

Original Research Article

Effect of Perinatal Asphyxia on Thyroid Stimulating Hormone and Thyroid Hormones

Gurjar Umesh¹, Gupta Palak², Gupta ML³

^{1,2} Post graduate Student, Department of Paediatrics, SMS Medical College, Jaipur, Rajasthan, India

³ Senior Professor & Unit Head, Incharge of Division of Cardiology, Department of Paediatrics, SMS Medical College, Jaipur, Rajasthan, India

*Corresponding author

Dr. Umesh Gurjar

Email: umeshgurjar31@gmail.com

Abstract: Less is known about the effect of perinatal asphyxia on fetal and neonatal thyroid hormone levels despite their importance. Only few studies carried out so far on this subject and even these have conflicting results. Aim of our study was to compare the serum levels of thyroid hormone (FT3&FT4) and TSH in term newborns with perinatal asphyxia and in healthy term newborns at 18 to 24 hr. after birth. And to find the association between severity of hypoxic-ischemic Encephalopathy and altered thyroid hormone (FT3&FT4) and TSH levels. It was a hospital based observational, Analytical, case-control study, 32 Term babies with perinatal asphyxia (as per NNF definition) were taken as cases and 32 healthy term newborns as controls. Thyroid hormones (FT3&FT4) and TSH levels from the blood collected between 18 and 24 hr. after birth were measured by Chemiluminescence immunoassay. The results were analysed using chi square, ANOVA and post HOC test. P value <0.05 was considered significant. Mean value of S.FT3, FT4 & TSH were significantly lower in the asphyxiated group (2.99 + 0.91, 1.47 + 0.39 & 6.61 + 3.40) than control group (5.08 + 1.01, 2.49 + 0.57 & 14.42 + 9.32). Asphyxiated neonates presented with significantly lower mean levels of FT3, FT4 and TSH with the advancing stages of HIE. Serum concentrations of FT3, FT4 & TSH were significantly lower in asphyxiated newborns than in normal newborns. Lower levels of FT3, FT4 & TSH had significant association with advance stages of HIE.

Keywords: Asphyxia, Hypoxic ischemic encephalopathy, hypothyroidism, Serum FT3, Serum FT4, Serum TSH

INTRODUCTION

Perinatal asphyxia is described as lack of oxygen, blood flow and /or gas exchange to the fetus or new born [1]. Neurological dysfunction is usually the most obvious presentation of perinatal asphyxia & its overwhelming nature often distracts our attention from the presence of other organ system dysfunction such as renal, GIT, cardiovascular and endocrine system[2]. Perinatal asphyxia triggers rapid alterations in the concentration of several hormones such as thyroid hormones, catecholamine, glucocorticoids, antidiuretic hormone, aldosterone, renin, atrial natriuretic peptide and insulin [3-6].

Less is known about the effect of perinatal asphyxia on fetal and neonatal thyroid hormone levels despite their importance. Only few studies carried out so far on this subject and even these have conflicting results [7, 8].

The objective of our study was to compare the serum levels of thyroid hormones (FT3&FT4) & TSH in term newborns with perinatal asphyxia and in healthy term newborns, in blood collected between 18 and 24 hr after birth. In additional objective was to see the effect of severity of Hypoxic-Ischemic Encephalopathy on Thyroid hormones (FT3&FT4) & TSH levels.

MATERIAL & METHODS

A hospital based prospective, case-control; observational, analytical study was conducted in the Neonatal units of department of paediatrics, S.M.S. Medical College Jaipur during the period of May 2014 to August 2015. Detailed history was taken, that included antenatal, natal and postnatal history, detailed physical examination was done and clinical course of these newborns was followed. Term babies having gasping, inadequate breathing or no breathing at 1 minute as per NNF definition of birth asphyxia were taken as Cases [9]. Healthy term newborns matched

with cases in terms of birth weight, gestational age, mode of delivery and sex, were taken as control.

The neonate of mothers who had used antihypertensive, corticosteroids, thyroid or antithyroid drugs during pregnancy, Preterm babies of <37 wk of age, neonates with septicemia, metabolic disorders or any congenital malformations and parent of newborn that refuse to give consent were excluded from the study.

Considering a significance level of $\alpha=0.05$ (type I error) and a statistical power of 90% ($\beta=0.10$) to detect a difference of 0.95, in the level of FT4, the sample size required was 30 in each group of cases and controls. We took 32 new-borns in each group.

Permission from ethical committee of the college was taken. Asphyxiated new-borns (Cases) underwent physical examination including their neurological assessment and HIE staging, according to the Levene's modification of Sarnat and Sarnat staging [10]. In all newborns, serum FT3, FT4 and TSH were measured between 18 and 24 hours of life. Blood sampling included 5 ml of blood in a plain vial

collected and processed within 2-3 hours of sampling. Chemiluminiscence immunoassay was used for determination of hormone levels. All samples were tested at central laboratory SMS hospital Jaipur, blinded to the patient's data. FT3 values were expressed in pg/ml; FT4 values were expressed in ng/dl and TSH values were expressed in uIU/ml.

Statistical analysis was performed with the SPSS, version 20 for Windows statistical software package (SPSS inc., Chicago, IL, USA). The Categorical data were presented as numbers (percent) and were compared among groups using Chi square test. Groups were compared for demographic data presented as mean and standard deviation and were compared using students t-test and ANOVA test, Probability P value <0.05 was considered statistically significant.

RESULTS

A total of 64 newborns were included in this study: 32 in the asphyxiated group and 32 in the control group. Patients from both groups were similar in terms of sex, birth weight, gestational age and mode of delivery. (Table 1)

Table 1: Clinical characteristics of the studied population

Characteristics		Asphyxiated group (n=32)	Control group (n=32)	P value
Birth weight		2.83 + 0.43	2.93 + 0.46	0.348 NS
Sex	Male	15(46.88%)	17(53.13%)	0.803 NS
	Female	17(53.13%)	15(46.88%)	
Wt. for Gestational age	AGA	25(78.13%)	28(87.50%)	0.557 NS
	SGA	6(18.75%)	3(9.38%)	
	LGA	1(3.13%)	1(3.13%)	
Mode of Delivery	Vaginal	17(53.13%)	16(50.00%)	1.000 NS
	Cesarean	15(46.88%)	16(50.00%)	

We found that the values of Serum FT3 between 18- 24 hours of life in the cases were low 2.99 ± 0.91 pg/ml as compared to 5.08 ± 1.01 pg/ml in the controls. The value- $5 \pm 9s$ of Serum FT4 in cases were found to be low 1.47 ± 0.39 ng/dl as compared to 2.49 ± 0.57 ng/dl in the controls. The values of Serum

Thyroid Stimulating Hormone (TSH) were also found to be low in cases 6.61 ± 3.40 mIU/ml as compared to 14.42 ± 9.32 mIU/ml in controls. These differences were highly significant ($P < 0.001$) for all hormone levels. (Table 2)

Table 2: Mean S.FT3, FT4 and TSH Levels in Cases and Controls

Serum Levels	Cases (n=32)	Controls (n=32)	P value
FT3(pg/ml)	2.99 ± 0.91	5.08 ± 1.01	<0.001
FT4(ng/dl)	1.47 ± 0.39	2.49 ± 0.57	<0.001
TSH(uIU/ml)	6.61 ± 3.40	14.42 ± 9.32	<0.001

We also observed that among the asphyxiated newborns (cases) those in HIE stage 1(N=6) the mean value for Serum FT3 was 3.4 ± 0.7 pg/ml as compared to 3.19 ± 0.99 pg/ml in HIE stage 2(N=14) and 2.39 ± 0.68 pg/ml in HIE stage 3(N=10), This difference was significant when compared between HIE Stage 1&2 and stage 1&3 but was not significant between stage 2&3.

Similarly mean value of FT4 in HIE stage 1, stage 2 and stage 3 was 1.81 ± 0.1 , 1.47 ± 0.13 and 1.07 ± 0.09 ng/dl respectively, this difference was significant when compared between all the three HIE Stages. The values of serum TSH in babies with HIE stage 1 was 8.82 ± 2.85 microU/ml as compared to 6.7 ± 3.42 microU/ml in HIE stage 2 and 4.51 ± 2.37 microU/ml in HIE stage 3.

This difference was significant only when compared between HIE Stage 1&3 but was not significant between stages 1&2 and 2&3. (Table 3) These results

showed significant effect on Thyroid hormones (FT3, FT4&TSH levels) with advancing HIE stages.

Table 3: Comparison of Mean S.FT3 Level in relation to HIE Stage of Asphyxiated newborns

Thyroid Profile	Stage of HIE			P Value LS		
	Stage 1 (Mean±SD)	Stage 2 (Mean±SD)	Stage 3 (Mean±SD)	1vs2	1vs3	2vs3
S.FT3(pg/ml)	3.4±0.7	3.19±0.99	2.39±0.68	<0.05S	<0.05S	>0.05NS
S.FT4(ng/dl)	1.81±0.14	1.47±0.13	1.07±0.09	<0.05 S	<0.05 S	<0.05 S
TSH(uIu/ml)	8.82±2.85	6.7±3.42	4.51±2.37	>0.05NS	<0.05S	>0.05NS

DISCUSSION

In our study, we assessed thyroid hormone and TSH levels in the blood (between 18 and 24 h after birth) of asphyxiated and Normal term newborns in order to investigate the effect of asphyxia on these hormone concentrations. The paired case-control methodology used in our study reduced the risk of confounding biases by neutralising the influence of several factors e.g. sex, gestational age, weight and mode of delivery on hormone levels.

Mean Thyroid hormone levels were significantly lower in asphyxiated group compared to control group. Our observations are similar to study done by Pereira *et al.*; [11] they had 17 cases of birth asphyxia and 17 controls. The median value of S.T3 between 18-24 hours of life in controls were 164.00 (56.96-222.5) ng/dl as compared to 40.8(37.4-80.4) ng/dl in cases (P= 0.003).The Mean value of S.FT4 level in cases was 1.85± 0.92 ng/dl as compared to 2.8± 0.74 U/L in the control group (P = 0.004). The median value of TSH for the control group was 14.5(12.9-17.85) microU/ml as compared to 9.1(6.34-12.95) micro U/ml in cases group (P = 0.008).

However another study conducted by Borges *et al.*; [8] evaluated the effects of asphyxia on thyroidal indices of term newborns and compared them to those of a control population. Blood was drawn from the cord and then serially at 5 min and 3, 24, and 48 h after delivery in all patients. Seven term healthy newborns (group 1)increased their free thyroxine (FT4) concentrations significantly after delivery from a mean of 0.94 +/- 0.13 ng/dl in cord blood to 2.6 +/- 0.6 ng/dl 48 h after delivery (p value less than 0.001 at 3, 24, and 48 h), FT3 levels increased from a mean level of 2.3 +/- 0.5 pg/ml in cord blood to a mean of 3.7 +/- 0.35 pg/ml 48 h after delivery (p value less than 0.001 at 24 and 48 h). Seven term newborns with transient low Apgar scores at birth (group 2) and seven term neonates born to mothers with toxemia or hypertension (group 3) failed to increase their FT4 and FT3 concentrations above baseline during the first 48 h of life. FT4 and FT3 values at 3, 24, and 48 h were significantly higher in the control group than in groups 2 and 3.

We found that among the asphyxiated group, Mean value of FT3 in HIE stage2 & stage 3 was significantly low than in HIE stage 1 (P <0.05). Mean value of FT4 was significant low when compared between all the 3 stages of HIE (P <0.05) and Mean value of TSH was significant low only in HIE stage 3 when compared to HIE stage 1(P <0.05). These results show significant effect of asphyxia on Thyroid profile (FT3, FT4&TSH levels) with advancing HIE stages.

Our results are similar to Pereira *et al.*; [11] they found that hormone alterations were more frequent in neonates presenting with moderate/severe hypoxic-ischemic encephalopathy. They compare asphyxiated babies with and without moderate/severe encephalopathy with control group, and found that asphyxiated babies with moderate/severe encephalopathy presented a significantly lower FT4 mean (1.44±0.63ng/dl) than those without disease (2.81±0.74ng/dl). However, no statistical difference was found between asphyxiated neonates without moderate/severe encephalopathy (2.31±1.03ng/dl) and controls. Similarly, the mean TSH values observed in asphyxiated babies with moderate/sever encephalopathy (7.70±3.51microU/ml) was significantly lower than those found in controls (14.80±4.13microU/ml).

Hence to conclude the Thyroid hormone levels and TSH were found to be low in asphyxiated babies in comparison to controls and this difference was also found among different stages of HIE.

The pattern of alterations found in the blood of asphyxiated newborns in our study may be due to occurrence of central hypothyroidism which results in low levels of thyroid hormones secondary to reduced production of TSH. However a larger study is needed to confirm our observations and inferences.

ACKNOWLEDGEMENTS-

We are grateful to Dr. Rashmi (PSM Dept.) for his assistance in the statistical analysis and to staff member of Central lab SMS Hospital Jaipur for support providing in the hormonal assay.

Conflict of Interest

None

REFERENCES

1. Anne R, Hanson and Janet and sons; Perinatal Asphyxia and Hypoxic Ischemic Encephalopathy, Lippincott Williams &Wilkins. 2011; 711-728.
2. Rajkumar PS, Bhatt BV, Sridhar MG, Balchander J, Konar BC, Narayanan P, *et al.*; Cardiac Enzymes Levels in Myocardial Dysfunction in Newborns with Perinatal Asphyxia. Indian J Pediatr. 2008; 75:1223-1225.
3. Kaneoka T, Ozono H, Goto U, Shirakawa K; Plasma adrenalin and noradrenalin concentration in fetomaternal blood and umbilical blood biochemical profilings. J Perinat Med. 1979; 7: 302-8.
4. DeVane GW, Porter JC; An apparent stress-induced release of arginine vasopressor by human neonates. J Clin Endocrinol Metab. 1980; 51: 1412.
5. Pereira DN, Procianoy RS; Transient elevation of aldosterone levels in perinatal asphyxia. Acta Pediatr. 1997; 86: 851-3.
6. Cheung CY, Brace RA; Fetal hypoxia elevates plasma atrial natriuretic factor concentration. Am J Obstet Gynecol. 1988; 159:1263-8.
7. Franklin RC, Carpenter LM, O'Grady CM; Neonatal thyroid function: Influence of perinatal factors. Arch Dis Child. 1985; 60:141-4.
8. Borges M, Lanes R, Moret LA, Balochi D, Gonzalez S; Effect of asphyxia on free thyroid hormone levels in full term newborns. Pediatr Res. 1985; 19: 1305-7.
9. NNF publication. National nomenclature and Data collection 1985, New Delhi, India.
10. National Neonatology Forum clinical practice guidelines follow up of high risk newborns 2010.
11. Denise N. Pereira, Renato S; Procianoy, Effect of Perinatal Asphyxia on Thyroid Hormones. J Pediatr (Rio J). 2001; 77(3):175-8.