International Journal of Children and Adolescents

Original Article
IJCA, Vol. 2, No. 4, Oct, 2016.1-4.

Determining mean level of thyroid hormones in 5th day, 2nd and 4th weeks in premature infants referred to NICUs of Aliasghar and Akbarabady Children Hospitals

Nasrin Khalesi: (**Corresponding author*) Department of Pediatrics, Iran University of Medical Sciences, Tehran, Iran. nasrinkhalesi1394@gmail.com
Maryam Sabouteh: Pediatrician and Neonatologist, Assistant Professor, Iran University of Medical Sciences, Tehran, Iran.

Received: 05 Jan 2016 Accepted: 10 May 2016

Abstract

Background and Objective: Thyroid function problems are often present with prematurity disorders. Thyroid hormones regulate growth and distinguish body organs; especially they affect central nervous system and metabolism of carbohydrates, lipids, and vitamins. Thus, these hormones should be evaluated. The present study aims to determine the mean level of thyroid hormones among premature infants referred to NICUs of Aliasghar and Akbarabadi hospitals in 5th day, 2nd and 4th weeks.

Methods: In this cross-sectional study 140 infants who referred to Aliasghar and Akbarabadi hospitals NICU since May 2012 were examined after obtaining written consent from their proxies. At the 5th day 1cc blood sample was taken; and the procedure was repeated at the 2nd and 4th weeks. TSH and T4 were measured and the mean was calculated for the 3 stages.

Findings: A total of 140 patients (80 boys) were evaluated. Gestational mean age was 31.91 weeks. At the 5th day the means of TSH and T4 were 4.16 and 8.71, at the 2nd week 4.47 and 8.12, and for the 4th week 4.08 and 8.76, respectively.

Conclusion: In current study TSH level at the 5th day was 4.16±3.3 and T3 serum level 8.71±3.4. TSH in 2nd week measuring was 4.47±2.5 and T4 was 5.12±2.9. At the 4th week the TSH level was 4.08±1.9 and T4 was 8.76±2.8. TSH level was independent from gestational age, but T4 serum level had direct association with gestational age. There was no relationship between thyroid hormones' level with birth weight, thyroid disorders history in infants' family, and consuming thyroid medications during pregnancy.

Keywords: Thyroid hormone, TSH, T3, T4, Gestational age, Prematurity, Akbarabady hospital, Aliasghar hospital

Introduction

Thyroid problems are always associated with prematurity disorders. Undeveloped hypothalamus- hypophysis-thyroid axis, depleted thyroid hormones after birth, non-thyroid diseases and drugs such as dopamine and steroids may cause thyroid dysfunction in preterm or premature infants. Furthermore, iodine deficiency or overdose can cause thyroid dysfunction (1). Despite preventive programs for iodine deficiency treatment, in some regions low iodine insufficiency is prevalent (2).

Thyroid hormones have an effect on development and distinguishing body organs especially central nervous system (CNS) and influence metabolism of carbohydrates, lipids, and vitamins (3). These hormones also play role in regulating neuropsychological functions in children and adults. Thyroid hormones have role in neural development, neurogenesis, myelination, dendritic growth and synapse formation. Besides, they play pivotal role in regulation of metabolism, reproduction system function, cardiovascular system and lung development (4).

Thyroid gland's production of thyroid hormones occurs during the third trimester of pregnancy, thus premature infants more probably suffer from hypothyroidism. Moreover, non-thyroid diseases can change metabolism and cause thyroid hormones disorder (5). Fetal serum T4 gradually

increases during mid-pregnancy period and while reaches to 11.5 µg/dl, and up to delivery time thyroid simulating-hormone (TSH) serum gradually increases to 10 mu/l (6). Thyroid function in premature newborns decreases quantitatively so that serum thyroxine (T4) level is lower than that of term infants but TSH and triiodothyronine (T3) is normal or lower than normal and free thyroxine (fT4) level is also low (7). Therefore, preterm infants often experience low T4 level during the first week of life and afterwards T4 level gradually increases up to six weeks of age which equals to that of term infants (7). This transient hypothyroxinemia is because of immature hypothalamus-hypophysis-thyroid axis and nonparticipation of maternal thyroid hormones (7).

Congenital hypothyroidism is one of the most important preventable maternal endocrine disorders which may cause main mental disability in future. Blood-TSH (b-TSH) evaluation for screening of thyroid disorders has been under consideration during current decades, though that screening has undergone some changes for racial and iodine resource differences in various people. Other permissive factors for changes in screening programs are increasing birth rate of preterm infants and 20% increase of survived infants with very low birth weight (VLBW) during recent 20 years (8).

Thyroid function disorder in VLBW infants, who are defined as those with birth weight of 1000-1499gr, is identified with sudden and delayed rise of TSH in time of delivery, low level of circulating T3 and T4 and fT4, and low serum-TSH (s-TSH) level (9).

In preterm infants (less than 37 weeks) coincident prevalence of atypical and primary congenital hypothyroidism is higher. Furthermore, congenital hypothyroidism in LBW infants (birthweight 1500-2499gr) and VLBW infants is more prevalent (10).

Transient rise of TSH in premature infants is seen frequently. Some studies assumed prematurity as an independent risk factor for hypothyroidism (11). Some other studies reported transient hypothyroidism more prevalent in preterm than term infants, while other studies reported the same prevalence rate for both groups (12).

Transient hypothyroxinemia is also a prevalent disorder among preterm infants which is identified with temporary low serum T4 and fT4 levels a normal TSH level is present. This disorder affects a wider range of infants with less than 30 weeks age and not only accompanies with neural side effects such as decrease of IQ but also can increase cerebral palsy (CP) risk (13).

Undeveloped hypothalamus-hypophysis-thyroid axis, immature production of thyroid hormones, immature hormones metabolism, and systemic diseases are among the most important factors affecting thyroid function in preterm infants (14).

Due to the high rate of premature infants with thyroid hormones disorders in Iran and giving a more precise thyroid function in these infants, we designed this study to determine mean thyroid hormones level in 5th day, 2nd and 4th weeks in premature infants hospitalized in NICUs of Aliasghar and Akbarabady hospitals in Tehran, Iran.

Methods

In this descriptive-cross sectional study we investigated all records of infants referred to NICUs of Akbarabady and Aliasghar hospitals since May 2012. Written consent was obtained from the patients' proxies. All patients gave a full history including gestational age, current age, sex, birth weight, kind of delivery, underlying diseases, pregnancy problems and reasons for hospitalization. Patients whose proxies were unsatisfactory to participate in this study were excluded. Also, patients whose mothers had active and uncontrolled thyroid diseases were excluded due to possibility of passing placental hormones between maternal blood and fetus. On the 5th day, 1 cc blood sample was taken and the procedure repeated on 2nd and 4th weeks. TSH and T4 levels were measured and mean level of hormones calculated in three steps.

Inclusion criteria were prematurity, and hospitalization in NICU. Exclusion criteria were proxies dissatisfactory to participate, maternal history of active and uncontrolled thyroid diseases, and major anomalies. In the performed analysis, p=0.05 was considered significant.

Results

Data for 140 infants (male=80 (57%)) were collected. Sonography-based gestational mean age was 31.91 weeks. Based on the sonography data, most people's gestational age (85%) has been between 29-34 weeks. Hypothyroidism was seen in only 5% of infants' families. About 95% (n=133) of mothers received no medications during pregnancy.

Only 2% (n=3) of infants had no diseases while birth and 98% (n=122) suffered from infant respiratory distress syndrome (IRDS).

A comparison among means of 3 times measuring TSH revealed a significant relationship (p=0.019). The relation between birth weight and TSH level was not significant (p=0.98).

The relationships between family history of thy-

Table 1. TSH and T4 levels were measured on the 5th day, 2nd and 4th weeks

Hormone		5th day after birth	2nd week after birth	4th week afterbirth
TSH	Mean	4.16	4.47	4.08
	SD	3.34	2.5	1.94
	95% confidence interval	3.61-4.72	4.05-4.89	3.76-4.41
T4	Mean	8.71	8.12	8.76
	SD	3.47	2.9	2.84
	95% confidence interval	8.13-9.29	7.63-8.6	9.24-8.29

roid diseases and means for TSH (p=0.071) and T4 (p=0628) were not significant.

Conclusion

In current TSH and T4 levels in 140 premature infants hospitalized in NICU were measured of whom 57% (n=80) were male and the rest were female. Mean gestational age was 31.91 weeks and most infants were born during 29-31 weeks. About 47% were low birth weight.

Based on the Chan et al (15) study fT4 level in VLBW infants has been 16.8±3.2 µmol/L and TSH 4.56±2.5 µmol/L. FT4 level had reverse relationship with gestational age as to the fT4 level decreased with increase of gestational age. TSH level had a very weak relationship with gestational age.

In our study, TSH level in 5th day was 4.16±3.3 µmol/L and serum T4 8.71±3.4 µmol/L. Second time (2nd week) TSH and T4 levels were 4.47±2.5 and 8.12±2.9 µmol/L, respectively. The last time (4th week) measuring yielded 4.08±1.9 and 8.76±2.8 µmol/L for TSH and T4 levels, respectively. Therefore, TSH level shows an increase in week 2 but in week 4 it decreases and reaches to 5th day level. However, T4 level is at the minimum in the 2nd week but again increases in week 4 to reach to the level 5th day after birth. Thus, it could be concluded that the TSH and T4 levels after 4 weeks after birth are similar to the 5th day levels, though they had some changes intermittently.

There was no significant relationship between serum TSH level and gestational age. However, decreasing gestational age was associated with increasing T4 levels for all three times measuring. Therefore, we can assume TSH level independent of gestational age but T4 has a direct relationship with gestational age.

In Sun et al study (16), TSH level was associated with birth weight but uncorrelated with weight of premature infants. Also, TSH levels were independent of sex.

In present study not only birth weight had no statistical relationship with TSH level, but also was independent of serum level. Similar to Sun et al study, we found no relationship between infants' sex and levels of thyroid hormones.

History of thyroid problems was seen in only in 5% of studied infants' mother or families. Nonetheless, we found no relationship between history of thyroid hormones problems in infants' families with hormones' levels. These two variables were independent.

In addition, only 2% (n=3) of mothers had consumed Levothyroxine during pregnancy which was found to be independent of TSH and T4 levels.

Conflicts of interest: None declared.

References

1. Joseph R. Mass newborn screening in Singapore—position and projections. Ann Acad Med Singapore. 2003. 32:318–323.
2. Woo HC, Lizarda A, Tucker R, Mitchell ML, Vohr B, Oh W, Phornphutkul C. Congenital hypothyroidism with a delayed thyroid-stimulating hormone elevation in very premature infants: incidence and growth and developmental outcomes. J Pediatr. 2011. 158:538–542.
3. Larson C, Hermos R, Delaney A, Daley D, Mitchell M. Risk factors associated with delayed thyrotropin elevations in congenital hypothyroidism. J Pediatr. 2003. 143: 587–591.
4. Clark SJ, Deming DD, Emery JR, Adams LM, Carlton EI, Nelson JC. Reference ranges for thyroid function tests in premature infants beyond the first week of life. J Perinatology. 2001. 21:531–536.
5. Carrascosa A, Ruiz-Cuevas P, Potau N, Almar J, Salcedo S, Clemente M, Yeste D. Thyroid function in seventy-five healthy preterm infants thirty to thirty-five weeks of gestational age: a prospective and longitudinal study during the first year of life. Thyroid. 2004. 14:435–442.
6. Kok JH, Hart G, Endert E, Koppe JG, De Vijlder JJM. Normal ranges of T4 screening values in low birth weight infants. Arch Dis Child. 1983. 58:190–194.

7. Dilli D, Oguz SS, Andiran N, Dilmen U, Buyukkagnici U. Serum thyroid hormone levels in preterm infants born before 33 weeks of gestation and association of transient hypothyroxinemia with postnatal characteristics. J Ped Endocrinol Metab. 2010. 23:899–912.
8. Adams LM, Emery JR, Clark SJ, Carlton EI, Nelson JC. Reference ranges for newer thyroid function tests in premature infants. J Pediatr. 1995. 126:122–127.
9. Reuss ML, Leviton A, Paneth N, Susser M. Thyroxine values from newborn screening of 919 infants born before 29 weeks' gestation. Am J Pub Health. 1997. 87:1693–1697.
10. Williams FLR, Mires GJ, Barnett C, Ogston SA, van-Toor H, Visser TJ, Hume R, with collaboration from the Scottish Preterm Thyroid Group. Transient hypothyroxinemia in preterm infants: the role of cord sera thyroid hormone levels adjusted for prenatal and intrapartum factors. J Clin Endocrinol Metab. 2005. 90:4599–4606.
11. Biswas S, Buffery J, Enoch H, Bland JM, Walters D, Markiewicz M. A longitudinal assessment of thyroid hormone concentrations in preterm infants younger than 30 weeks' gestation during the first 2 weeks of life and their relationship to outcome. Pediatr.2002; 109:222–227.
12. Williams FLR, Simpson J, Delahunty C, Ogston SA, Bongers-Schokking JJ, Murphy N, vanToor H, Wu SY, Visser TJ, Hume R, with collaboration from the Scottish Preterm Thyroid Group. Developmental trends in cord and postpartum serum thyroid hormones in preterm infants. J Clin Endocrinol Metab.2004; 89:5314–5320.
13. Van Wassenaer AG, Kok JH, Dekker FW, De Vijlder JJM. Thyroid function in very preterm infants: influences of gestational age and disease. Pediatric Research.1997;42:604–609.
14. Fisher DA. Thyroid system immaturities in very low birth weight premature infants. Semin Perinatol.2008;32(6):387–97.
15. Chan DK, Tagamolila V, Ardhanari J, Lim XY, Wong J, Yeo CP. Reference Range of thyroid hormones in very low birth weight infants at the time of discharge, Thyroid. 2014 Jan 1;24(1):73-7.
16. Sun X, Lemyre B, Nan X, Harrold J, Perkins SL, Lawrence SE, Barrowman N. Free thyroxine and thyroid-stimulating hormone reference intervals in very low birth weight infants at 3–6weeks of life with the Beckman Coulter Unicel DxI 800. Clin Biochem. 2014 Jan 31;47(1):16-8.