Cord Blood Thyrotropin Screening for Congenital Hypothyroidism

Three Years’ Experience on the Island of Saint Lucia

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ABSTRACT

Cord blood thyrotropin (TSH) screening for congenital primary hypothyroidism has been in effect on the island of St. Lucia for the past three years. Umbilical cord blood samples are obtained on Guthrie filter paper and then transported 3,000 miles to Loyola University of Chicago and delivered to the Illinois State Metabolic Screening Laboratory. There TSH is measured by radioimmunoassay (RIA). After three years, 1,789 newborns have been screened, and the mean value is 6.23 ± 0.13 μIU per ml. This mean value is less than previously reported by us in 1986 (10.23 ± 0.29 μIU per ml). It is concluded that this screening service continues to be possible far removed from the population under observation. No case of primary hypothyroidism has been detected. Our decreased mean TSH value is due to the new method currently used by the Illinois State Metabolic Screening Laboratory. Congenital hypothyroidism will not be missed provided internal controls are established and rigidly observed.

Introduction

Three years ago screening for primary congenital hypothyroidism began on the island of St. Lucia. Congenital hypothyroidism is the most preventable cause of mental retardation. It has an incidence of one in 4,000 live births in North America, one in 3,500 infants in most European countries, and one in 2,637 in Finland. No neonatal screening program existed in the Caribbean. Our study was undertaken in St. Lucia, in the Lesser Antilles, in the Caribbean because of an ongoing commitment to medical care.
HYPOTHYROIDISM CORD BLOOD THYROTROPIN

between Loyola University of Chicago, School of Medicine and the St. Jude Hospital in St. Lucia.

Materials and Methods

St. Lucia is an island in the Caribbean Sea located 24 miles south of Martinique at a latitude of 13° 53' and a longitude of 60° 58'. The island has an area of 238 square miles. The population of 115,000 individuals is mostly black, black-white, and a few East Indians. St. Jude Hospital, where the studies are being undertaken, is situated in the southern part of the island in a rural area, near the city of Vieux Fort. St. Jude Hospital has 110 beds and approximately 1,000 deliveries per year with the average post-partum stay of 12 hours. Births are attended by locally trained midwives with obstetrical back-up as needed.

Cord blood samples are collected on Guthrie filter paper by the midwife at the time of delivery. Samples are sent to LUMC Loyola University Medical Center (LUMC) every two weeks through the mail after being carried to the mainland (USA) by volunteers leaving the island. Then from LUMC, the samples are delivered to the Illinois State Metabolic Screening Laboratory where TSH levels are measured by radioimmunoassay. Rabbit TSH antiserum is added to 3.3 mm blood spot discs and incubated at 18°C to 25°C for 16 to 18 hours. Radioactive TSH (I125) is then added and incubated at 18°C to 25°C for five hours. A precipitating solution of goat antiserum is added, and, after precipitation and centrifugation, the bound fraction is counted by gamma counter. Standard levels of TSH at 0, 10, 20, 30, 40, 100, and 200 μIU per ml adjusted for a hematocrit of 65 by the company.

Results

There have been 1,789 samples collected and processed in this ongoing program. A scattergram of TSH results is shown on figure 1. The mean TSH value is 6.23 ± 0.13 μIU per ml. This mean value is less than previously reported by us in 1986 (10.23 ± 0.29 μIU per ml). However, our values remain well below the upper limit of normal cord blood TSH values reported by Foley, Klein, and Foley in Pittsburgh and by Virtanen in Finland (60 μIU per ml and 50 μIU per ml, respectively).

Our turnover time of 33 days, which is defined as the interval between the date of collection and the date TSH results are known to us, has not improved.

No other damaged sample has been found since the report of one sample denatured by direct exposure to sunlight while on a surgical instrument tray covered by a metal top.

Discussion

Cord blood TSH values have been used for screening for congenital hypothyroidism in Pittsburgh during one of the first pilot programs in 1973 and in Finland since 1979 with complete coverage of their 63,000 annual births. Using the date of Foley, Klein, and Foley in Pittsburgh and Virtanen's data in Finland, cord blood TSH values >50 μIU per ml were adopted as our abnormal values. The TSH values are high soon after birth because of the physiologic thyrotropin releasing factor surge, but they decrease to much lower values within the next few days.7

Drawbacks of cord blood TSH screening, such as with twin pregnancy, have been reported in our initial paper. However, it was chosen because of the short post-partum stay of our population.

Reviewing our data, new problems became apparent.

1. Our mean value was much lower than previously reported, 6.23 ± 0.13 μIU per ml (figure 1) versus 10.23 ± 0.29
μIU per ml. The most striking difference, however, was 450 samples with a TSH value of less than one μIU per ml.

The major concern was the possibility of denaturation of the samples by heat. However, the study done by the Centers for Disease Control (CDC) on degradation of thyroid stimulating hormone spotted on filter paper shows that TSH remains stable up to 72 days at 23°C and 37°C. These temperatures represent the normal range of temperatures in the Caribbean. Furthermore, no evidence of heat denatured hemoglobin was found.

Investigating it further, it was found that a new kit using different antibodies was in use since November 14, 1985 at the State Laboratory. To verify that the change in method was responsible for our lower values, our results were divided in two groups. One group consisted of the TSH values measured by the previous radioimmunoassay, and the other group included the TSH values calculated by the current radioimmunoassay.

In figure 2 is a scattergram of all the TSH values from July 1984 to November 14, 1985. The mean value in this scattergram is 9.46 μIU per ml which is not very different from our previously reported mean of 10.23 μIU per ml.
In figure 3 is a scattergram of the TSH values from November 15, 1985. The mean value calculated from this scattergram is 3.17 μIU per ml.

2. Reliability of any cord blood TSH value less than 50 μIU per ml was counted as being normal, regardless of the method used.

The CDC undertook a nationwide survey in 1979 to investigate the reliability of the different methods used by multiple laboratories in the United States for screening for primary congenital hypothyroidism. Their conclusion was that the incidence of error was low if laboratories respected their cut-off point. Our cut-off point would be the 99th percentile of the St. Lucia population. These values are 27 μIU per ml using the previous radioimmunoassay and 23 μIU per ml by the current radioimmunoassay.

Conclusion

After reviewing the data of three years it was concluded that:

1. Screening programs for neonatal hypothyroidism continue to be possible in laboratories far removed from the population under observation.

2. Our lower mean TSH of 6.23 ± 0.13 μIU per ml is due to the new kit used by the Illinois State Metabolic Screening Laboratory and not to the improper handling of the samples.

3. The cut-off point for our St. Lucia population has been established by us. It is 23 μIU per ml by the currently used radioimmunoassay.

4. No case of congenital hypothyroidism has been detected when a T4 level was measured for all the babies whose cord TSH levels were greater than the previously mentioned values.

References


