Correlation of Third Day TSH and Thyroxine Values with Bilirubin Levels Detected by a Neonatal Screening System

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ÖZET

Yenidoğan tarama programında saptanan 3. gün TSH ve tiroksin değerlerinin bilirubin düzeyleri ile ilişkisi

Amaç: Tüm yenidoğanlarda konjenital hipotiroidi ve metabolik hastalık taramaları için postnatal yaklaşık 72. saatte kan örneği alınmaktadır. Bu zaman yaklaşık bilirubin seviyelerinin pik yaptığı döneme karşılık gelmektedir. Aynı anda alınacak kan testlerinde serum bilirubin seviyelerinin ölçülmesi yüksek düzeydeki bilirubin seviyelerinin saptanmasını sağlayacaktır. Bu çalışma postnatal 3. günde alınan kan örneklerinde TSH, T4 ve total bilirubin seviyeleri arasındaki ilişkiyi araştırmak amacıyla yapılmıştır.

Gereç ve Yöntem: Bu çalışma hastanemiz pediatri bölümünde 1 Ocak 2008 ile 30 Ocak 2008 tarihleri arasında sezeryanla doğmuş 450 full-term yenidoğan üzerinde retrospektif olarak yapılmıştır. Tüm veriler SPSS 15.0 ile analiz edilmiştir. Tiroid hormonları ile total bilirubin seviyeleri arasındaki ilişki Pearson's Korelasyonu ile değerlendirilmiştir.

Bulgular: Yenidoğanların hastaneden taburcu olma zamanı ortalama 76±1,2 saat idi. Ortalama doğum tartısı 3306±432 g ve ortalama gestasyon yaşı 269±8 gün (384/7±11/7 hafta) idi. Çalışma grubundaki yenidoğanların ortalama T4 ve TSH seviyeleri ise sırasıyla 13,73±2,22 µg/dl ve 6,96±3,97 mU/mL bulundu. Ortalama total bilirubin seviyesi ise 8,95±3,23 mg/dl idi. The Pearson's Korelasyon analizine göre TSH ve total bilirubin seviyeleri arasındaki ilişkiyi gösteren r değeri -0.19 bulundu, istatistiksel olarak anlamlıydı ancak bu ilişki çok güçlü değildi.

Sonuç: Bulgularımız sağlıklı yenidoğanlarda, eş zamanlı ölçülen T4, TSH ve bilirubin seviyelerinin tarama amacıyla oldukça yararlı olduğu ancak klinik olarak önemli bir korelasyon göstermediğini ortaya koymaktadır

Anahtar kelimeler: Tiroid Stimulan Hormon (TSH), tiroksin (T4), total bilirubin

ABSTRACT

Correlation of third day TSH and thyroxine values with bilirubin levels detected by a neonatal screening system

Objective: For the purpose of screening for congenital hypothyroidism and metabolic diseases blood is drawn for analysis from all newborns about 72 hours of postnatal age, which coincides with the approximate peak-time of bilirubin levels. Adding the measurement of serum bilirubin concentrations to the blood tests in programs of this kind will serve to detect high levels of bilirubin. The present study was designed to investigate a relationship, between neonatal TSH, T4 and total bilirubin levels in the blood samples of postnatal third day.

Material and Methods: The population of the present study, which was conducted retrospectively in department of pediatrics in our hospital, was 450 healthy full-term newborns who had been born by cesarean section during the period January 1, 2008 and April 30, 2008. All data were analyzed by using SPSS 15.0 . Correlation between total bilirubin and thyroid hormone levels was computed by the Pearson's correlation coefficient.

Results: The mean age of the neonates when discharged from the hospital after birth was 76±1.2 hours. The mean birth weight was 3306±432 g and the mean gestational age was 269±8 days (384/7±11/7 weeks). The mean serum levels of T4 and TSH in the neonates of the study group were 13,73±2,2 µg/dl and 6,96±3,97 mU/mL respectively. The mean serum level of total bilirubin in the study group was 8,95±3,23 mg/dl. The Pearson's correlation analysis revealed that r was -0.19 between TSH and total bilirubin levels and was significant but not so much powerful.

Conclusion: Our results suggest that simultaneously measurement of T4, TSH, and bilirubin levels is a useful clinical tool for screening but there seems to be no significant clinical correlation between these parameters in healthy term newborns.

Key words: Thyroid-stimulating hormone (TSH), thyroxin (T4), total bilirubin

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INTRODUCTION

Jaundice is one of the most frequent clinical signs of newborns detected in the first week of life. Jaundice develops as an effect of indirect hyperbilirubinemia in 30-50% of term infants and in 80% of preterm infants (1). Congenital hypothyroidism (CHT) is well known cause of prolonged unconjugated hyperbilirubinemia and appears to be associated with the delayed maturation of hepatic uridine diphosphate glucoronyl transferase (UDPGT) enzyme activity (2,3). Because thyroid hormones act practically in all tissues of the body and influence enzyme concentration and activity, the metabolism of substrates, vitamins and mineral salts, basal metabolism

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or calorigenesis; they also stimulate the consumption of oxygen and act in other endocrine systems (4). On the other hand, it is also accepted that physiological jaundice in the newborn is developing as a result of deficiency in UDPGT activity. UDPGT activity steadily increases with birth, reaching adult values in 14 weeks (5). Prolonged jaundice is seen in approximately 10% of newborns with hypothyroidism (6). But also hypothyroidism has been reported in studies on the etiology of jaundice that develops within the first week of life (7,8,9). Today, as healthy newborns are discharged from the hospital at an early stage after delivery, the diagnosis, monitoring and timely treatment of jaundice becomes more problematic (10). It is a fact that some term infants are seen to experience a severe jaundice in short time after birth (11). Normally, in the first days after birth serum bilirubin concentrations increase and generally peak on the third day (12). In many countries, newborns are subjected to screening programs to detect metabolic and endocrine diseases. For this purpose, blood is drawn for analysis from all newborns about 72 hours of postnatal age, which coincides with the approximate peak-time of bilirubin levels. Adding the measurement of serum bilirubin concentrations to the blood tests in programs of this kind will serve to detect high levels of bilirubin (13). In view of the above, the present study was designed to investigate a relationship, if any, between neonatal thyroid-stimulating hormone (TSH), thyroxin (T4) and total bilirubin levels in the blood samples of postnatal third day.

MATERIAL AND METHODS

The population of the present study, which was conducted retrospectively in department of pediatrics in our hospital, was 450 healthy full-term newborns (≥38 weeks of gestation) who had been born by cesarean section during the period January 1, 2008 and April 30, 2008. Neonates with congenital hypothyroidism, cephal hematoma, maternal thyroid disease, small for gestational age (birth weight less than 2500 gram), neonates with Rh izoimmunation, ABO incompatibility with hemolysis, glucose-6-phosphate dehydrogenase deficiency, serious diseases or congenital anomalies and neonates delivered by vaginal route were excluded from the study. Glucose-6-phosphate dehydrogenase values are detected in neonates with hyperbilirubinemia requiring phototherapy. Our hospital accepted a discharge policy of ≥72 hours for newborns delivered through cesarean section and ≥48 hours for newborns delivered vaginally. All of the maternal blood groups are analyzed by our obstetric and gynecology department during pregnancy. Additionally we investigate of all neonates' blood groups from cord blood. A follow-up evaluation within 48 to 72 hours after discharge is offered to all neonates. Individual serum bilirubin concentrations were measured with direct spectrophotometry (Bilirubin Analyser Bil Micrometer, Kohsoku Denki Co, Ltd, Tokyo, Japan) in venous blood samples before discharge taken as a part of a neonatal screening program for phenylketonuria, metabolic diseases and hypothyroidism.

All data were analyzed by using SPSS 15.0 for Windows (SPSS, Chicago, IL). Correlation between total bilirubin and thyroid hormone levels was computed by the Pearson's correlation coefficient. Written consent was obtained from parents of all neonates for blood samples.

RESULTS

During the study period, a total of 592 live births took place at our hospital. One hundred and forty two neonates did not meet the enrollment criteria. After exclusion of those babies meeting the exclusion criteria the remaining 450 neonates (229 male and 221 female) constituted our study population. The mean age of the neonates when discharged from the hospital after birth was 76±1,2 hours. Neither any baby nor any mother included in the study had clinical symptoms of hypothyroidism. The mean birth weight was 3306±432 g and the mean gestational age was 269±8 days (384/7±11/7 weeks). The mean serum levels of T4 and TSH in the neonates of the study group were 13,73±2,22 μg/dl and 6,96±3,97 μU/mL respectively. The mean serum level of total bilirubin in the study group was 8,95 ± 3,23 mg/dl Table 1. Etiology of hyperbilirubinemia

Table 1: Serum Concentrations of TSH, Thyroxin (T4) and Total Bilirubin (N=450)

	Minimum	Maximum	Mean	Standard Deviation
TSH (μU/ml)	0,69	19,49	6,96	3,97
T4 (μg/dl)	7,85	19,92	13,73	2,22
Bilirubin (mg/dl)	1,1	25,7	8,95	3,23

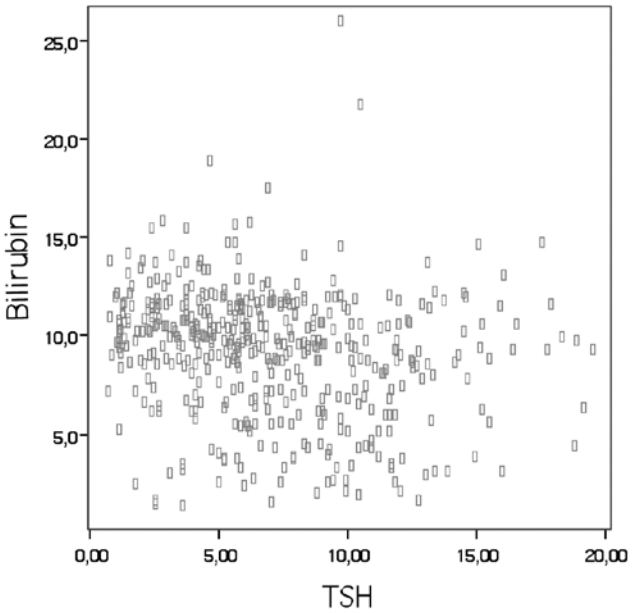

Figure 1. Correlation of TSH and Total Bilirubin Levels

above the threshold values requiring phototherapy was breast milk jaundice. The Pearson's correlation analysis revealed that r was -0.19 between TSH and total bilirubin levels and was significant but not so much powerful (Figure 1). According to the analysis, total bilirubin values decreased as TSH increased. There was no significant correlation between T4 and total bilirubin (r=-0.02) and between TSH and T4 (r=-0,04) serum levels.

DISCUSSION

Hyperbilirubinemia is one of the most frequent causes for readmission of neonates to hospital in the first week of life (14). The American Academy of Pediatrics (AAP) guideline on management of hyperbilirubinemia recommends that every newborn be assessed for the risk of developing severe hyperbilirubinemia, by using predischarge total serum bilirubin (TSB) or transcutaneous bilirubin (TcB) measurements and/or assessment of clinical risk factors before discharge (15). Universal bilirubin screening with either TcB or TSB measurements was associated with increased identification of newborns needing phototherapy and a significantly lower incidence of severe hyperbilirubinemia. Normally, the serum bilirubin concentration increases during the first days of life, usually reaching peak values at about third day after birth (12). In the present study, we attempted to investigate the correlation of third day T4 and TSH values with total bilirubin levels. In our hospital screening for congenital hypothyroidism is conducted by serum T4 and TSH testing and simultaneously serum bilirubin levels. The thyroid hormone levels in the present study were evaluated after 72 hours of postnatal age to avoid physiological changes in the hormonal levels during first 3 days of life. Because maturation of the hypothalamic-pituitary-thyroid axis feedback relationship occurs during the second half of the gestation, but it is not complete after birth. Immediately after birth, there is a TSH surge to 60-80 mU/mL in 30 minutes, likely as a result of the stress of delivery and clamping of the cord. Then serum TSH levels decreases slowly over the next two days in full term infants. But this adaptation timing is different in preterm infants. But this adaptation timing is different in preterm infants (16). Therefore neonatal screening should be performed in the nursery room, ideally between 3 and 5 days after birth (17). Early in the experience of newborn screening programs, most used a primary T4 and TSH test strategy to detect with congenital hypothyroidism (16,17).

McElduff et al. reported higher TSH levels at the third day of life in neonates delivered by cesarean section (18). The difference was not significant, but the number studied was small. On the other hand Turan et al. reported that thyroid function tests does not show significant variations according to the mode of delivery and the type of anesthesia used (19). In our study we wanted to eliminate confounding factors such as gestational age (by including only term babies) and mode of delivery (only cesarean section delivery).

As a result, our results suggest that simultaneously measurement of T4, TSH, and bilirubin levels is a useful clinical tool for screening but there seems to be no significant clinical correlation between these parameters in healthy term newborns. We can speculate that clinical conditions like jaundice resulting from thyroid hormone levels as in congenital hypothyroidism will depend on the degree and duration and will affect basically all tissues to a lower or greater extent including bilirubin metabolism. As this period is being very dynamic and influenced by several factors, further studies are needed with larger sample size to establish the correlation of thyroid hormones and bilirubin levels in the first days of hypothalamic-pituitary-thyroid axis maturation.

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