

# DETECTION THROUGH SCREENING OF MATERNAL THYROTOXICOSIS INDUCED CENTRAL HYPOTHYROIDISM IN NEWBORNS

Roy Joseph<sup>1,2</sup>, Yung Seng Lee<sup>1</sup>, Steven Chin Yuen Ng<sup>2</sup>, Kah Yin Loke<sup>1</sup>

<sup>1</sup>Department of Pediatrics, National University of Singapore;

<sup>2</sup>Department of Neonatology, National University Hospital

**Abstract.** Use of a third generation TSH assay enabled extremely low values of TSH to be detected through newborn screening. The use of a supplemental free thyroxine improved testing specificity. The hypothyroidism observed is believed to be secondary to suppression of the hypothalamic-pituitary-thyroid axis by placentally transferred maternal thyroxine.

## INTRODUCTION

Maternal thyrotoxicosis is a common complication of pregnancy and the likelihood of the baby developing drug induced hypothyroidism and/or neonatal thyrotoxicosis is well known. The use of a third generation thyrotropin (TSH) assay enhances the ability to identify accurately low TSH levels in newborn serum. Two cases of this less well-known complication of central hypothyroidism secondary to maternal Thyrotoxicosis (Matsuura *et al*, 1997) have been detected through the cord blood newborn screening program.

## MATERIALS AND METHODS

Thyroid dysfunction screening is part of the cord blood newborn screening program at the National University Hospital. Further evaluation of babies occurred if either the cord TSH was greater than 25 mIU/l or less than 1.6mIU/l (Joseph *et al*, 1993). These TSH values represent the 97<sup>th</sup> and the 0.5 centiles respectively. The TSH assay was done using the Ortho Clinical Diagnostics Vitros Eci assay and assay time was about 38 minutes. During the period January 1988 to April 2001, 7716 newborns were screened using a TSH testing protocol.

## RESULTS

In this cohort there were 20 babies with cord TSH of <1.6 mIU/l. In 12 of them, the free thyroxine (fT4) levels were in the normal range (12-20 pmol/l) and they were not evaluated further. The remaining 8 when evaluated on Day 4 showed 3 different patterns of fT4 values. One had a very high value, 5 had normal values

and 2 had extremely low fT4 values. These two babies were evaluated further (Lee *et al*, 2002).

The first baby had a cord TSH of 0.2 mIU/l and a fT4 of 11.7 pmol/l. When evaluated on Day 4, the TSH remained low (0.49 mIU/l). The FT4 had fallen markedly to 6.8 pmol/l. The second case had in the cord specimen, undetectable levels of TSH and a FT4 of 24.9 pmol/l. When evaluated on Day 4, the TSH remained low at 0.03 mIU/l and the FT4 had fallen to 9.5 pmol/l. Both babies did not have low birth weight, nor were they dysmorphic. They were well at birth and remained asymptomatic in the newborn period. Radiological examination of the knee showed ossification centers appropriate for the gestational age.

Both mothers were known thyrotoxic who were poorly compliant with therapy and had become clinically and biochemically toxic during their third trimester of pregnancy. Towards the end of the first week of life, a TRH stimulation test was done on both newborns using a TRH dose of 7 µg/kg. The basal TSH values (mIU/l) were 1.01 and 0.09 respectively. The "peak" values drawn 20 minutes after TRH administration were 2.16 and 0.31. This pattern of poor TSH response confirmed that the hypothyroidism was pituitary/hypothalamic in origin. A CT scan in the first, and cortisol and growth hormone levels in the second, showed no abnormalities.

Soon after, they were both started on replacement thyroxine 12.5 µg daily (about 4 µg/kg). They remained asymptomatic, and grew normally both physically and mentally. At about 4 months of age and while on the same daily thyroxine dose of 12.5 µg, their TSH/fT4 values were normal at 1.5/16.5 and 1.2/13.6 respectively.

## DISCUSSION

Screening for hypothyroidism using TSH is designed to detect primary hypothyroidism. A third generation TSH assay used in newborn screening at the University Hospital in Singapore is capable of accurately measuring very low TSH levels (lower limit of detection is 0.03 mIU/l). Babies with low TSH levels have been routinely evaluated in order to detect central (i.e. non- primary) hypothyroidism. Confirmation of central hypothyroidism has been achieved by measuring the fT4 levels in babies with a low TSH value. The identification of 2 babies with central hypothyroidism from a population of 7716 gives a preliminary incidence of 1 in 3858, (almost as high as that reported for primary hypothyroidism, 1 in 3500). Their fT4 levels in the newborn period were extremely low and if not corrected would in all probability have resulted in some inhibition of their physical and mental development. That the babies were asymptomatic highlights the vital role of screening. The history of poorly controlled maternal thyrotoxicosis in both, raises the need to biochemically and critically evaluate in the newborn period, the infant of the thyrotoxic mother (Matsuura *et al*, 1997; Slyper and Shaker, 1989). This evaluation needs to be carried out even if the initial screening results are normal.

The observation of maternal thyrotoxicosis induced neonatal central hypothyroidism is recent and probably follows the use of a primary TSH screen for hypothyroidism. The pathogenesis has not been defined. The initiating event is probably the transport across the placenta in the third trimester of excessive maternal thyroid hormones (Momotani *et al*, 1986; Vulmsa *et al*, 1989 ). The maternal hormones suppress the maturing fetal hypothalamic-pituitary thyroid axis (Mandel *et al*, 1990). The mechanism of suppression may be due to alteration of the set point for feedback control or by a reduction of the capacity for pituitary TSH secretion (Mandel *et al*, 1986).

Long term follow up of the thyroid function and the physical and mental development of these babies are required for accurate prognostication.

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