

Original Research Article

Effect of perinatal asphyxia on thyroid stimulating hormone and thyroid hormone levels in a rural tertiary care center in Mandya district of Karnataka, India

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ABSTRACT

Background: Studies have shown a difference between serum concentrations of TSH, T4, T3 and FT4 in asphyxiated newborns than in normal newborns which suggesting abnormal thyroid function in asphyxia. We planned this study to assess and compare the effect of perinatal asphyxia on thyroid stimulating hormone and thyroid hormone levels.

Methods: This was a tertiary care teaching hospital based, prospective case control study conducted on normal full term and full term asphyxiated neonates delivered and admitted in the neonatal intensive care unit at Adichunchanagiri Institute of Medical Sciences, B. G. Nagara, Karnataka, India from December 2012 to May 2014.

Results: The means for thyroid hormones, in cord blood, were similar in both groups, except rT3 are higher for non-asphyxiated new born as compared to asphyxiate ones. In newborns with 18-24 hours of life, lower levels of T4, T3, FT4, and TSH were observed in asphyxiated newborns, in which the basal levels (in cord blood) with exception of FT4, failed to increase.

Conclusions: Our study suggests that lower T4, free T4, and T3 levels are secondary to lower TSH levels in asphyxiated newborns; also, peripheral metabolism of T4 in asphyxiated infants can be altered due to low T3 and normal reverse T3 levels.

Keywords: Asphyxia, TSH, Thyroid hormone levels

INTRODUCTION

The thyroid hormones, thyroxine (T4) and triiodothyronine (T3), are tyrosine-based hormones produced by the thyroid gland. An important component in the synthesis is iodine. The thyronines act on the body to increase the basal metabolic rate, affect protein synthesis and increase the body's sensitivity to catecholamines (such as adrenaline) by permissiveness. The thyroid hormones are essential to proper development and differentiation of all cells of the human body. These hormones also regulate protein, fat, and carbohydrate metabolism, affecting how human cells use

energetic compounds. Numerous physiological and pathological stimuli influence thyroid hormone synthesis.¹

The thyroid hormone, thyroxine binding globulin and thyroid stimulating hormone concentrations in term and preterm infants at birth, over the neonatal period, and during early infancy is in a state of flux during the perinatal period.^{2,3}

However, very little data available which attempt to evaluate the possible effect of perinatal asphyxia on neonatal thyroid function.^{4,5}

The cord serum rT3 concentration was not influenced by maturity, birth-weight, or neonatal risk factors, whereas these factors did affect the concentrations of T3, T4, and TBG. There is no arteriovenous rT3 concentration difference across the placenta; therefore the cord rT3 reflects the systemic rT3 concentration in the baby at birth. As rT3 in the neonate largely, if not entirely, derives from thyroxine from the fetal thyroid, measurement of the cord rT3 concentration may be a good immediate screening test for neonatal hypothyroidism.⁵

Few studies have shown a difference between serum concentrations of TSH, T4, T3 and FT4 in asphyxiated newborns compared to normal newborn which suggests central hypothyroidism secondary to asphyxia. Moreover, asphyxiated newborns with moderate/severe hypoxic-ischemic encephalopathy present a greater involvement of the thyroid function and consequently a greater risk of death.⁶

We have planned this prospective institutional study of serum concentrations of thyroid hormones - T4, T3, free T4 (FT4) and reverse T3 (rT3) and thyroid-stimulating hormone (TSH) found in the umbilical cord blood of term newborns.

Objective of this study was the serum concentrations of thyroid hormones - T4, T3, free T4 (FT4) and reverse T3 (rT3) and thyroid-stimulating hormone (TSH) found in the umbilical cord blood of term newborns with and without asphyxia and those found in their arterial blood collected between 18 and 24 hours after birth.

METHODS

Place of this study was Adichunchanagiri institute of medical sciences, B. G. Nagar, Karnataka, India. And the duration of this study was December 2012 to May 2014. Prospective case control study was designed. And sample size was 50 neonates samples.

The sample size was estimated on the basis of a single proportion design. We assumed the confidence interval of 95% and confidence level of 14.5%. The sample size actually obtained for this study was 50 neonates.

Data collection

The study was a prospective case control study conducted on normal full term and full term asphyxiated neonates admitted in the Neonatal Intensive Care Unit. A total of 50 neonates on (n=25) normal full term and (n=25) full term asphyxiated neonates who were treated for the diagnosis of perinatal asphyxia were enrolled for the study.

Study tools

- Pre designed pretested proforma for data collection

- T4, T3, FT4, and TSH were measured by radioimmunoassay (Accu Bind VAST ELISA Kits, Monobind Inc., Ca., USA)
- rT3 was dosed with reverse T3 kit, also by the radioimmunoassay method (ELISA Kit, CEC022 Ge, Monobind Inc., Ca., USA)
- The values of FT4 and T3 were expressed in ng/dl, TSH in mU/ml, those of total T4 in mg/dl, and those of rT3, in ng/ml.

Study population consisted of full-term asphyxiated newborns with 1 and 5 minute Apgar scores < 7 were included in asphyxiated newborns and infants with Apgar score of 7 and above were included as non-asphyxiated group.

RESULTS

A total of 50 newborns were included and analyzed in our study. The mean gestational age of the infants was 39.32±1.115 months with average birth weight was 3002.0±1963.9 and in our study 54% of the newborns were females. In our study 40 (80%) were born to primipara and 10 (20%) to multipara.

Table 1: Demographic data of the newborns.

Demographic data		N = 50
Gestational age (weeks)		39.32±1.115
Birth weight (grams)		3002.0±1963.9
Sex	Male	23 (46.0%)
	Female	27 (54.0%)

Table 2: Distribution of APGAR score among all neonates.

APGAR score	Median (minimum-maximum)
At 1 minute	6 (1 -10)
At 5 minute	7.5 (1 -10)

APGAR score distribution of newborns at 1 min and at 5 min was 6 and 7.5 respectively. Among all neonates delivery methods of new born were 33 (66.0%) unassisted, 7 (14.0%) forceps, 6 (12.0%) emergency caesarean and 4 (8.0%) elective caesarean respectively.

The mean values in respect to umbilical cord blood and blood of newborns of T4 was 10.80±2.204 and 12.26±3.089 mg/dl respectively, T3 was 65.66±18.947 and 102.70±62.612 ng/dl respectively, FT4 was 1.36±0.273 and 2.344±0.5365 ng/dl respectively, rT3 was 1.728±0.5151 and 2.344±0.5365 ng/dl respectively and TSH was 12.16±3.316 and 11.98±3.473 mU/ml respectively for all newborn babies.

The plasma concentration of thyroid hormones namely T4, T3, FT4, rT3 and TSH in the umbilical cord blood in respect of Asphyxiated and non-Asphyxiated new born were compared. P values in respect of each of these

indices are also mentioned against each. Ongoing through the table we observe that while p values in respect of rT3

and TSH are significant (p<0.05) the same are non-significant in respect of T4, T3 and FT4 (p>0.05).

Table 3: Distribution T4, T3, FT4, rT3 and TSH of umbilical cord blood and blood of newborns.

	No of newborn	Umbilical cord blood		Blood of newborns	
		Mean±SD	Range	Mean±SD	Range
T4 (mg/dl)	50	10.80±2.204	(7 -15)	12.26±3.089	(7 - 19)
T3 (ng/dl)	50	65.66±18.947	(41 -110)	102.70±62.612	(35 - 173)
FT4 (ng/dl)	50	1.36±0.273	(1 - 2)	2.344±0.5365	(1.4 - 3.1)
rT3 (ng/ml)	50	1.728±0.5151	(0.5 - 3.1)	1.422±0.2427	(0.8 - 1.8)
TSH (m U/ml)	50	12.16±3.316	(5 -19)	11.98±3.473	(5 - 19)

Table 4: Plasma concentration of thyroid hormones in umbilical cord blood of asphyxiated and non-asphyxiated neonates.

Umbilical cord blood	Group		P value
	Asphyxiated	Non-asphyxiated	
T4 (m g/dl)	11.12±2.088	10.48±2.312	0.309
T3 (ng/dl)	68.96±21.868	62.36±15.234	0.222
FT4 (ng/dl)	1.37±0.273	1.36±0.279	0.878
rT3 (ng/ml)	2.016±0.3671	1.440±0.4839	0.000
TSH (m U/ml)	14.12±2.804	10.20±2.566	0.000

Table 5: Distribution of plasma concentration of thyroid hormones in asphyxiated and non-asphyxiated newborns with 18-24 hours of life.

Newborns	Group		P value
	Asphyxiated	Non-asphyxiated	
T4(m g/dl)	9.76±1.480	14.76±2.067	0.000
T3(ng/dl)	40.88±4.146	164.52±4.976	0.000
FT4(ng/dl)	1.856±0.2274	2.832±0.1994	0.000
rT3(ng/ml)	1.528±0.1671	1.316±0.2625	0.001
TSH(m U/ml)	9.32±2.155	14.64±2.289	0.000

Table 6: Distribution of thyroid hormones levels in asphyxiated newborns with 18-24 hours of life.

Asphyxiated	No	Mean±SD	P value
T4 (m g/dl)	Stage 1	10	9.40±0.843
	stage 2	14	10.21±1.626
	Stage 3	1	7.00±0.0
T3 (ng/dl)	Stage 1	10	41.60±4.600
	stage 2	14	40.00±3.721
	Stage 3	1	46.00±0.0
FT4 (ng/dl)	Stage 1	10	1.760±0.2271
	stage 2	14	1.914±0.2179
	Stage 3	1	2.000±0.0
rT3 (ng/ml)	Stage 1	10	1.430±0.1889
	stage 2	14	1.600±0.1177
	Stage 3	1	1.500±0.0
TSH (m U/ml)	Stage 1	10	9.90±2.514
	stage 2	14	8.93±1.940
	Stage 3	1	9.00±0.0

Among both the groups the plasma concentration of thyroid hormones in asphyxiated and non-asphyxiated newborns within 18-24 hours of life were recorded. We observed that the concentrations in respect of all the thyroid hormones except for rT3 are higher for non-asphyxiated new born as compared to asphyxiated ones. P values are significant in respect of all the hormones as indicated in the Table 5.

The thyroid hormones like T4 (mg/dl), T3 (ng/dl), FT4 (ng/dl), rT3 (ng/ml) and TSH (m U/ml) in cases of new born after 18-24 hours of life were studied. It has given a comparative value in respect of hypoxic ischemic encephalopathy for asphyxiated new born. Ongoing through the Table 6 we find that P value in respect of rT3 (ng/ml) are statistically significant whereas values are non-significant in respect of T4 (m g/dl), T3 (ng/dl), FT4 (ng/dl) and TSH (m U/ml) ($p>0.05$).

DISCUSSION

The effect of hypoxia on thyroid hormones has been long recognized. In animals, hypoxia reduces thyroid function and extra thyroidal metabolism of T4. Similarly, Moshang et al found an increase in the levels of rT3 in patients with acute hypoxemia, suggesting a reduction in its degradation.⁷ In the same study, patients with chronic hypoxemia showed decreased levels of T3, and increased rT3 levels, revealing alterations in extra-thyroidal metabolism. The action of these hormones on the synthesis of mitochondrial enzymes and structural elements is extremely important, in addition to participating in thermogenesis, water and electrolyte transportation, and in the growth and development of the central nervous system and skeleton. Low levels of thyroid hormones in non-thyroidal illnesses are associated with poor prognosis

Table 7: Sample size, objective and outcomes.

Author	Year	Design	Sample size	Objective	Outcome
Pereira DN et al ⁸	2001	A case-control study	34	Effect of perinatal asphyxia on thyroid hormones	Lower T4, free T4, and T3 levels are secondary to lower TSH levels in asphyxiated newborns
Borges M et al ⁹	1985	Prospective case control study	21	To study the effect of asphyxia on free thyroid hormone levels in full term newborns	A rapid increase in thyroid-stimulating hormone values by 5 min after delivery (to a mean±SD of 18.6±3, 20±3.5, and 17.7±5 uU/ml in groups 1, 2, and 3, respectively), followed by a progressive thyroid-stimulating hormone decline to levels similar to baseline over the following 48 h, was noted in all three groups of subjects.
Wilson DM et al ¹⁰	1982	Prospective	96	To assess serum free thyroxine values in term, premature, and sick infants	T3, T4, free T4 correlated positively with increasing gestational age and birth weight, and was lower in infants with RDS.

The mean for thyroid hormones, in cord blood, were similar in both groups, except rT3 are higher for non-asphyxiated new born as compared to asphyxiated ones. This is similar to what has been reported by Pereira DN et al and Borges et al.^{8,9} they did not find differences in the concentration of FT4 and FT3 in cord blood, and those presented by Franklin et al which did not find statistical differences in the concentration of T4, T3, rT3, FT4, TBG, and TSH between normal and asphyxiated newborns.¹¹ The increase of rT3 observed in cord blood may indicate an alteration in the peripheral metabolism of thyroid hormones through the inhibition of 5' - deiodinase activity, which is similar to what occurs in acute hypoxia.

On the other hand, in newborns with 18-24 hours of life, lower levels of T4, T3, FT4, and TSH were observed in asphyxiated newborns, in which the basal levels (in cord blood), with exception of FT4, failed to increase. Borges et al.⁸ found that FT4 and FT3 levels failed to increase within the first 48 hours of life in the group of asphyxiated newborns, even though their TSH levels were normal.

The importance of thyroid hormones to the normal development of the brain and intellectual function, and their relation with patient's prognosis requires follow-up studies that correlate hormonal alterations with the occurrence of neurological sequelae. Studies that evaluate

the role of T4 and/or T3 restoration in patients with subnormal hormonal levels should also be considered.

CONCLUSION

Our study suggests that lower T4, free T4, and T3 levels are secondary to lower TSH levels in asphyxiated newborns; also, peripheral metabolism of T4 in asphyxiated infants can be altered due to low T3 and normal reverse T3 levels.

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