Original Paper

TRANSIENT HYPOTHYROXINAEMIA IN FULL TERM LOW BIRTH WEIGHT NEONATES

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Abstract

This prospective study was done in Combined Military Hospital, Dhaka from July 2002 to June 2003 to document the postnatal changes of thyroid hormones in full term low birth weight (LBW) neonates. The parameters were- serum TT_4 (total thyroxin), TT_3 (total triiodothyronine), FT_4 (free thyroxin) and TSH (thyroid stimulating hormone). Twenty seven healthy full term neonates formed the control group (group A) who were studied on day 5 to observe the base line data. Study group (group B) consisted of 27 low birth weight (LBW) neonates. They were studied twice on day 5 (B_1) and day 45 (B_2). The mean ± SD gestational age was 38.41±0.93 and 38.63±1.08 weeks in group A and B respectively. The mean ± SD birth weight were 3.41±0.55 and 2.11±0.33 kg in group A and B respectively and the difference was statistically significant (p <0.0001). All neonates of group A had normal serum levels of TT_4, TT_3, FT_4 and TSH on day 5 but in LBW full term neonates though FT_4 level remained within normal range, 48% neonates of group B had significantly decreased levels of TT_4, TT_3 and TSH (p<0.001) but on day 45 all of these hormone levels were significantly increased (p<0.001) and attained normal values. This study showed that 48% LBW neonates had transient hypothyroxinaemia on day 5 which was corrected spontaneously by day 45.

Key word : Hypothyroxinaemia, Low birth weight (LBW).

Introduction

Low birth weight (LBW) neonates are major concern of the health sector in Bangladesh like many other developing countries of the world. In Bangladesh maternal malnutrition, poor hygiene and sanitation, lack of education, social stigmas etc are responsible for high incidence of LBW neonates. LBW neonates have a greater morbidity and mortality due to their functional immaturity of various organs resulting in deranged biochemical, metabolic and endocrine functions[1,2,3].

Neonatal screening for congenital hypothyroidism is important because mental retardation may be avoided if treatment is started early[4]. Thyroid hormone secretion in cord blood are greatly related with gestational age and birth weight[5]. Congenital hypothyroidism is a relatively common disorder in the neonate with an incidence of 1 in 4000 infants in USA[6,7]. In Bangladesh the incidence is higher and is about 5% LBW infants have an incidence of permanent hypothyroidism equal to that in full term infants[8], but they have disproportionately high incidences of transient hypothyroidism[9].

Serum levels of thyroid hormones at different time interval were measured in LBW neonates by different study groups. They found significant differences between cord values and the results at different postnatal ages[4,5,10,11]. Most of the studies reported that the LBW neonates usually have lower serum levels of total thyroxine (TT_4), total triiodothyronine (TT_3) and free thyroxine (FT_4) with higher or normal TSH level in comparison to full term neonates[9,12,13]. On the contrary, Frank et al[9] (1996) observed a normal serum FT_4 in LBW neonates. It has been proposed that hypothyroxinaemia found in LBW neonates does not require replacement therapy as it is transient in nature and is corrected spontaneously within 4-8 weeks after birth[3,5,10,13]. But Frank[9] et al (1996) recommended that infants with transient hypothyroidism should be treated as soon as the diagnosis is made. It is reported that replacement therapy showed a reduction of morbidity of these neonates[14].

So neonatal screening for transient hypothyroidism has a great role in reduction of sufferings of LBW neonates. The present study was designed to assess the thyroid hormonal changes in full term LBW neonates postnatally in terms of serum TT_4, TT_3, FT_4 and TSH levels.

Materials and Methods

This prospective study was done in Combined Military Hospital (CMH), Dhaka from July 2002 to June 2003. Healthy full term neonates (weight > 2.5 Kg) and low birth weight full term neonates (weight < 2.5 Kg) were included in the study. Fifty four neonates irrespective of sex were selected for the study. They were grouped as

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group A containing 27 apparently healthy full term neonates. Base line data was observed by studying them on day 5. Group B included 27 LBW full term neonates and were selected as study group. They were studied on day 5 (B_1) and on day 45 (B_2). Neonates having birth asphyxia, major congenital anomalies or maternal history of taking antithyroid drugs were excluded from the study. Healthy full term neonates were selected from labour ward of CMH Dhaka delivered by caesarean section, babies of Rh negative mother and babies of twin pregnancy. LBW neonates were selected from admitted patients of neonatal ICU and paediatric OPD of CMH Dhaka.

Serum levels of TT_4, TT_3, FT_4 and TSH were measured by Electrochemiluminescent assay at Armed Forces Institute of Pathology (AFIP), Dhaka. SPSS (Version 10.0) was used to analyze the data. Test of significance were done by unpaired and paired 't' test and 95% confidence level was taken as a level of significance.

Results

The mean ± SD (standard deviation) gestational ages were 38.41±0.93 and 38.63±1.08 weeks in group A and B respectively (table-I).

Table-I: Gestational age of different groups of neonates.

Group	Number	Age in completed weeks Mean±SD	p value
A	27	38.41±0.93 (Range = 7-40)	>0.05
B	27	38.63±1.08 (Range = 37-40)	

Note: Unpaired't' test was done between A &B

Gestational age of group B was almost within the same range to that of group A. The mean ± SD birth weight were 3.41±0.55, 2.11±0.33 in group A and B respectively & the difference is statistically significant (p<0.001).

Table-II: Birth weight in different groups of neonates.

Group	Number	Birth weight (Kg) (mean ± SD)	p value
A	27	3.41 ± 0.5 (2.5-4.2)	<0.001
B	27	2.11 ± 0.33 (0.8-2-4)	

Note: Unpaired't' test was done between A &B

TT_4: The mean ± SD serum TT_4 were 184.6± 10.2 nmol/L, 123.1± 43.6 nmol/L and 160.4± 27.7 nmol/L in group A,B_1 on day 5, in B_2 on day 45 respectively (table-III). Mean TT_4 was significantly(p <0.001) lower in group B_1 compared to that of group A. Mean TT_4 were significantly (p< 0.001) increased in group B_2 than that of B_1. 48% LBW neonates had lower level of TT_4 on day 5 and 100% of them attained normal values by day 45.

Table-III: Serum levels of TT_4 in different groups.

Groups	TT_4 (nmol/L) (mean ± SD)	p value
A	184.6± 10.2	
B_1	123.1 ± 43.6	< 0.001
B_2	160.4 ± 27.7	< 0.001

Note: Unpaired t test was done between A & B_1 & paired 't' test was done between B_1 & B_2. Normal reference value of TT_4;1-2 weeks:126-214nmol/L, 1-2 months:93-189nmol/L, Adult: 59-135nmol/L(Whitley1999)[15]

TT_3: The mean ±SD serum TT_3 were 2.28±0.33 nmol/L, 1.52 ± 0.64 nmol/L and 2.13±0.43 nmol/L in groups A,B_1 and B_2 respectively (table-IV).

Table-IV: Serum levels of TT_3 in different groups.

Groups	TT_3 (nmol/L) (mean ± SD)	p value
A	2.28 ± 0.33	
B_1	1.52 ± 0.64	< 0.001
B_2	2.13± 0.43	< 0.001

Note: Unpaired t test was done between A & B_1 & paired't' test was done between B_1 & B_2. Normal reference value of TT_4: 1-5 days:1.54-11.0 nmol/L, 1-11months:1.62-3.77 nmol/L, Adult: 1.08-3.14nmol/L[15]

The mean TT_3 was significantly (p<0.001) lower in group B_1 than that of group A. TT_3 level increased significantly (p<0.001) in group B_2 compared to B_1. Fourty eight percent LBW neonates had lower TT_3 on day 5 and 100% of them were corrected on day 45 .

FT_4: The mean ± SD serum FT_4 were 19.33±2.77 p mol/L, 18.78±9.23 p mol/L and 20.81±3.17 pmol/L in groups A, B_1 and B_2 respectively (table-V).

Table-V: Serum levels of FT_4 in different groups.

Groups	FT_4 (pmol/L) (mean ± SD)	p value
A	19.33 ± 2.77	
B_1	18.78 ± 9.23	>0.05
B_2	20.81 ± 3.17	>0.05

Note:Unpaired t test was done between A & B_1 & paired't' test was done between B_1 & B_2. Normal reference value of FT_4: 1-3 days:26-63.1pmol/L,1week-1year :12-33pmol/L, Adult: 10.3-34.7pmol/L[16]

Serum FT_4 was lower in B_1 than that of A, but that was not statistically significant (p>0.05). But this lower level of FT_4 in LBW neonates was within normal range. Subsequently FT_4 level increased in group B_2 in comparison to that of B_1 but the difference was not statistically significant (p>0.05).

TSH: The mean ±SD serum TSH were 3.96±0.39 mIU/ml, 2.69±1.14 mIU/ml and 2.41±0.93mIU/ml in groups A, B_1 and B_2 respectively (table-VI). Serum TSH

was significantly ($p<0.001$) lower in group B_1 than that of A. Subsequently TSH levels were decreased significantly ($p<0.001$) in groups B_2 than that of B_1.

Table-VI: Serum levels of TSH in different groups.

Groups	TSH (mIU/L) (mean ± SD)	p value
A	3.96 ± 0.39	
B_1	2.69 ± 1.14	<0.001
B_2	2.41 ± 0.93	<0.001

Note: Unpaired t test was done between A & B_1 & paired't' test was done between B_1 & B_2. Normal reference value of TSH : 1-4days:1.0-39.0mIU/L, 2weeks-20weeks 1.7-9.1 mIU/L, Adult: 0.4-4.2mIU/L[16]

Discussion

This prospective study was done to observe the postnatal changes of thyroid hormones in full term LBW neonates. All parameters were also measured in healthy full term neonates on day 5 to observe the base line data. The mean serum TT_4, TT_3, FT_4 and TSH in healthy full term neonates were within normal range on day 5 and the results matches with the findings of other workers[8,9,17,18]. Mean serum TT_4 levels were significantly lower ($p<0.001$) in full term LBW neonates than that of full term neonates on day 5. The low TT_4 in full term LBW neonates increased to normal by day 45. These results are similar to those of other workers[8,19]. Similarly mean TT_3 in full term LBW neonates were also significantly ($p<0.001$) lower than that of full term neonates on day 5. Parveen et al[8] reported the similar findings. This low TT_3 in full term LBW neonates increased significantly ($p<0.001$) to normal on day 45. Similar results are also reported by Delange et al[19]. The mean serum levels of FT_4 were lower in full term LBW neonates on 5th day of their life in comparison to that of full term neonates, but these were within normal range. Franklin, Purdie and O'Grady[13] also had similar results. These low FT_4 level in full term LBW neonates increased on day 45. But the differences were not statistically significant. Serum levels of TSH in full term LBW neonates and healthy full term neonates were within normal range throughout the study period. Wassenaer et al[20], Hadeed et al [21] and Rapaport R[22] reported similar results.

On day 5, 48% full term LBW neonates had lower levels of TT_4, TT_3 and thereby showed hypo function of thyroid. However, all these full term LBW neonates attained normal values on day 45. The serum TSH levels in all full term LBW and full term neonates were within normal range throughout the study period. Similar results are reported by different workers[3,5]. The exact cause and mechanism involved in this type of transient hypo function of thyroid is poorly understood. The likely causes are immaturity of hypothalamo-pituitary-thyroid axis, maternal iodine deficiency, immaturity of enzymatic mechanisms of hormone synthesis, decreased response of thyroid gland to TSH etc. However, almost all the above mentioned factors might act temporarily resulting in transient hypothyroxinaemia in full term LBW neonates [23-25].

Conclusion

In this study, 48% full term LBW neonates had transient hypothyrxinaemia as revealed on day 5 and all of them attained normal values by day 45. Despite their state of hypothyroxinaemia all the full term LBW neonates had normal TSH level throughout the study period. The exact mechanism of this transient hypothyroxinaemia in full term LBW neonates is poorly understood. The present study indicates that the hypothyroxinaemia in full term LBW neonates may be due to immaturity of the hypothalamo-pituitary-thyroid axis as they all had normal TSH level.

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