Cord Blood Thyrotropin Screening for Primary Hypothyroidism on Carribean Island: A Rapid Communication*

W. P. ZELLER, MD,†‡ C. SAJOUS, MD,‡
G. S. AHMED, MD,‡ C. L. ANDERSON, MD,‡
M. BROOKS, MD,‡ and R. DOBBINS§

†‡Departments of Pediatrics and Internal Medicine,
Loyola University of Chicago, Stritch School of Medicine
and
§Newborn Metabolic Screening Laboratory,
the Illinois Department of Public Health
Chicago, IL 60153

ABSTRACT

Screening programs using determinations of serum thyroxine have demonstrated that congenital hypothyroidism occurs in one in 4,000 live births in North America. More than 90 percent of affected infants have primary hypothyroidism with elevated plasma thyrotropin (TSH) levels. Since the feasibility of newborn screening and incidence of congenital hypothyroidism in other less well developed areas of the world is not well defined, a study was undertaken of neonatal primary hypothyroid screening in infants born on the Carribean island of St. Lucia in the Lesser Antilles. Three hundred thirteen cord blood samples were collected on filter paper and transported 3,000 miles to Loyola University of Chicago, Stritch School of Medicine (LUMC). From LUMC, the samples were transported to the Illinois State Metabolic Screening Laboratory for determination of TSH by radioimmunoassay (RIA). In this group of newborns, the mean TSH level in cord blood was 10.23 ± 0.29 μIU per ml (SEM). It is concluded that screening programs for neonatal primary hypothyroidism can be performed using reference laboratories far removed from the population under observation.

Introduction

Congenital hypothyroidism is the most preventable cause of mental retardation.

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† Address reprint requests to W. P. Zeller, M.D., Department of Pediatrics, Loyola University, Stritch School of Medicine, 2160 S. First Avenue, Maywood, IL 60153.

It has an incidence of one in 4,000 live births in North America,6 one in 3,500 infants in most European countries,2 and one in 2,637 in Finland.12 The first pilot screening programs began in the early 1970's in Pittsburgh, PA with cord blood thyrotropin (TSH) measurements,9 in Quebec with dried blood filter paper T4 concentrations,3 and in Belgium with
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Whereas the retrospective surveys had placed the incidence of primary congenital hypothyroidism at one in 7,000 live births, the results of newborn screening programs show that the incidence is much higher. No neonatal screening program exists in the Caribbean. Our study was undertaken to determine whether or not a reference laboratory could be used to detect primary hypothyroidism in St. Lucia, the Lesser Antilles in the Caribbean. This location was chosen because of an ongoing commitment to medical care between Loyola University of Chicago, School of Medicine (LUMC) and the St. Jude’s Hospital in St. Lucia.

Materials and Methods

St. Lucia is an island in the Caribbean 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 persons is mostly black, black-white, and a few East Indians. St. Jude Hospital, where the studies were undertaken, is situated in the southern part of the island in a rural area, near the city of Vieux Fort. St. Jude has 110 beds, approximately 1,000 deliveries per year, and the average post-partum stay is 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 vaginal delivery or Cesarean section. Samples are sent to LUMC every two weeks through the mail after being hand carried to the mainland (USA) by volunteers leaving the island. Then, the samples are taken from LUMC and delivered to the Illinois State Metabolic Screening Laboratory, where TSH levels are measured by radioimmunoassay. Goat antihuman TSH antisera is added to 4.76 mm blood spot discs and incubated at 25°C for 24 hours. Radioactive TSH (I$^{125}$) is then added and incubated at 25°C for four hours. A precipitating solution of polyethylene glycol and donkey antigoat gamma globulin is added and, after precipitation and centrifugation, the bound fraction is counted by the gamma counter. Standard levels of TSH at 0, 10, 20, 30, 40, 100, and 200 μIU per ml adjusted for hematocrit of 55 percent are provided by the company.

Results

There have been 313 samples collected and processed in this ongoing program. A scattergram of TSH results is shown in figure 1. The mean TSH was 10.3 ± 0.23 μIU per ml (SEM). This mean TSH value compares very well with the serum values of Klein, Agustin, and Foley. However, our values are well below the upper limit of normal value of 60 μIU per ml on filter paper as described by Foley et al.

Our turnover time, which is defined as the interval between the date of collection and the date of TSH results, averaged 33 days. Only one sample could not be processed because of damage by heat. The sample had been placed in a surgical instrument tray covered by a metal top and left in direct sunlight. The heat denatured the hemoglobin and was not able to be accurately processed.

Discussion

Cord blood TSH values have been used for screening of 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. In Pittsburgh, Foley, Foley, and Klein, after screening 44,919 patients, determined that a TSH value in cord blood greater than 60 μIU per ml was abnormal; however, the Pittsburgh children with primary
hypothyroidism all had a TSH value >69 μIU per ml. Virtanen\(^1\) in Finland, in the first phase of the screening, had set the upper limit for normal cord TSH values at <44 μIU per ml. Because of the number of false positive (0.21 percent), abnormal values in cord blood were TSH value >50 μIU per ml or TSH range of 45 to 59 μIU per ml with T4 <10 μg per dl. This TSH value >50 μIU per ml has been adopted as our abnormal value.

At birth, the blood TSH values are high because of the physiologic thyrotropin releasing factor surge and this decreases to much lower values within the next few days.\(^7\) Infants with congenital hypothyroidism can be detected by cord TSH screening.\(^2\,3\,4\,5\)

One disadvantage of screening cord blood noted in the Finnish program was multiple monochorionic pregnancy where a hypothyroid infant may be missed if there is a mixing of blood with a euthyroid twin, even in the absence of feto-fetal transfusion syndrome. Therefore, monochorionic twins should be re-screened two weeks after birth.\(^12\) Recall has recently been incorporated by us on all twins to remove this variable from our cord TSH screening.

Despite these drawbacks, our neonatal screening is done by cord blood TSH because of the short post-partum stay of the population. The TSH value >50 μIU per ml has been adopted as abnormal to reduce our false positive and still have no false negatives.\(^12\) The other problems facing us are:

A. Collection of Samples

All deliveries are attended by midwives. Through the midwife, it is possible to make health care professionals understand the importance of (1) screening every child, (2) labeling each sample properly, and (3) filling each circle completely on the filter paper. (After a few mislabeled and poorly collected samples, the collection is now running smoothly.)

B. Distance

The samples need to be mailed to the laboratory at regular intervals. A long transit time could decrease the TSH level and delay synthroid replacement.\(^5\,10\) During the first two or three
months, the samples were kept three weeks or more before being shipped. At present, they are mailed regularly at two week intervals.

C. Recalls

All the patients leave the hospital and return to remote rural areas with no modern communication facilities. The elevated TSH levels have been difficult. However, recalls have been possible, and, to date, there have not been any TSH values >40 µIU per ml.

Conclusion

After reviewing our data for the first 18 months of the project, it is concluded that:

1. Screening programs for neonatal hypothyroidism can be performed in laboratories far removed from the population under observation. The turnover time would still be reasonable to institute treatment and prevent mental retardation.

2. Because of the limited sample size, continued screening and expansion of the screening program is necessary to determine the incidence of congenital hypothyroidism in the island of St. Lucia and the Caribbean.

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