SCREENING

Sensitivity versus specificity: neonatal screening for congenital hypothyroidism

Newborn screening for congenital hypothyroidism (CH) with a TSH cut-off point of 20 mU/l misses an appreciable number of permanent CH cases, according to the results of a Greek neonatal screening program published in the *Journal of Clinical Endocrinology and Metabolism*. However, lowering the TSH cut-off to 10 mU/l identified children with CH who would otherwise have escaped diagnosis.

Previous studies have highlighted that some cases of CH are missed during screening, a finding that was also observed in the Greek neonatal program, in which a 20 mU/l TSH cut-off value was used. This finding prompted Mengreli *et al.* to evaluate the consequences of lowering the TSH threshold to 10 mU/l. The aim of the 3-year prospective study was twofold: to uncover the number of cases previously missed by screening (false negatives) and to identify the underlying pathogenetic cause in these missed cases.

Mengreli *et al.* evaluated a population of 311,390 newborns who underwent screening for CH at a single center in Greece. Of the infants diagnosed with CH ($n = 200$), 56 (28%) presented with TSH values between 10 mU/l and 20 mU/l. Follow-up of 47 infants with CH indicated that 40 (85.1%) suffered from permanent CH, a higher incidence than previously thought. Examination of the underlying causes of permanent CH revealed that eight infants (20%) had an anatomical defect of the thyroid gland, whereas the remainder had a functional defect. Premature birth was associated with a high probability of missed diagnosis of permanent CH.

> “...the lower cut-off applied resulted in improved sensitivity ... [but with] an increase in the number of false-positive results...”

Lowering the TSH cut-off point to 10 mU/l not only resulted in a 10-fold increased recall rate, but also demonstrated that a sizable number of CH cases were missed by use of the higher TSH threshold. Nonetheless, the lower TSH cut-off point increased the number of false-positive results by 10-fold. The aim of an effective screening program is to deliver high sensitivity (no missed cases) while retaining specificity (a low number of false-positive results). Mengreli highlights that “although the lower cut-off applied resulted in improved sensitivity, on the other hand, an increase in the number of false-positive results was observed, constituting a serious drawback.” Mengreli concludes that further studies of the utility of their modified CH screening cut-off value for TSH are still required.

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Original article Mengreli, C. *et al.* Screening for congenital hypothyroidism: the significance of threshold limit in false-negative results. *J. Clin. Endocrinol. Metab.* doi:10.1210/jc.2010-0057