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EFFECT OF PERINATAL ASPHYXIA ON THYROID HORMONE LEVELS IN TERM NEONATES

Paediatrics

Dr Pawan Kumar. S* Associate Professor, Department Of Pediatrics, Raja Rajeswari Medical College And Hospital Banglore. *Corresponding Author

Dr Ravali Polepaka Junior Resident, Department Of Pediatrics Raja Rajeswari Medical College And Hospital Banglore.

Dr Auti Sharan Kumar Junior Resident, Department Of Pediatrics Raja Rajeswari Medical College And Hospital Banglore.

Dr Adarsh. E Hod And Professor, Department Of Pediatrics, Raja Rajeswari Medical College And Hospital Banglore.

KEYWORDS

INTRODUCTION

Perinatal asphyxia is the one of major public health problem in the world. It is the major cause of morbidity and mortality. It accompanies one of the three most common causes of death along with prematurity and bacterial infections.[1] Asphyxia is a term used to indicate the consequences of complete lack of oxygen as a result of a number of primary causes. Hypoxia refers to decreased arterial concentration of oxygen. Ischemia refers to blood flow to cells or organs that is insufficient to maintain the normal function of the organs. Perinatal asphyxia provokes multiple alterations in the body due to failures in the gas exchange system. Among these alterations we find hypoxia, hypercapnia, and decrease of blood pH. It causes decreased perfusion to the tissues causes diving seal reflex which causes shunting of blood away from lung, kidney, GIT, skin to brain, adrenals and heart.[2] Cellular dysfunction occur as a result of diminished oxidative phosphorylation and ATP production. Impaired oxidative phosphorylation can occur during the primary hypoxic ischemic insults as well as during a secondary energy failure that usually occurs approximately 6 to 24 hours after the initiating insult. Cell death can be either immediate or delayed, and either necrotic or apoptotic. In hypoxic adults and older children effect of hypoxia on thyroid metabolism has been studied.[3-8] Effect of hypoxia on thyroid indices in term new-born have also been evaluated with conflicting results.[8-10] For the development of central nervous system thyroid hormone plays a pivotal role. In non-thyroidal illnesses low level of thyroid hormones are associated with poor prognosis. The present study was conducted to evaluate the effect of perinatal asphyxia on level of thyroid hormones by comparing thyroid profile in cord blood and venous blood at 48-72 hours after birth in new-borns with and without asphyxia.

METHODS

It was a prospective case control study conducted 60 asphyxiated neonates (cases) and 60 full term healthy non-asphyxiated neonates (controls) born at Rajarajeswari medical college and hospital, Bangalore, India from December 2019 to June 2021 after getting approval from the Institutional ethical committee. Cases selected were full-term asphyxiated newborns with APGAR of less than or equal to 5 at 5 minutes or Umbilical vein blood pH <7.1 and base deficit -12 or requiring ventilation more than 10 minutes. Controls were full-term newborn with 1 and 5-minute Apgar scores greater than or equal to 8 and Umbilical vein blood pH greater than or equal to 7.2, who had similar birth weight, gestational age, type of delivery, colour and sex. Cases and controls were matched in terms of gestational age, type of delivery, ethnic group, birth weight and sex. New-borns with any congenital malformation or diseases or born to a mother with abnormal thyroid profile or if mother taking any drugs like antihypertensive, diuretics, corticosteroids and anti-thyroid drugs or parents not giving consent were excluded from the study.

Gestational Age Assessment:

The New Ballard Score (NBS)[30] was used to estimate gestational age (GA) in all the cases and control newborn within 48hours of birth. The assessment was done by a single non blinded observer for all the cases and control. APGAR score was recorded at 1 and 5 minutes after the birth. Diagnosis of asphyxia and its severity grading would be done on the basis of Sarnat and Sarnat staging.

Immediately after birth, umbilical cord was clamped in two different points, and a blood sample was collected for blood gas analysis and determination of TSH. All the asphyxiated newborns were admitted to an intensive care unit. The controls were healthy newborns, who received assistance in the same neonatal care and who were fed on demand. 48-72 hours after birth, a blood sample was collected for venous blood andlevels of thyroid hormones of each newborn in both groups were determined. Severity of hypoxic ischemic encephalopathy assessed by Sarnat and Sarnat Staging and asphyxiated baby were graded as HIE I, HIE II and HIE III. FreeT4, and TSH were measured by radioimmunoassay method. The values of free T4 were expressed in ng/dl, TSH in mIU/dl.

All the new-borns with birth asphyxia were admitted in neonatal intensive care unit under strict observation for vitals, urine output and kept nil by mouth. Hydration was maintained and given intravenous fluid. All healthy term new-born were given to mother and received feeding on demand. Both the groups were kept under observation till discharge or death.

RESULTS

The demographic profiles of the babies in both groups were comparable with regards to gestational age, birth weight, and sex. There were no differences between the groups concerning gestational age (38.83±2.0; 38.03±1.9 weeks: asphyxiated and non-asphyxiated, respectively), birth weight (3,008.0 ± 1100.0; 2,996.0± 1059.2 grams: asphyxiated and non-asphyxiated, respectively), sex (19/11and 17/13: M/F in both groups respectively). The p value was not significant (P>0.05).

There was no significant difference between asphyxiated and non-asphyxiated babies in terms of mother age, mother's thyroid status, mode of delivery, parity of mother, sex of baby, and birth weight of babies (Table 1). All the babies (in both the groups) were term babies with no significant difference in gestational age.

The group of asphyxiated newborns presented significantly lower 1- and 5-minute Apgar scores. This shows the highly significant correlation of Apgar score at 1 and 5 minute. (p<.001) (figure 1)

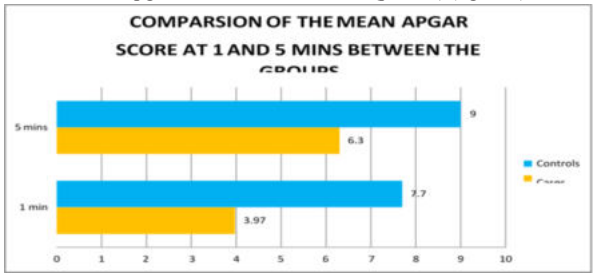

Figure 1: Distribution Of APGAR Score Among Cases And Controls

Table 1: Distribution Of Cases And Controls In Cases And Controls

Demographic data	Group		P value
	Cases	Controls	
Gestational age(weeks)	38.83±2.0	38.03±1.9	0.12
Birth weight(grams)	3008.0±1100.0	2996.0±1059.2	0.832
Sex(Male: Female)	(19:11)	(17:13)	0.59

The plasma concentration of thyroid hormones namely TSH in the umbilical cord blood in respect of Asphyxiated and non-Asphyxiated new born were compared. The cord TSH was higher in asphyxiated newborns, with significant p value (<0.05). (table 2)

Table 2: Plasma Concentration Of Thyroid Hormones In Umbilical Cord Blood Of Cases And Controls

Umbilical cord blood	Group		P value
	Cases (Asphyxiated)	Controls (Non-asphyxiated)	
TSH	19.87±7.22	7.89±3.61	0.001

Among the cases and controls the plasma concentration of thyroid hormones

in asphyxiated and non-asphyxiated newborns within 48-72 hours of life were

recorded. We observed that the concentration in respect of all the thyroid hormones free T4 and TSH are higher for Non-asphyxiated new born as compared to asphyxiated ones. P values are significant (p<0.05) (table 3)

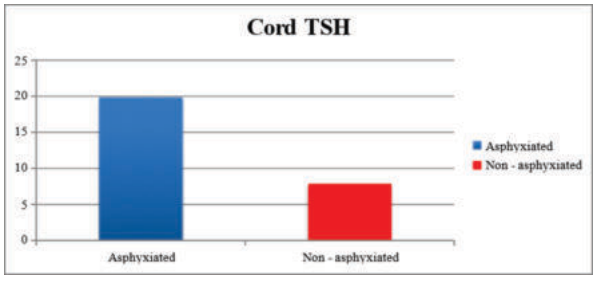

Figure 2: Distribution of plasma concentration of TSH in umbilical cord blood among cases and controlsTable 3: Distribution of plasma concentration of thyroid hormones in cases and controls with 48-72 hours of life

Table 3: Distribution Of Plasma Concentration Of Thyroid Hormones In Cases And Controls With 48-72 Hours Of Life

Blood of newborns	Group		P value
	Cases (Asphyxiated)	Controls (Non-Asphyxiated)	
FT4(m g/dl)	2.08±0.54	2.47±0.41	0.000
TSH(m U/ml)	7.30±2.95	9.19±3.24	0.000

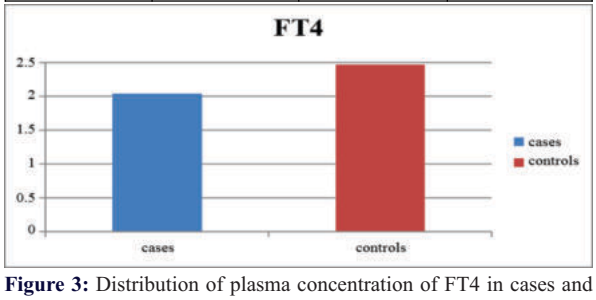

Figure 3: Distribution of plasma concentration of FT4 in cases and controls at 48-72 hours of life

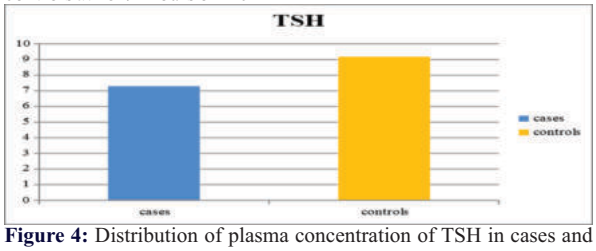

Figure 4: Distribution of plasma concentration of TSH in cases and controls at 48-72 hours of life

Table 4: Distribution Of Hypoxic Ischemic Encephalopathy (HIE) Stage In Cases Group

Parameters	HIE Stages	N	Mean±SD	P value
Ft4	HIE stage 1	12	1.996±0.578	0.607
	HIE stage 2	17	2.195±0.501	
	HIE stage 3	1	2.000±0.0	
TSH	HIE stage 1	12	6.498±2.712	0.112
	HIE stage 2	17	8.412±2.602	
	HIE stage 3	1	4.820±0.0	

Among all, 30 neonates were normal in control group but among the 30 neonates in the case group, 12 (40%) had mild HIE, 17(56.7%) had moderate HIE and 1(3.3%) had severe HIE during the course in NICU. (table 4)

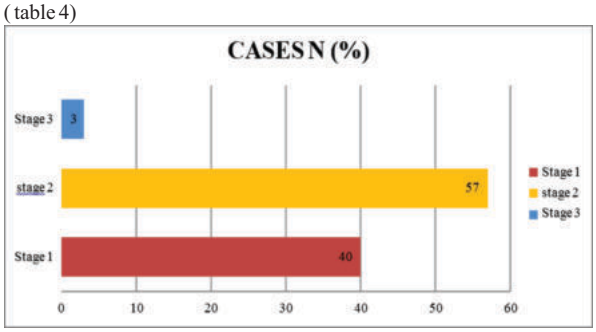

Figure 5: Distribution of Hypoxic ischemic encephalopathy (HIE) Stages in cases group

DISCUSSION

Several studies evaluated the effect of hypoxia in alteration of thyroid function with conflicting results. It may be due to methodological differences among the studies. Several factors studied to influence the thyroid function. Various perinatal factors such as gestational age, weight, sex, mode of delivery, Eclampsia, APH, Birth Asphyxia, PROM, HIV status, maternal age and thyroid status etc. have been studied for influence on cord blood T3, T4 and TSH. [11-15]

Moshang et al compared alteration of thyroid function in acute versus chronic hypoxia in children around 2-16 years and found elevated serum rT3 and decreased serum T3 concentrations (indicating extra thyroid metabolism).[7]

Warner S et al, they observed that hypoxia leads to activation of deiodinase type 3 in turn inactivates the peripheral conversion of T4 to T3.[16]

Borges et al reported that in spite of the maximal TSH surge, in asphyxiated new-borns serum fT3 and fT4 levels failed to increase and concluded that the alterations in the thyroid function observed in asphyxiated new-borns may be caused by the low consumption of oxygen with low metabolic rate, suggesting that asphyxia plays an important role in thyroid metabolism.[17]

Tahivoric HF et al studied the serum concentration of thyroid hormone levels (T4, fT4 , rT3 , T3, TSH and TBG) in cord blood at birth and serum on 5th day of life he concluded that neither hypoxia nor the method of delivery had any influence on the peripheral metabolism of thyroid hormones.[18]

Joshi et al also studied influence of perinatal factors on thyroid profile.[19] They collected umbilical cord blood sample for assessment of TSH and T4 in 830 new-borns.

They found that birth asphyxia had significant influence on cord blood TSH as compared to normal new-born.Durga et al measured cord blood TSH in 100 live newborn infants.[20] They observed that requirement of resuscitation in initial steps and low APGAR scores at 1 minute result in significantly raised cord blood TSH (P<0.05).

To substantiate our findings, studies with larger sample size and multiple numbers of blood samples at different duration after birth are needed to establish whether these effects are transient or permanent. Further studies to supplement thyroid hormone may be considered since it's a curable cause via thyroid replacement.

CONCLUSION

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

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