The Practice and Limitations of Screening for Congenital Hypothyroidism in Selected Hospitals in Sri Lanka

Damayanthi Kusum Kumari Nanayakkara

(MBBS, MPhil)

Nuclear Medicine Unit

Faculty of Medicine

A thesis submitted to the Faculty of Medicine in fulfilment of the requirements for the degree of

Doctor of Philosophy

of the

University of Peradeniya

Sri Lanka

April 2007

Abstract

The Practice and Limitations of Screening for Congenital Hypothyroidism in Selected Hospitals in Sri Lanka

The global incidence of congenital hypothyroidism (CH) is approximately 1:3000 of all births. Geographical regions with recognised iodine deficiency show a higher incidence of CH (1:700). However, clinical features of CH are subtle at birth and need biochemical methods for early detection. Neonatal screening for CH is not a routine practice in Sri Lanka. Hence, the diagnosis is based on "clinical features". This thesis aims to determine the major limitations in the current practice, to find out the burden of thyroid dysfunction in early infancy and finally to assesses the feasibility of conducting a routine neonatal screening program in Sri Lanka. The initial field experience and the pilot study results are reported here.

The first was a retrospective study that looked at the current practice of using clinical features for the diagnosis CH. Confirmatory tests were done on serum. The second was a prospective study that was carried out at the first triple vaccination to measure serum thyroid stimulating hormone (TSH) and free thyroxin in clinically normal infants. The third study was a pilot study carried out at the time of BCG vaccination using filter paper blood spot assay technique. After obtaining consent from the parents filter paper blood samples were collected by heel-stick or venepuncture method. Air-dried blood samples were tested for TSH using neonatal blood spots TSH kits (immunoradiometric assay method, skyBio.Ltd.UK).

Neonates with blood spot TSH above 20mU/L were identified as at risk and recalled for confirmation with serum analysis. Hypothyroidism was confirmed by elevated serum TSH associated with low free T4. Serum TSH above 20mU/L or blood spot TSH above 6.0mU/L was considered as hyperthyrotropinemia. Infants with abnormal thyroid functions were closely followed up.

Both first and second studies found a high frequency of thyroid dysfunction i.e., hypothyroidism and marginal hyperthyrotropinemia. The first study also found that prolonged neonatal jaundice was significantly associated with CH. However, in the absence of a routine biochemical screening programme in Sri Lanka, delay in diagnosis of CH is inevitable. The pilot study screened 4352 neonates. Total coverage from each hospital was over 90% with sample rejection rate at 1.5% (95%CI 1.1%-1.9%). The average sampling time was 1.2±1.5 days and 75% (95% CI 74%-76%) were screened within 48hours of birth. The mean TSH value was 5.9mU/L in this study group. Using TSH cut off (blood spot) at 20mU/L, 52 neonates were identified at risk and 1.2% (95% CI 0.9%-1.5%) were recalled. This confirmed 4 true, 5 unclassified cases of CH. The incidence of true CH was 1:1088, whereas including transient cases; the total incidence was high as 1: 483.

These studies showed that thyroid dysfunction in neonates in this area were higher compared to global figures. It is comparable to the figures seen in countries with iodine deficiency. Prolonged neonatal jaundice was found to be a significant clinical tool in the diagnosis of CH in the absence of a routine screening program. However, there are some limitations in the current clinical practice.

If these limitations are corrected, there is a greater chance of improving the early diagnosis of CH using clinical methods and biochemical confirmation.

The pilot study discusses the high frequency of true CH and unclassified thyroid dysfunction in this region and may be in the rest of Sri Lanka. It is justified to establish as routine screening for CH as soon as possible. It is technically feasible to carry out screening of newborn babies in hospital at the time of BCG vaccination before discharge from the postnatal ward. The methodology used in the pilot study could be satisfactorily modified to expand the programme of screening to the district, provincial and national level. I would recommend following the same process use in the pilot study for the future programmes.