.535	1.744	0.091
	Measurement 2- 3	0.15	2.397	0.489	0.302	0.765

clinical deficiency during three months survey. The mean TSH level first decreased on second measurements and after three months increased just above the initial level. The mean FT4 level also decreased after one month and increased in third analysis. But it not reached the initial level. The mean levels of both investigated hormones decreased at second measurement and increased at end of the study. All mean and particular hormone levels remained in normal laboratory range. We did not demonstrate in our research normal negative connection between TSH and FT4 present physiologically in humans. The mechanism of negative feedback with hypophysis influence opposite changes between TSH and thyroid hormones, when one increase another decrease in answer [5-7].

Large, once given iodine dose in adults with no personal and familiar history of latent or overt thyroid diseases in contrast media recommended while CT is performed is safe and does not cause any statistically significant thyroid hormonal changes. Opposite results to our study showed Hintze et al. who collected not selected patient group in region of moderate iodine deficiency and showed that iodine-induced hyperthyroidism developed among patients with low-risk of thyroid disease and apparently hormonal gland in ultrasound examination before study inclusion. The data of another scientists also agree with Hintze results [8-10]. But most authors warn against possibility of thyroid functional deficiency after iodine contrast in patients from "thyroid" high-risk group. Mostly they are oldest patients with enlarged thyroid volume, especially with multinodular goiter, or possible autonomy, low TSH, likewise younger people with genetic predisposition to autoimmunology [11,12].

Also among patients with prior personal or family history of thyroid disease. These groups should be under clinical control after the procedure to quick diagnose any thyroid insufficiency, either subclinical or overt, as well hypothyroidism as hyperthyroidism. If any clinical symptoms appear, hormonal examination and if needed treatment are included. We know from literature that iodine contrast can develop hypothyroidism especially among children with immature escape phenomenon. As well

hyperthyroidism to even thyroid storm leading to death was described [13-16]. Nevertheless one consider that prophylaxis should be not provided even in cases of iodine-induced hyperthyroidism generally, but after individual consideration. Incidence of prevention adverse effects with metimazole or perchlorate can be greater higher than risk of iodine induced thyrotoxicosis development [17,18]. Fasbender et al. showed, that not initial level of TSH, but thyroid morphology is more precise iodine-induced hyperthyroidism predictor than basal TSH decrease. But from practice point of view and up to our results it is difficult to agree with Fasbender conclusions because as practitioners we often observe low TSH which is not marker of hyperthyroidism but connected with age (older patients) and especially touched with chronic illnesses. Doctor who knows that iodine contrast can induce pathologic thyroid process at high-risk patients group let him for appropriate direction such patients. It makes possible to decrease time to proper diagnosis and faster introduce treatment even before development overt symptoms, just in latent, subclinical phase [19,20].

A single, large dose of iodine contained in contrast media used to computed tomography is safe, does not cause thyroid hormonal abnormalities and not need control after procedure. Iodine contrast media can be use in wide spectrum with no harm to thyroid gland function and hormonal equilibrium.

References

1. Szybiński Z., Delange F., Lewinski A., et al. A programme of iodine supplementation using only iodised household salt is efficient - the case of Poland. *Eur. J. Endocrinol.*, 2001; 144: 331-337.
2. Tedelind S., Larsson F., Johanson C., et al. Amiodarone inhibits thyroidal iodide transport in vitro by a cyclic adenosine 5'-monophosphate- and iodine-independent mechanism. *Endocrinology*, 2006; 147: 2936-2943.
3. Dohan O., Carrasco N. Advances in Na(+)/I(-) symporter (NIS) research in the thyroid and beyond. *Mol Cell Endocrinol*, 2003; 213: 59-70.
4. Delange F. Iodine deficiency in Europe and its consequences: an update. *Eur. J. Nucl. Med. Mol. Imaging*, 2002; Suppl.2: 404-416.
5. Carayon P., Niccoli-Sire P., Lejeune P.J., et al. Guidelines for the diagnosis and monitoring of thyroid disease. *Ann. Biol. Clin.*, 2002; 60: 331-338.

6. Becker D.V., Braverman L.E., Delange F., et al. Iodine supplementation for pregnancy and lactation-United States and Canada: recommendations of the American thyroid association. *Thyroid*, 2006; 16: 949-951.
7. Eisenberg M., Samuels M., DiStefano J.J. 3rd. L-T4 bioequivalence and hormone replacement studies via feedback control simulations. *Thyroid*, 2006; 16: 1279-1292.
8. Hintze G., Blombach O., Fink H., et al. Risk of iodine-induced thyrotoxicosis after coronary angiography: an investigation in 788 unselected subjects. *Eur. J. Endocrinol.*, 1999; 140: 264-267.
9. Skare S., Frey H. Iodine-induced thyrotoxicosis in apparently normal thyroid glands. *Acta Endocrinol. (Copenh)*, 1980; 94: 332-336.
10. Savoie J.C., Massin J.P., Thomopoulos P., et al. Iodine-induced thyrotoxicosis in apparently normal thyroid glands. *J. Clin. Endocrinol. Metab.*, 1975; 41: 685-691.
11. Laurberg P., Jorgensen T., Perrild H., et al. The Danish investigation on iodine intake and thyroid disease, DanThyr: status and perspectives. *Eur. J. Endocrinol.*, 2006; 155: 219-28;
12. Knudsen N., Bulow I., Jorgensen T, et al. Goitre prevalence and thyroid abnormalities at ultrasonography: a comparative epidemiological study in two regions with slightly different iodine status. *Clin Endocrinol (Oxf)* 2000 ; 53: 479-85;
13. Blattmann H., Reinhardt M., Schumichen C., et al. Thyrotoxic crisis after exposure to iodine. A case with fatal outcome. *Radio-loge*, 1994; 34: 487-490.
14. Del Cerro M.M., Fernandez R.A., Guerta G.L., et al. Thyroid function alterations in children with congenital cardiac disease after catheterization with iodinated contrast media. *Revista Espanola de Cardiologia*, 2000; 53: 517-524.
15. Gartner W., Weissel M. Do iodine-containing contrast media induce clinically relevant changes in thyroid function parameters of euthyroid patients within the first week? *Thyroid*, 2004; 14: 521-524.
16. Weber C., Scholtz G.H., Lamesch P., et al. Thyroidectomy in iodine induced thyrotoxic storm. *Experimental and Clinical Endocrinology and Diabetes*, 1999; 107: 468-472.
17. Lawrence J.E., Lamm S.H., Braverman L.E. The use of perchlorate for the prevention of thyrotoxicosis in patients given iodine rich contrast agents. *J. Endocrinol. Invest.*, 1999; 22: 405-407.
18. Van der Molen A.J., Thomsen H.S., Marcos S.K. Effects of iodinated contrast media on thyroid function in adults. *Eur. Radiol.*, 2004; 14: 902-907.
19. Fassbender W.J., Schluter S., Stracke U., et al. Thyroid function after iodine-containing contrast media agent administration in coronary angiography: a prospective study of euthyroid patients. *Z. Kardiol.*, 2001; 90: 751-759.
20. Fassbender W.J., Vogel C., Doppl W., et al. Thyroid function, thyroid immunoglobulin status, and urinary iodine excretion after enteral contrast-agent administration by endoscopic retrograde cholangiopancreatography. *Endoscopy*, 2001; 33: 245-252.

Correspondence address

Andrzej Biłan
Klinika Chorób Wewnętrznych
Uniwersytet Medyczny w Lublinie
20-081 Lublin, ul. Staszica 16
tel/fax (+84)815327717
e-mail: andrzej.marek.bilan@gmail.com