Hypothyroxinemia Of Prematurity Was Not Associated With Adverse 5-year Neurodevelopmental Outcome Very Low Birth Weight Infants

Lay Ong, Tan¹, Mary Grace, Tan¹, Woei Bing, Poon¹

¹ Department of Neonatal & Developmental Medicine, Singapore General Hospital, Singapore

INTRODUCTION

The association between hypothyroxinemia of prematurity with delayed development and cerebral palsy is controversial. The predictive value of late thyroid function tests in VLBW infants, after 2 weeks of life, for long term neurodevelopment is contentious.

AIMS

1) To compare 5 year neurodevelopmental outcomes of very low birth weight (VLBW) infants with hypothyroxinemia of prematurity against those without.

2) To review predictive values of cord TSH, predischARGE thyroid function at term/near term for neurodevelopment and growth at 5 years.

METHODS

Retrospective cohort study in a single tertiary neonatal centre of VLBW infants admitted between 2008 to 2011. Routine cord TSH and pre-discharge thyroid function tests at term or near term equivalent age were analysed. Additional thyroid function tests performed inpatient, as well as the lowest fT4 and highest TSH, were also analysed. Comparisons were made between all abnormal and normal thyroid function controls. Patients requiring thyroid replacement were also analysed and compared to those with normal thyroid function tests.

The outcome data were at 2 year corrected age included growth parameters, Bayley scales of infant and toddler development – third edition and Vineland II adaptive behaviour scales (VABS).

The outcome data at 5 years old included growth parameters, Wechsler Preschool and Primary Scale of Intelligence (WPPSI III), Bracken School Readiness Assessment, VABS and Beery Test of Visual-Motor Integration. A multi-logistic regression model was used incorporating gestation, gender, duration of NICU and the individual thyroid tests looking at prediction of neurodevelopment.

Linear correlation analysis of the respective thyroid parameters were done, taking into account the gestational age, gender and duration of NICU stay. Correlation coefficient (unadjusted and adjusted), R square and standardised R square were done. Categorical data was analysed using chi square. Continuous data was analysed Mann whitney U test.

RESULTS

A total of 105 patients were analysed in this study. 15 patients were excluded due to mortality.

Table 1: Demographic characteristics

Baseline characteristics		
Gestational age at birth (weeks, mean)		28.6
Birth weight (gram, mean)		1041
Sex (male, n)		54
Race n (%)	Chinese	68
	Malay	17
	Indian	4
	Others	14
Cord TSH done (n)		87
Day of life TFT done before discharge (mean)		62
Post menstrual age TFT done before discharge (weeks, mean)		37.5
Levothyroxine needed (n)		3
Hypothyroxinemia of prematurity (n)		15
Primary hypothyroidism (n)		3

Table 2: relationship between Cord TSH and neurodevelopmental outcome at 5 years old

Cord TSH	Pearson's R	R square	Standardised coefficient	P-value
WPPSI Full scale IQ	0.556	0.359	0.316	0.048
Bracken School readiness composite standard score	-0.099	0.261	-0.110	0.364
Beery VMI	0.358	0.407	0.465	0.013

Table 3: relationship between TFT before discharge and neurodevelopmental outcome at 5 years old

fT4 before discharge	Pearson's R	R square	Standardised coefficient	P-value
Bracken School readiness composite standard score	0.203	0.200	0.205	0.214
Beery VMI	0.366	0.241	0.389	0.05
TSH before discharge	Pearson's R	R square	Standardised coefficient	P-value
WPPSI verbal IQ score	0.374	0.262	0.308	0.032
Processing speed IQ	0.286	0.259	0.323	0.038
Shape mastery level	0.278	0.212	0.220	0.132
VABS daily living skill	0.963	-	-	0.009

Table 4: relationship between hypothyroxinemia of prematurity with neurodevelopmental outcome at 5 years old

	Mean (Hypothyroxinemia of prematurity)	Mean (normal TFT)	P-value
WPPSI full scale score	97.4	93.2	0.485
VABS Adaptive Behaviour Composite score	70	52.8	0.624
Bracken school readiness composite standard score	88.7	92.2	0.554
Beery VMI	106.4	104.6	0.769

Table 5: relationship between infants on thyroxine replacement with neurodevelopmental outcome at 5 years old

	Pearson's R	R square	Standardised coefficient	P-value
WPPSI performance score IQ	-0.063	0.184	-0.095	0.499
WPPSI processing speed IQ	0.537	0.426	0.502	0.001
WPPSI full scale IQ score	-0.084	0.223	-0.199	0.188
Beery VMI	-0.356	0.302	-0.303	0.074

CONCLUSION

Different thyroid function tests, even in VLBW infants without congenital hypothyroidism, predict for different aspects of neurodevelopment and growth at 5 years. Hypothyroxinemia of prematurity was not associated with neurodevelopmental delay.

REFERENCES

- Osborn, David A., and R. W. Hunt. "Prophylactic postnatal thyroid hormones for prevention of morbidity and mortality in preterm infants." (2007): CD005948-CD005948.
- Scratch SE, Hunt RW, Thompson DK, Ahmadzai ZM, Doyle LW, Inder TE, Anderson PJ. Free thyroxine levels after very preterm birth and neurodevelopmental outcomes at age 7 years. Pediatrics. 2014 Mar 1; peds-2013.
- Lee JH, Kim SW, Jeon GW, Sin JB. Thyroid dysfunction in very low birth weight preterm infants. Korean journal of pediatrics. 2015 Jun 1;58(6):224-9.
- Hashemipour M, Hovsepian S, Ansari A, Keikha M, Khalighinejad P, Niknam N. Screening of congenital hypothyroidism in preterm, low birth weight and very low birth weight neonates: A systematic review. Pediatrics & Neonatology. 2017 Jul 22.

PATIENTS. AT THE HEART OF ALL WE DO.