Intellectual outcome at childhood in congenital hypothyroidism according to etiology and treatment related factors

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Introduction: **The intellectual outcome in children with congenital hypothyroidism detected by neonatal screening is generally good. The aim of this study was to evaluate the intellectual outcome in patients with congenital hypothyroidism at childhood and to identify factors that may affect intellectual development.**

Method: **The intelligence quotient (IQ) of 126 patients with congenital hypothyroidism was evaluated at childhood using the Korean Wechsler Intelligence Scale for Children. We retrospectively reviewed their clinical datas to know etiology, thyroid function status, L-thyroxine dose at diagnosis and normalization duration of TSH. Etiology – dyshormonogenesis (Type 1), agenesis (Type 2), hypoplasia (Type 3) and ectopic thyroid (Type 4) - was sorted by imaging including ultrasonography and Tc-99m scintigraphy at diagnosis.**

Result: **The mean IQ of patients tested at childhood was 103.3 ± 11.5. Total IQ, verbal IQ and performance IQ of patients was not significantly different according to etiology. Mean IQ of patients with thyroid agenesis was lower than patients with thyroid dysgenesis, but there was no statistical significance. In multivariate linear regression analysis, pretreatment thyroid function, age at treatment and normalization duration of TSH were not determinants of IQ. L-thyroxine dose was statistically significant determinant of total, verbal and performance IQ.**

Table 1. Baseline characteristics per subtype in children with congenital hypothyroidism

Variable	Total (N=128)	Type 1 (N=53)	Type 2 (N=7)	Type 3 (N=41)	Type 4 (N=27)	p-value
Age (year)	7.2 ± 2.2	7.1 ± 2.1	9.2 ± 4.9	7.1 ± 1.7	6.8 ± 1.8	0.646
Sex						0.086
Male	55 (43.0%)	20 (37.7%)	3 (42.9%)	24 (58.5%)	8 (29.6%)	
Female	73 (57.0%)	33 (62.3%)	4 (57.1%)	17 (41.5%)	19 (70.4%)	
Weight (kg)	4.5 ± 1.0	4.3 ± 0.7	4.1 ± 0.8	4.7 ± 0.9	4.7 ± 1.7	0.118
Status at diagnosis						
TSH	140.9 ± 158.4	159.1 ± 160.2	240.3 ± 231.0	49.1 ± 47.9	226.5 ± 179.9	<0.001[1-3, 2-3, 3-4]
FT4	0.7 ± 0.5	0.5 ± 0.4	0.1 ± 0.1	0.9 ± 0.4	0.8 ± 0.7	<0.001[1-3, 2-3, 2-4]
Status at NST						
TSH	113.7 ± 116.0	107.5 ± 92.6	295.2 ± 269.5	58.6 ± 44.4	185.9 ± 142.3	<0.001[1-3, 1-4, 3-4]
FT4	0.8 ± 0.9	0.6 ± 0.7	0.1 ± 0.1	1.2 ± 1.0	0.9 ± 0.8	<0.001[1-3, 2-3, 2-4]
Treatment-related factor						
Onset duration (days)	43.2 ± 73.6	29.5 ± 15.5	19.4 ± 7.8	42.1 ± 32.9	77.8 ± 157.4	0.001[1-3, 2-3]
Dose (g)	47.5 ± 7.7	47.9 ± 5.5	50.6 ± 13.1	45.5 ± 8.6	49.8 ± 7.1	0.444
Dose/weight (g/kg)	10.9 ± 2.7	11.5 ± 2.4	12.7 ± 3.7	9.9 ± 2.4	11.4 ± 3.2	0.217
Normalization duration of TSH (days)	125.2 ± 154.5	124.8 ± 172.6	194.8 ± 272.9	120.1 ± 151.7	116.5 ± 64.4	0.688

Data were reported as mean±standard deviation for continuous variables and n (%) for categorical variables.
P-values were calculated by Kruskal-Wallis test for continuous variables and chi-square test or Fisher's exact test for categorical variables.
Posthoc comparison with Bonferroni's correction : i-j means that there exists the significant difference between type i and type j. (i, j=1,2,3,4).

Table 2. IQ per subtype in children with congenital hypothyroidism

Variable	Total (N=128)	Type 1 (N=53)	Type 2 (N=7)	Type 3 (N=41)	Type 4 (N=27)	p-value
Total IQ	103.3 ± 11.5	103.0 ± 10.3	92.1 ± 14.5	105.5 ± 12.0	103.4 ± 11.0	0.085
Verbal IQ	101.7 ± 14.0	100.2 ± 13.0	93.3 ± 14.0	105.0 ± 15.3	101.9 ± 12.9	0.118
Performance IQ	104.9 ± 12.2	105.7 ± 11.6	90.9 ± 16.3	106.1 ± 10.9	105.0 ± 12.5	0.13

Table 3. Univariate linear regression analysis for IQ score in children with congenital hypothyroidism

Variable	Total IQ		Verbal IQ		Performance IQ	
	B (95% CI)	p-value	B (95% CI)	p-value	B (95% CI)	p-value
Subtype2 (vs. type1)	-10.89 (-19.85, -1.93)	0.018	-6.96 (-17.98, 4.06)	0.214	-14.82 (-24.25, -5.4)	0.002
Subtype3 (vs. type1)	2.59 (-2.05, 7.22)	0.271	4.75 (-0.95, 10.45)	0.101	0.42 (-4.46, 5.29)	0.865
Subtype4 (vs. type1)	0.46 (-4.8, 5.73)	0.862	1.61 (-4.87, 8.09)	0.624	-0.68 (-6.22, 4.86)	0.809
Age (year)	-0.88 (-1.78, 0.02)	0.055	-0.86 (-1.98, 0.25)	0.128	-0.9 (-1.85, 0.05)	0.063
Female	4.51 (0.51, 8.52)	0.027	6.63 (1.81, 11.45)	0.007	2.4 (-1.9, 6.7)	0.272
Weight (kg)	2.12 (-0.29, 4.52)	0.084	3.38 (0.43, 6.34)	0.025	0.85 (-1.63, 3.34)	0.496
TSH at diagnosis	-0.01 (-0.02, 0)	0.143	-0.01 (-0.03, 0)	0.108	-0.01 (-0.02, 0.01)	0.347
FT4 at diagnosis	-0.12 (-4.3, 4.06)	0.956	0 (-5.17, 5.17)	1	-0.23 (-4.42, 3.96)	0.913
Onset duration of treatment (days)	0 (-0.03, 0.03)	0.976	0.02 (-0.02, 0.06)	0.342	-0.02 (-0.05, 0.01)	0.222
Dose (g)	-0.41 (-0.71, -0.11)	0.008	-0.33 (-0.71, 0.06)	0.097	-0.5 (-0.8, -0.19)	0.002
Dose/weight (g/kg)	-1.62 (-2.48, -0.76)	<0.001	-1.86 (-2.95, -0.78)	0.001	-1.38 (-2.27, -0.48)	0.003
Normalization duration of TSH (days)	0.01 (-0.01, 0.02)	0.276	0.01 (-0.01, 0.03)	0.273	0.01 (-0.01, 0.02)	0.45

B : regression coefficient.

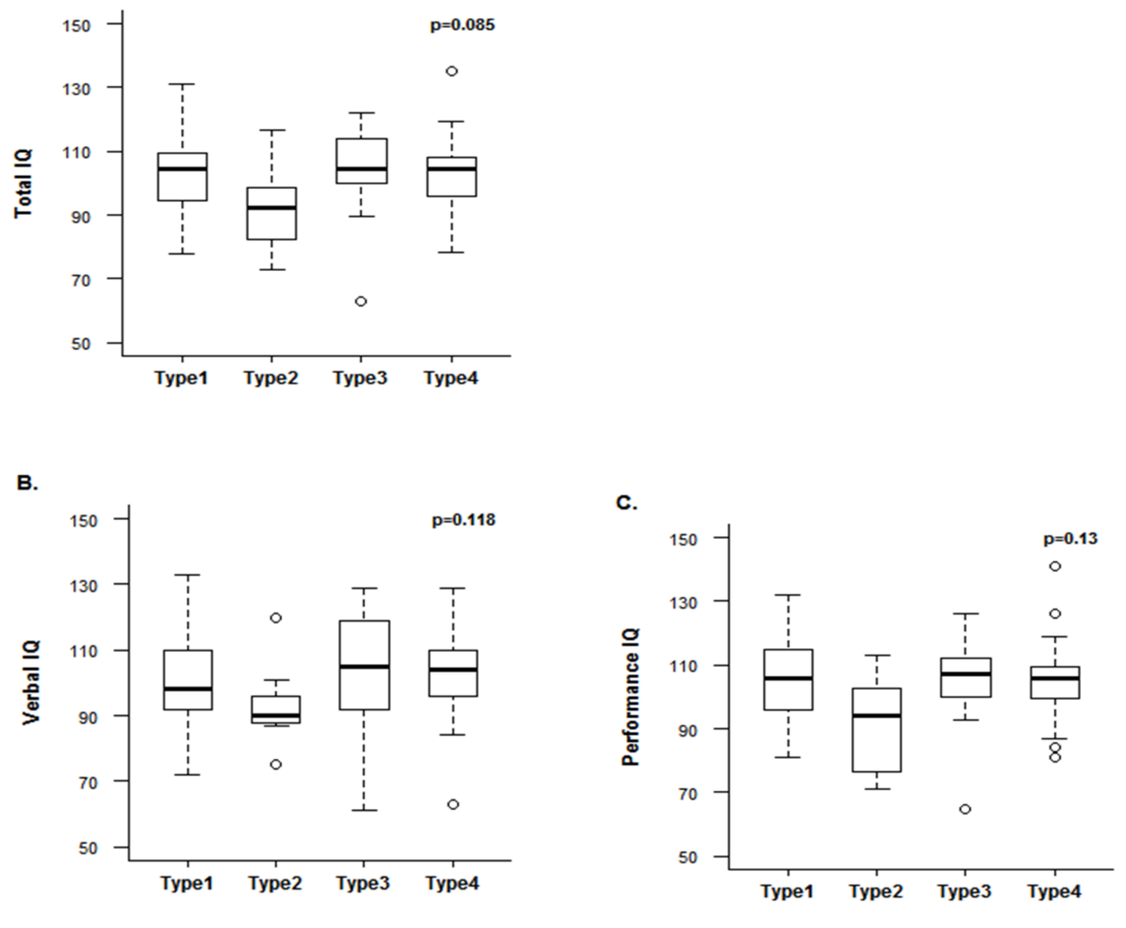

Figure 1. IQ per subtype in children with congenital hypothyroidism

Conclusion: **IQ of children with treated congenital hypothyroidism were within normal range. Treatment pattern was important for intellectual outcome rather than etiology and severity of congenital hypothyroidism.**

References : **1. Aleksander PE, Brückner-Spieler M, Stoehr AM, Lankes E, Kühnen P, Schnabel D, et al. Mean High-Dose l-Thyroxine Treatment Is Efficient and Safe to Achieve a Normal IQ in Young Adult Patients With Congenital Hypothyroidism. J Clin Endocrinol Metab 2018;103(4):1459-1469**

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