Secretary's Advisory Committee on Newborn Screening

Meeting (by teleconference): Thursday, October 12, 2017

Report on Nomination to Newborn Screening for Carnitine

Palmitoyltransferase 1A Deficiency in Wisconsin

The advisory committee considered whether Carinitine Palmitoyltransferase 1A deficiency should be added to the Wisconsin mandatory newborn screening panel.

Carnitine palmitoyltransferase 1A (CPT1A) is an enzyme in the liver that is involved in transportation of long chain fatty acids into the mitochondria where they are broken down, processed, and stored (fatty acid oxidation). CPT1A deficiency is a rare metabolic disorder resulting in impaired mitochondrial fatty acid oxidation and accumulation of long chain fatty acids in the liver. Most affected individuals are asymptomatic at birth and usually present with hypoketotic hypoglycemia and sudden onset of liver failure during periods of increased energy demands. In newborns symptoms usually manifest with concurrent febrile or gastrointestinal illness and the onset is rapid. These episodes of metabolic crisis are potentially fatal and multiple episodes of decompensation cause neurological damage. CPT1A deficiency has also been associated with an increased risk of developing serious infection and renal tubular acidosis. CPT1A deficiency is inherited in an autosomal recessive fashion. Heterozygotes are asymptomatic and each child of individuals who are carriers has a 25% chance of being affected. The estimated overall prevalence is 1:500,000 to 1:1,000,000 newborns however, in the native Alaskan population the prevalence is 1.3:1,000 and in the Hutterite population the carrier rate may be as high as 1:16.

The committee considered whether CPT1A deficiency met each of the following nine criteria:

1. Mandated testing should be limited to conditions that cause serious health risks in childhood that are unlikely to be detected and prevented in the absence of newborn screening.
2. For each condition, there should be information about the incidence, morbidity, and mortality and the natural history of the disorder.
3. Conditions identified by newborn screening should be linked with interventions that have been shown in well-designed studies to be safe and effective in preventing serious health consequences.
4. The interventions should be reasonably available to affected newborns.
5. Appropriate follow-up should be available for newborns that have a false positive newborn screen.
6. The characteristics of mandated tests in the newborn population should be known including specificity, sensitivity, and predictive value or other convincing medical evidence (experience, natural history, or literature).
7. If a new sample collection system is needed to add a disorder, reliability and timeliness of sample collection must be demonstrated.
8. Before a test is added to the panel the details of reporting, follow-up, and management must be completely delineated including development of standard instructions, identification of consultants, and identification of appropriate referral centers throughout the state/region.

9. Recommendations and decisions should include consideration of the costs of the screening test, confirmatory testing, accompanying treatment, counseling, and the consequences of false positives. The mechanism of funding those costs should be identified. Expertise in economic factors should be available to those responsible for recommendations and decisions.

The committee unanimously agreed that criteria 1, 2, 3, 4, 7, and 8 were met and the majority of the committee agreed that criteria 5 and 9 were met. The committee unanimously voted that more information was needed to meet criterion six.

With regard to the view that more information is needed to meet criterion six, it is impossible to know the characteristics of this test because we have never screened for CPT1A deficiency. Because of the rarity of this condition, false positives are not anticipated and confirmatory genetic testing, that is readily available, will be used routinely. Collateral issues seen with other disorders seem unlikely, as unaffected individuals are unlikely to be identified; this is not a condition with late onset variants; and the treatment appears to be of low risk. It is unknown how many worldwide have been treated for CPT1A deficiency, but there are no known complications of treatment. Parental knowledge that their child has a propensity to decompensate with fasting is the key to treating this disorder.

A motion was made and seconded to add CPT1A deficiency to the required newborn screening panel. The committee voted unanimously to recommend the addition of CPT1A deficiency to the mandatory panel and the meeting concluded.

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