RELATIONSHIP BETWEEN MEAN ARTERIAL PRESSURE AND THE LEVEL OF TSH IN STROKE PATIENTS

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Keywords: *hypertension, subclinical hypothyroidism, stroke*

Abstract: *According to the literature, hypothyroidism is a risk factor for high blood pressure (BP) and atherosclerotic diseases. This research aims at examining the role of thyroid hormone deficiency in the development of hypertension and ischemic diseases. The study was conducted on 154 patients who suffered a stroke and a control group consisting of 15 patients with normal thyroid function without signs and symptoms of stroke. Our research confirmed that subclinical hypothyroidism (SHT) could increase the risk of diastolic hypertension. Significantly elevated values of differentiated blood pressure (dfBP) can be considered as an indicator of arterial stiffness in SHT.*

INTRODUCTION

Hypertension is a major risk factor for atherosclerotic diseases. The incidence of stroke is 3 times higher in hypertensive people correlated with both systolic value and the diastolic one. Any increase by 20 mmHg in systolic blood pressure (sBP) and by 10 mmHg in diastolic BP (dBP) multiplies by 2 the risk of stroke at any age.(1)

Several biological mechanisms are known to be associated with an increased risk for hypertension, weight gain, insulin resistance, hyperlipidemia, hypothyroidism.(2)

Hypothyroidism is associated with hypertension in 3% of the cases.(3)

The mechanism responsible for arterial hypertension (AHT) in thyroid insufficiency could be arterial vasoconstriction, stiffness of arterial walls and impaired contractility of the heart. Hypertension, most commonly diastolic, is increased in patients with hypothyroidism due to increased peripheral vascular resistance.(4)

Some researchers believe that in subclinical hypothyroidism (SHT), only the arterial mechanism appears to be involved in diastolic hypertension without the participation of the heart.(5,6,7)

It has been found that in the normotensive patients who became hypothyroid (with thyroid hormone replacement therapy), hypertension occurs.(8) In hypothyroid patients with AHT, the treatment with thyroxine normalizes elevated BP.(9)

In previous studies, it has been shown that hypothyroidism is associated with increased vales of dBP and decreased pulse rate. On the other hand, the incidence of hypothyroidism is increased in patients with AHT compared to the general population.(10,11,12,13)

We started from the idea that the process of atherogenesis may be due or can be accelerated and exacerbated by thyroid hormone deficiency, so early identification of SHT can help preventing or delaying the development of cerebral ischemic diseases.

Clinical hypothyroidism is associated with AHT, but it is unclear if this is true for SHT.

PURPOSE

This research aims at examining the role of thyroid hormone deficiency in the development of AHT and ischemic diseases.

MATERIALS AND METHODS

The study was conducted on 154 patients who had suffered a stroke, hospitalized in the Asklepios Neurology Clinic in Schildautal, Germany between 2013 and 2015 and a control group consisting of 15 patients with normal thyroid function without signs and symptoms of stroke, aged between 61 and 80 years old, hospitalized in the Endocrinology Clinic from Sibiu between 2014 and 2015.

After applying the inclusion and exclusion criteria, of the total of 154 stroke patients, 116 patients were included in the study.

Exclusion criteria were: patients receiving amiodarone treatment, previously diagnosed with hypothyroidism or hyperthyroidism, severe obesity, chronic heart failure, severe systemic disease, renal and hepatic chronic diseases, malignancies.

Thyroid function assessment was conducted as part of the routine evaluation of all patients admitted to the clinic for cerebrovascular events.

Euthyroidism or normothyroidism (NT) was defined as thyroid stimulating hormone (TSH) and free thyroxine (FT4) within normal reference range.

Symptomatic subclinical hyperthyroidism was defined as TSH concentration below the normal lower limit and increased FT4. In subclinical hyperthyroidism, TSH concentration is low and FT4 is normal.

The diagnosis of stroke was determined by clinical and laboratory tests. We performed the following laboratory examinations: brain magnetic resonance imaging (MRI) brain computed tomography (CT), angio-MRI or angio-CT for intracranial vascular exploration, Doppler ultrasound for extracranial vascular exploration, electrocardiogram, electroencephalogram, chest X-ray, lumbar puncture, oximetry.

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Article received on 27.06.2016 and accepted for publication on 16.09.2016
ACTA MEDICA TRANSILVANICA September 2016;21(3):38-40

Laboratory tests performed were the following: blood count, blood ionogram, hemostasis exploration, blood sugar, liver samples, C-reactive protein, lipidogram, hormonal dosages, namely TSH, FT4 and free triiodothyronine (FT3).

The values considered normal were the following: cholesterol <200 mg/dl, LDL-cholesterol ≤ 130 mg/dl, triglycerides ≤ 130 mg/dl, TSH between 0.35-4.94 μU/ml, FT4 between 1.71-3.71 pg/ml, FT3 between 0.7-1.48 ng/dl.

BP was measured by a mercury sphygmomanometer. The optimum value (according to the World Health Organization) for sBP was 120 mmHg and 80 mmHg for dBP.

Mean BP (mBP) replaces the instantaneous values (systolic and diastolic) with a unique value, which would achieve the same circulatory flow in the conditions in which the flow would be continuous and not pulsed. It can be approximated by the formula: mBP = + dBP (sBP - dBP/3).

Differential BP or pulse pressure (dfBP) is given by the difference between sBP and dBP. Their changes characterize two types of pressure curves: divergent: sBP increases, dBP decreases; converging: sBP decreases, dBP increases.

RESULTS

After subtracting the number of patients with subclinical hyperthyroidism of those 116, it results that of 103 patients with stroke, 8 (7.76%) had SHT.

After subtracting the number of patients with SHT of those 116, it results that of 108 patients with stroke, 13 (12.03%) had subclinical hyperthyroidism.

SHT incidence is higher, 11.94%, if we refer only to the 67 stroke patients between 61 to 80 years old, age group that included all 8 patients with SHT.

To compare the biological parameters in stroke patients and subclinical disthyroidism forms, of the total (67) of stroke patients without clinical disthyroidism forms aged between 61 and 80 years old, there have been randomly selected 15 patients as controls.

In stroke patients without SHT, mean value ± standard deviation (M±SD) of BP (145.33 ± 18.27/85.67±11.63) indicate that they showed stage 1 hypertension (table no.1).

In patients with stroke and SHT, M±SD of BP (133.75 ± 14.33/87.5 ± 9.26) indicates that they presented prehypertension or high mBP (table no. 2).

Table no. 1. Values of TSH and BP in patients with stroke and NT

No.	Gender	Age (years)	TSH (μU/ml)	sBP (mmHg)	dBP (mmHg)	mBP (mmHg)	dfBP (mmHg)
1	M	70	1.396	150	85	107	65
2	M	80	1.778	145	80	102	65
3	M	82	0.99	125	80	95	45
4	F	73	1.202	140	85	103	55
5	M	72	0.776	125	70	88	55
6	M	80	1.523	160	100	120	60
7	F	69	2.410	170	105	127	65
8	F	73	1.785	140	85	103	55
9	F	80	1.491	120	70	87	50
10	F	79	1.754	165	95	118	70
11	M	63	2.038	170	100	123	70
12	F	70	1.243	140	80	100	60
13	F	78	0.806	120	75	90	55
14	M	70	0.812	140	75	97	65
15	F	69	1.597	170	100	123	70
	M±DS	73.87±5.59	1.44±0.47	145.33±18.27	85.67±11.63	103±10.03	60.33±7.67

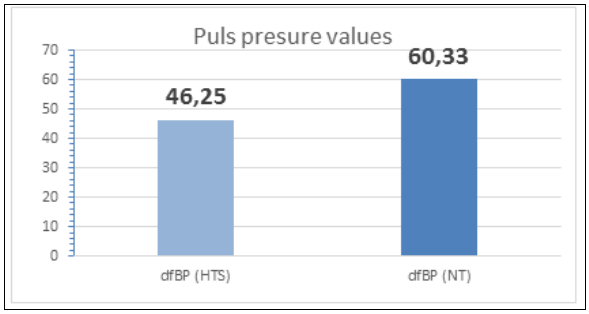
Table no. 2. Values of TSH and BP in patients with stroke and SHT

No.	Gender	Age (years)	TSH (μU/ml)	sBP (mmHg)	dBP (mmHg)	mBP (mmHg)	dfBP (mmHg)
1	F	79	13.298	135	90	105	45
2	F	69	15.797	120	85	97	35
3	F	75	15.797	130	80	97	50
4	B	78	7.088	160	100	120	60
5	B	67	5.286	140	95	110	45
6	B	67	5.924	145	90	108	55
7	F	76	9.735	120	70	87	50
8	F	71	17.686	120	90	100	30
	M±DS	72.75±4.86	11.33±4.93	133.75±14.33	87.5±9.26	105.53± 13.55	46.25±9.91

Table no. 3. Demographic data and values of TSH and BP in patients with stroke and SHT compared with patients with stroke and without SHT

Measured variables	Stroke and SHT	Stroke without SHT	T Student test
No. of patients	8	15	
Age (years)	72.75±4.86	73.87±5.59	P=0.319 p<0.05 (NS)
Men	3	7	
Women	5	8	
TSH (0,35-4,94 μU/ml)	11.33±4.93	1.44±0.47	P=0.001 p<0.05
FT4 (0,7-1,48 ng/dl)	1,20±0,14 ng/dl	1,10±0,17 ng/dl	P=0.367 p<0.05 (NS)
sBP (< 120 mmHg)	133.75±14.33	145.33±18.27	P=0.067 p<0.05 (NS) p<0.01
dBP (< 80 mmHg)	87.5±9.26	85.67±11.63	P=0.352 p<0.05 (NS) p<0.01 (NS)
mBP (mmHg)	105.53±13.55	103±10.03	P=0.641 p<0.05 (NS) p<0.01 (NS)
dfBP (mmHg)	46.25±9.91	60.33±7.67	P=0.0005 p<0.05

Figure no. 1. Values of dfBP in patients with SHT compared with NT patients



DISCUSSIONS

In our research, BP average values were not significantly different from statistical point of view.

sBP had lower values (M ± SD:133.75±14.33 mmHg) in patients with stroke and SHT versus patients suffering from stroke but without SHT (M ± SD:145.33±18.27 mmHg). The latter showed, if we consider sBP values, prehypertension or high mBP. The difference between the two groups was not statistically significant at $p<0.05$ but it was statistically significant at $p<0.01$.

dBP was higher in patients with stroke and SHT (87.5 ± 9.26) compared with dBP in patients without SHT (85.67 ± 11.63 mmHg), though in statistical terms, dBP differences were insignificant. The same can be said for mBP.

The biggest differences ($p<0.05$) in our research were found for dfBP values. dfBP in patients with SHT was 46.25 ± 9.91 mmHg, while in NT and stroke patients, it was 60.33 ± 7.67 mmHg. Other authors as well have reached comparable results to ours.(10,11,12,13)

The pathophysiological explanation of convergent blood pressure in patients with SHT could be bradycardia, vasoconstriction and peripheral vascular resistance present in thyroid hormone deficiency. dfBP also depends on the pulse wave velocity which is the gold standard of arterial stiffness. Increased pulse wave velocity is an indication of early vascular aging, being also present in SHT.(14,15)

It has been found (16) that the prevalence of ATH in patients with SHT was significantly higher than in normal control group. Rotterdam study showed that SHT was an independent risk factor for myocardial infarction and atherosclerosis. Blood hypercoagulability, increased blood viscosity, lipid anomalies in patients with SHT may increase the risk of atherosclerosis, factors that may also be involved in the pathogenesis of BP increase.(5,16,17,18)

Over time, much emphasis was put on dBP compared with sBP as a predictor of cardiovascular morbidity and fatal events. However, a large number of observational studies showed that cardiovascular morbidity and mortality is in a constant relationship with both dBP and sBP.

Our research allows us to conclude that ATH is an associated risk factor in patients with SHT. Consequently, all patients at risk of stroke should be screened for thyroid insufficiency, and thyroid investigation to be considered part of stroke risk stratification.

We consider that our study has limitations regarding the small number of subjects included in the study. Even in these circumstances, it can be said that SHT is associated with increased pulse pressure, increased risk factor for cerebrovascular disease.

CONCLUSIONS

1. Our research confirmed that SHT could increase the risk of diastolic hypertension.
2. Significantly increased values of dfBP can be considered as an indicator of arterial stiffness in SHT.
3. Screening for hypothyroidism is essential if the patient has an increased level of cholesterol, excess weight and increased dfBP. Early diagnosis and thyroid replacement therapy timely applied may reduce cardiovascular risk.

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