Screening for Congenital Hypothyroidism

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Congenital hypothyroidism (CH) is a treatable cause of intellectual disability in children, hence the importance of newborn screening for hypothyroidism.

First time newborn screening for a congenital disorder was done by Prof. Dr. Robert Guthrie in 1960, in USA for phenylketonuria.[1] Screening was done first time in 1965. This led to early diagnosis and treatment of hypothyroidism which in turn improved intellectual outcome in babies born with CH. This created a worldwide interest in screening for hypothyroidism. In India screening for CH was done first time at B. J. Wadia Hospital, Mumbai in 1982 using cord blood sample.[2]

Incidence of CH as obtained from neonatal thyroid screening programs ranges from 1:3000 to 1:4000 live births.[3] Cause of CH can be attributed to ethnicity, consanguinity, nutritional and environmental factors including iodine deficiency.

Types of CH based upon their cause can be classified into

1) Agenesis (22%-42%)
2) Ectopy (35%-42%)
3) Gland in place defect (24%-36%)

Clinical features of CH include mental retardation, developmental delay, delayed psychological development, congenital anomalies of heart, epilepsy, infantile cerebral palsy, hoarseness of voice, feeding problems, hypotonia, umbilical hernia, dry skin, jaundice. This causes a considerable financial and emotional burden on parents to manage such children. Hence there is a need of newborn screening program to detect congenital disorder as early as possible.

Wilson – Jungner in 1996 have given a criteria for selection of disorder in newborn screening program.[4] These are as follows:

1) The condition should be an important health problem.
2) Natural history of the condition should be well understood.
3) It should be detectable at an early age.
4) Treatment at an early stage should be beneficial.
5) Suitable test should be devised for early detection.
6) The test should be acceptable.
7) Intervals for repeating the test should be available.
8) Adequate health service provision should be made for the extra clinical workload resulting from screening.
9) The risk both physical and psychological should be less than the benefits.
10) The cost should be balanced against the benefits.

When to Screen

Primary TSH based CH screening is practical and cost effective. TSH surge in newborn starts 30 mins after birth, peaks at 24hrs and persists for 48-72 hrs. Thus cord blood is spared of this effect. So sample for screening should be taken from cord blood or postnatal day3 - day5 sample. This largely eliminates false positive result due to TSH surge.[5]

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The advantage of cord blood sample screening is that it is painless and can be done in early discharge cases. But its disadvantage is that it cannot be used for screening of other metabolic disorder which are dependent on feeding.

The advantage of postnatal sample is that it can be used to test other metabolic disorders dependent on feeding like galactosemia, phenylketonuria while its disadvantage is that it requires a longer stay in hospital or revisit to hospital if mother gets discharged early.

Method

Cord blood is taken in a plain vacutainer and sent to lab for testing. Alternatively postnatal sample can be collected and sent. Sample is collected by heel puncture on the plantar surface of the foot. Circles are drawn on filter paper which is directly applied to puncture area. Blood sample should completely fill the circles. It is then air dried for 4 hrs at room temperature and then sent to lab. The filter paper should be attached to a card which carries all the information about the baby.

Which test TSH or T4

An ideal screening test should be highly sensitive and specific. 3 main screening types used are

1) Primary T4 screening
2) Primary TSH testing
3) Simultaneous T4 and TSH measurement

Primary TSH based CH screening is more specific, practical and cost effective.[6] Main drawback of primary TSH screening is that it may miss infants with delayed rise of TSH which is seen in preterm babies due to immaturity of the hypothalamic-pitutary-thyroid axis. It also cannot detect cases of central CH, hypothyroxenemia and infants with thyroid TBG deficiency. Confirmatory test is done if TSH is greater than cut-off value.

Recommendations for recall testing are:[7]

1) TSH > 20 mIU/L is the cut-off for recall.
2) TSH > 40 mIU/L is recommended for defining screen positive cases for immediate recall for venous blood confirmatory test.
3) TSH from 20-40mIU/L should have a second TSH screen at 7-10 days of age. TSH in this range can often be false positive or there may be transient hypothyroidism. Transient CH is common in premature infants in iodine deficient areas.

Case of central CH can be identified by primary T4 testing. There is higher chance of false positive result in case of primary T4 testing. Also it fails to detect newborn with compensated form of CH (where T4 levels are normal and TSH levels are high) which is commonly seen in ectopic thyroid, the most common cause of CH.

Abnormal values i.e. T4<6.5 microgram/dl or TSH >20 mIU/L should always be confirmed by a repeat testing of venous blood sampling.[9] Age related TSH cut off (>34 mIU/L) is recommended for samples taken between 24-48 hrs of age.

Overall primary TSH assay is the recommended method for screening.

TSH Cut Off

For TSH levels from 20 – 40 mIU/L, a repeat filter paper sample or a repeat serum sample should be taken at 7-10 days of age. This will allow the neonatal factors causing a false positive result to settle down. If the repeat TSH is > 20 mIU/L for age < 2 wks or > 10 mIU/L for age >2 wks , confirmatory test by fT4 and TSH should be done.[8]

For TSH > 40 mIU/L, newborn should be immediately recalled. Venous blood sample is sent for fT4 and TSH testing by chemiluminescence or ELISA assay.

Treatment with levothyroxine is started in following condition –

1) fT4 < 12pmol/L or <1.1 ng/dl, irrespective of TSH value.
2) fT4 < 15 pmol/ L or < 1.17 ng/dl with venous TSH >20 mIU/L if age is <2wks and >10 mIU/L if age is >2 wks.
3) Normal T4/fT4 with persistently elevated TSH > 10 mIU/L at age > 3 wks.

In newborn with TSH >= 80 mIU/L, therapy should be started immediately without waiting for the result of confirmatory test. All the preterm and low birth weight infants should undergo screening at 48-72 hrs of age.

Imaging is done for assessing the severity and cause of CH. Imaging should never cause a delay in initiation

of treatment. It should just be used to assess the severity and cause of disease. The thyroid gland should be imaged using either scintigraphy or ultrasonography or both.

Treatment

Levothyroxine is the drug of choice for treatment of hypothyroidism. It should be started as soon as possible and not later than 2 wks after birth. The dose is adjusted between 10-15 microgram/kg per day.

Follow up test should be done after 1-2 wks of start of treatment. Subsequent evaluation should take place every 2 wks until TSH value reaches normal. Then every 1-3 months until the age of 1 year. Then every 2-4 months until the age of 3 years. Thereafter every 3-12 months until growth is complete.

Conclusion

Hence we see that there is a definite need to include newborn screening in the public health program like immunization program. There is a considerable financial and emotional burden on the parents of child who develops the complication of congenital hypothyroidism. Screening the newborn for congenital hypothyroidism is the most cost effective way to prevent it.

One such platform to introduce newborn screening in national program is Rashtriya Bal Swasthya Karyakram (RBSK) which is launched by Ministry of Health and Family Welfare, Government of India under National Rural Health Mission. It involves screening of children from birth to 18 years of age for 32 common health conditions. Children who screen positive are provided with further follow up and treatment. At present screening of Congenital Hypothyroidism is optional for states and UTs. They may include it depending on epidemiological situation and availability of testing.

Now that an initiative has been started, we are hopeful that screening for Congenital Hypothyroidism will soon be made mandatory in national health program.

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