Thyroid Function Test in Sick Premature Infants

دراسة وظائف الغدة الدرقية لدى المرضى من الاطفال الخدج حديثي الولادة

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الخلاصة:

الهدف: هرمون الغدة الدرقية مهم لنمو وتطور الدماغ وخاصة لدى الاطفال الخدج وذلك لأنهم معرضون لمضاعفات مستقبلية في تطور الجهاز العصبي .أجريت هذه الدراسة لمعرفة وظائف الغدة الدرقية لدى المرضى من الاطفال الخدج والعوامل المؤثرة عليها.

المنهجية:أجريت دراسة مقطعية على خمسين طفل خديج (مولود قبل ٣٧ أسبوع من العمر الحملي) في مستشفى الزهراء التعليمي للفترة من الأول من آذار ولغاية الأول من تشرين الثاني ٢٠١٢ .تم اختيار العينة بشكل عشوائي. أخذت عينة من الدم في اليوم الثالث من العمر لغرض فحص وظائف الغدة الدرقية . كان جميع المرضى يعانون من مضاعفات الولادة المبكرة مثل عسر التنفس الولادي ،اليرقان ، تسمم الدم الجرثومي ،نقص السكر في الدم ومضاعفات أخرى. تمت دراسة وظائف الغدة الدرقية لدى هذه العينة وتأثير العمر الحملي ومضاعفات الولادة المبكرة عليها . وكذلك تمت دراسة تأثير العوامل المتعلقة بالأم على وظيفة الغدة الدرقية لدى الرضيع مثل داء السكري وارتفاع ضغط الدم وتاريخ العائلة مثل وجود أمراض الغدة الدرقية لدى العائلة وقصور النمو أو الاختلال العقلي .

النتائج: أظهرت الدراسة إن طفل واحد (٢%) لديه نقص في عمل الغدة الدرقية وكان هذا الطفل لديه تاريخ عائلي للتخلف العقلي .وكان (٤%) من الاطفال لديه نقص مؤقت في هرمون الثايروكسين و(٢٠%)من الاطفال لديه ارتفاع معتدل للهرمون المحفز للغدة الدرقية(TSH) أما باقي الاطفال (٧٤%) فكانت نتيجة وظائف الغدة الدرقية طبيعية، وكان جميع الاطفال في الدراسة لديه مضاعفات كتسمم الدم الجرثومي وعسر التنفس الولادي ونقص السكر في الدم واختلاجات عصبية ساهمت في اختلال في عمل الغدة الدرقية .

الاستنتاج: يجب اخذ وظيفة الغدة الدرقية بنظر الاعتبار لدى الاطفال الخدج وذلك لضمان تطور طبيعي وحياة طبيعية في المستقبل.

التوصيات: ننصح بإجراء فحص وظائف الغدة الدرقية لكل الاطفال حديثي الولادة وخاصة الخدج .

Abstract:

Background: Thyroid hormones are essential for brain development. Transient hypothyroxinemia early in life may increase the risk of neurodevelopment disabilities in preterm infant .

Objectives: to study thyroid function among preterm infants & factors that may affect the results .

Methods: This study was done on 50 preterm infants in Al-Zahraa teaching hospital from the period of 1st of March to 1st of November 2012. Thyroid function test was done to those neonates within the first 3 days of life. All the patients complain of complications of prematurity. Factors related to the neonate as gestational age ,birth weight , sex and complications of prematurity were studied in relation with the results of thyroid function test. Also factors related to the mother as diabetes mellitus, hypertension & family history of thyroid disease & mental retardation was taken into consideration.

Results: Thirty seven (74%) of neonates have normal thyroid function test, one neonate (2%) has hypothyroidism, 2 (4%) neonates have transient hypothyroxinemia and 10 (20%) neonates have transient moderate elevation of TSH (10 - 30μU/ml).The preterm with hypothyroidism have family history of mental retardation. and the hypothyroid state could be related to familial cause rather than prematurity. Statistical analysis was done by using SPSS version 17.

Conclusion: Although the study shows no statistical relation between gestational age &complications of prematurity with thyroid function test results, thyroid screening for premature infants especially those with complications should be taken into consideration for better outcome.

Recommendation: we recommend neonatal screening for thyroid function especially for preterm infants.

Key wards: premature infants ,thyroid function test , hypothyroxinemia

INTRODUCTION:

Thyroid hormones are important for stimulation of growth and development of various tissues at critical periods including the central nervous system and skeleton & is known to regulate neurodevelopment, probably from early fetal life onwards [(1).]

Thyroid hormone deficiency can cause long term morbidity in terms of behavior, locomotor ability, cognition and hearing ability, if the onset is early in development [(2)]. Since the introduction of neonatal screening for congenital hypothyroidism in the 1970's it became clear that preterm infants have lower plasma concentrations of (free)T4 and (free)T3 than full term infants of the same postnatal age and this has raised an ongoing discussion on the need for thyroid hormone supplementation in preterm infants in order to improve clinical and neurodevelopmental outcome[(3)].

During fetal life, the thyroid gland develops with production of thyroxin (T4) and triiodothyronine (T3) and secretion into the serum from about 12 weeks gestation, the levels of which increase to term. Approximately one third of maternal T4 crosses the placenta to the fetus. Maternal T4 may play a role in fetal development, especially that of the brain, before the synthesis of fetal thyroid hormones begins. The fetus of a hypothyroid mother may be at risk for neurologic damage, and a hypothyroid fetus may be partially protected by maternal T4 until delivery[(4)].

Postnatal thyroid function in preterm babies is qualitatively similar but quantitatively reduced compared with that of term infants. After preterm birth, TT4 and TT3 levels remain lower than in term born infants during the first weeks[(5)].This period during which total and free T4 (and T3) levels are low is generally referred to as transient hypothyroxinemia of the preterm infant **.Hypothyroxinemia** of the prematurity was defined as total T4 level <60 nmol/ l and TSH level <7 μU/ ml in the initial test.

Hypothyroidism was defined as total T4 level <60 nmol/l in conjunction with TSH level > 10 μU/ ml or as a TSH level > 30 μU / ml in conjunction with any level of total T4.

Transient TSH elevation was defined as normal total T4 level with moderately elevated TSH level (10 – 30) μU/ ml and TSH level will normalized in the follow up test without treatment[(6)].

PATIENTS & METHODS

Across sectional study was done on 50 preterm babies. These cases were collected randomly from the nursery care unit, neonatal care unit, and emergency unit in Al Zahraa teaching hospital in Al Najaf from the period between 1rst of March to 1rst of November 2012.All of them with complications of prematurity like RDS, apnea, jaundice, sepsis, hypoglycemia and convulsion. The selection of cases were limited to those with gestational age ranging from 27 to 36 weeks. Gestational age was obtained by last menstrual period (LMP), U/S & Ballard score. A written informed consent for investigation was filled by the parents of the infants included in the study & the study

was approved by the ethical committee in the hospital.The blood samples were taken from peripheral blood on day 3 postnatal and send to the laboratory were TSH ,T3 and T4 were estimated by using VIDAS TSH,T3 and T4 which is an automated quantitative test for use on the VIDAS family instruments for the determination of TSH,T3 and T4 in human serum or plasma (lithium heparin) using ELFA technique (Enzyme linked Fluorescent assay).TSH level is considered normal if between (0.25 – 5) µU/ml. T3 normal value between (0.92 – 2.33) nmol/l and for T4 was (60 – 120) nmol/l.We analyzed the effect of GA, Sex, birth weight and systemic complications of prematurity on thyroid function. Also we analyzed the effect of maternal factors (as age, parity ,history of diseases in the mother as diabetes mellitus, hypertension &thyroid disease, drug history and family history of thyroid disease.

Statistical analysis: Statistical analysis was done by using SPSS (statistical package for social sciences) version 17.To evaluate the impact of the studied risk factors on the results ANOVA was used. We set p value <0.05 as significant.

Objectives: to study the thyroid function among preterm infants &factors that may affect the results.

RESULTS:

The study was conducted on 50 preterm neonates (i.e. gestation age <37 weeks). Their gestational age ranged from 27-36 weeks.

Table(1) Demographic characteristics of the preterm neonates

Characteristic	Number n=50	%
Gender		
male	33	66
female	17	34
Birth weight(gm)		
1000 – 1499	15	30
1500- 1999	21	42
2000- 2500	14	28
Gestational age (wks)		
27- 28	4	8
20- 30	8	16
31- 32	15	30
33- 34	8	16
35- 36	15	30
Mode of delivery		
Vaginal	18	36
Cesarean section	32	64

Table(2) Results of thyroid function tests among sick premature neonates

Results of TFT	No.	Percentage
Normal	37	74%
Hypothyroxinemia(Low T4, normal TSH)	2	4%
Transient ↑TSH(moderate elevation in TSH with normal T4)	10	20%
Moderate ↑TSH , low T4	0	0%
Hypothyroidism	1	2%
Total	**50**	**100%**

Table 2 shows that 37 neonates (74%) had normal thyroid function test ,13 (26%) neonates had abnormal TFT & only one(2%) of them had Hypothyroidism .

table(3) The effect of gestational age on the results of thyroid function test.

Gestational age (weeks)	Normal TFT (n=37)	Hypothyroxinemia (Low T4, normal TSH) (n=2)	TSH(10-30 µU/ml), normal T4(n=10)	Hypothyroidism TSH >30µU/ml (n=1)
27-28	4(10.81%)	0	0	0
29-30	4(10.81%)	1(50%)	2(20%)	1(100%)
31-32	10(27.02%)	1(50%)	4(40%)	0
33-34	7(18.91%)	0	1(10%)	0
35-36	12(32.43%)	0	3(30%)	0
P value	**0.54**			

Table 3 shows that there is no significant difference between the different gestational age in relation to thyroid function test results(p=0.54)

Table(4) Distribution of the results of thyroid function test according to the sex of neonates

Sex	Normal (n=37)	Hypothyroxinemia (Low T4, normal TSH) (n= 2)	TSH(10-30µU/ml, normal T4)(n=10)	Hypothyroidism TSH >30µU/ml (n=1)
Male	24 (64.86%)	2(100%)	6(60%)	1(100%)
Female	13 (35.14%)	0	4(40%)	0
P value		**0.63**		

Table 4 present that there is no significant difference between both sexes in regard to the results of thyroid function test(p=0.63)

Table(5) Distribution of the results of thyroid function test according to the birth weight of the neonates .

Birth weight	Normal (n=37)	Hypothyroxinemia (Low T4, normal TSH) (n=2)	TSH(10-30µU/ml, normal T4) (n=10)	Hypothyroidism TSH >30µU/ml (n=1)
1000-1499	11(29.72%)	1(50%)	2(20%)	1(100%)
1500-1999	16(43.24%)	1(50%)	4(40%)	0
2000-2500	10(27.04%)	0	4(40%)	0
P value	**0.66**			

Table 5 reveals that there is no significant difference between birth weight of the neonates in regard to the results of thyroid function test (p=0.66).

Table(6) distribution of thyroid function test results according to possible maternal & neonatal risk factors.

Risk factors	Normal (n=37)	Hypothyroxinemia (Low T4, normal TSH) (n=2)	TSH(10-30µU/ml, normalT4 n=10	Hypothyroidi-sm TSH >30µU/ml (n=1)	P value
Neonatal Respiratory distress	25(67.5%)	2(100%)	8(80%)	1(100%)	0.6
Sepsis	11(29.7%)	2(100%)	2(20%)	0	0.13
Jaundice	21(56.7%)	0	4(40%)	0	0.25
Apnea	16(43.2%)	1(50%)	4(40%)	0	0.84
Hypoglyce-mia	9(24.3%)	0	4(40%)	1(100%)	0.11
Convulsion	2(5.4%)	0	0	0	0.86
Maternal Hypertensi-on	2(5.4%)	0	1(10%)	0	0.91
diabetes	2(5.4%)	0	2(20%)	0	0.46
thyroid disease	5(13.5%)	0	1(10%)	0	0.89

History of mental retardation	3(8.1%)	0	2(20%)	1(100%)	0.26
History of child death	5(13.5%)	1(50%)	3(30%)	0	0.42

Table 6 shows that no specific neonatal or maternal risk factor for abnormal thyroid function test & most of neonates have more than one risk factor.

DISCUSSION:

Thyroid hormones are essential for brain development. Very preterm infants who are at risk of neurodevelopment disabilities also have low T4 level and free T3 values in the first week after birth . This transient hypothyroxinemia may in part be the cause of neurodevelopmental problems[(2)].This study shows that 37 (74%) of preterm neonates have normal thyroid function test and 2(4%) have transient hypothyroxinemia and only one preterm neonate have hypothyroidism. There is difficulty in screening for congenital hypothyroidism in preterm neonates due to the immaturity of the hypothalamic –pituitary – thyroid axis, and the effect of intercurrent illness and drug on thyroid function and it may be unwise not to re-screen infants for congenital hypothyroidism at term[(7)]. The use of prophylactic Thyroid hormone in preterm infants to reduce morbidity and improve the neurodevelopmental outcome are not supported by many studies [(8)]. In this study the patient who has hypothyroidism has gestational age (29 – 30 weeks) and the 2 preterm neonates with transient hypothyroxinemia have gestational age (29 - 32 weeks)but the study shows no statistically significant relation between gestational age & thyroid function test results in contrast to other studies which found that gestational age was the only factor which could affect the thyroid function during the first 2 weeks of life [(9,10)] but in these studies they did repeated follow up thyroid function test which was not done in this study. The incidence of congenital hypothyroidism in preterm infants is similar to term infants , profound abnormality of thyroid function test can occur in preterm babies with transient hypothyroidism but both categories of hypothyroidism (permanent and transient) can be detected by a once –only TSH screening strategy with a relatively low cut –off [(11)]. This study showed that the preterm with hypothyroidism have VLBW, and the 2 babies with transient hypothyroxinemia have weight (1000 – 2000 grams) with no significant effect of birth weight of the neonates on the results of thyroid function test. There is no evidence of an association between birth weight and adult pituitary - thyroid axis set point after control for genetic and environmental factors could be demonstrated[(12)]. Regarding other risk factors (e.g. respiratory distress syndrome, sepsis, apnea & others) The preterm neonate with hypothyroidism has family history of mental retardation, respiratory distress syndrome (RDS) and hypoglycemia, and the 2 neonates with hypothyroxinemia have RDS, sepsis, and apnea attacks. Our study corresponds with two studies done in Amsterdam, both studies demonstrate abnormal thyroid function test in sick premature infant [(13)].The most common disorder associated with abnormal TFT in preterm infants was RDS [(14)]. A study showed

significant effect of hypoxia and sepsis on thyroid function and the depth and duration of hypothyroid condition depends on the gestational age, degree of hypoxia and the gravity of the infectious process[15].Regarding the neonate who has family history of mental retardation, the abnormal thyroid function could be related to familial causes rather than prematurity itself.

In comparison with other studies e.g. a study done in Iran showed that the prevalence of hypothyroidism was observed in 13% in preterm infants & 2% had permanent hypothyroidism[9]& in Australia a study showed that the incidence of hypothyroxinemia was 58%[16] while in Korea hypothyroxinemia was observed in 28% of preterm infants &12% were diagnosed with hypothyroidism [17]. these studies have results higher than our study &this variation could be attributed to the difference in sample size. Iraqi people themselves are susceptible for hypothyroidism because they have severe iodine deficiency status as graded by WHO [18].Since congenital hypothyroidism is the commonest treatable cause of mental retardation &most infants with congenital hypothyroidism appear normal at birth or show no signs, neonatal thyroid screening programs were performed in many countries for early diagnosis & treatment of hypothyroidism [19] Iraq is one of the countries lacking this important neonatal screening program.

CONCLUSION :

Since there is improvement in the care of preterm and very low birth weight infants lead to improvement of their survival rate and in order to decrease their disabilities as a results of complications of prematurity we have to take into consideration the state of thyroid function since thyroid hormone is important in brain development and prematurity and its complication affect thyroid function .

RECOMMENDATION:

1-Screening program for detection of thyroid function in the neonatal period especially for preterm infants should be encouraged in Iraq.

2-Effort should be concentrated on the health of pregnant women to decrease the incidence of preterm delivery & it's complications.

3-further studies to be done on a larger sample of neonates with follow up of their outcome is recommended.

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