SCRENNING FOR INBORN ERRORS OF METABOLISM BY TANDEM MASS SPECTROMETRY IN SINGAPORE

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A newborn may appear healthy at birth, but be at risk of serious health issues later in life due to an undiagnosed disorder. Newborn screening is a preventive health measure to detect and treat disorders that can result in early mortality or lifelong disability. In Singapore, newborns are screened for G6PD enzyme deficiency, congenital hypothyroidism, congenital hearing impairment, and more recently, inborn errors of metabolism (IEM).

The metabolic screen test

In 2006, a new newborn screening test was introduced to the public health system to detect IEM disorders. Called the metabolic screen, the test utilises tandem mass spectrometry (TMS) technology, allowing doctors to screen for many IEM conditions with a few drops of blood.

IEM disorders are collectively grouped as fatty acid oxidation disorders, amino acidopathies and organic acidemias. Left untreated, they can lead to prolonged ill health, learning disabilities or even death.

The metabolic screen is performed within days of a baby’s birth. A few drops of blood are drawn from the newborn’s heel (Figure 1) and sent to the Biochemical Genetics Laboratory at KK Women’s and Children’s Hospital (KKH).

There, the blood sample is screened for over 30 IEM conditions using a tandem mass spectrometer (Figure 2).

The metabolic screen has a sensitivity of 100 percent, a specificity of 99.8 percent and a positive predictive value of 20 percent. This means one in every five newborns with a positive screen is diagnosed with an IEM disorder.

To date, over 135,000 newborns in Singapore have undergone the metabolic screen, and 44 cases of IEM have been detected. Although each individual disorder is rare, the combined detection rate for the screened population is about 1 in 3,000. This incidence rate is similar to many other newborn screening programmes in the United States and the Australasia region.

Benefits of metabolic screening

Newborn metabolic screening enables early identification and treatment, so that mortality, morbidity and disability can be prevented.

Example: A recent newborn who tested positive for methylmalonic acidemia began to show biochemical signs of metabolic acidosis and hyperammonaemia even as he looked well during a clinical evaluation on day four of life. Acting on rapid follow-up laboratory and diagnostic findings, triggered by the metabolic screen result on day three of life, doctors were able to initiate early treatment and appropriate management for this child. He is currently healthy and developing normally.

It is also not uncommon for an abnormal newborn screening result to uncover an undiagnosed maternal IEM condition. Since 2006, seven such cases have been identified - two cases of 3-methylcrotonyl-CoA carboxylase deficiency, two cases of vitamin B12 deficiency and three cases of primary carnitine deficiency.

Integrated care for newborns with IEM conditions

The metabolic screen is part of a much larger, integrated preventive system. Early detection, quick action and intervention are crucial for the process to succeed.

When the laboratory at KKH identifies a significantly out-of-range result for a newborn screening test, the metabolic team is notified, and a metabolic specialist contacts the baby’s paediatrician to discuss the result, outline the possible diagnosis and recommend additional tests for further investigation. The baby’s parents are informed of the abnormal result by the paediatrician, following which the metabolic specialist contacts the parents to explain the findings, provide advice and arrange for a clinic visit.

In the case of a definite IEM being diagnosed, a shared care model is offered together with the paediatrician. This entails general paediatric care such as vaccinations and developmental checks being carried out by the paediatrician, with patient visits to the metabolic clinics for advice about management of the IEM.

Risks for unscreened newborns

Newborn screening is not compulsory; however opting out of the test carries risks for newborns. Since the metabolic screen was introduced, six infants who did not undergo testing presented with clinical symptoms of IEM and received treatment at KKH. Unfortunately, most of these children suffered irreversible developmental and neurological complications.

CONCLUSION

The proportion of newborns undergoing IEM screening by TMS has increased to over 65 percent in 2012. Participation by public and restructured hospitals is largely universal. However, only half of the newborns in private hospitals undergo newborn screening despite a 50 percent share in the annual live birth population in Singapore.

It is likely that a significant number of undiagnosed IEM cases exist in the community, either because the test was not offered, or was declined or unavailable before 2006. Thus it is essential for obstetricians and paediatricians to educate prospective parents on the availability and need for newborn screening, to help them make an informed decision. The optimal result would be for all newborns to undergo newborn screening as part of their basic standard of care.

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