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ORIGINAL ARTICLE

A three-year follow-up of congenital adrenal hyperplasia newborn screening☆,☆☆

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KEYWORDS
Congenital Adrenal Hyperplasia;
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Abstract
Objective: congenital adrenal hyperplasia (CAH) newborn screening can prevent neonatal mortality in children with the salt-wasting form of the disease and prevent incorrect gender assignments, which can occur in females. However, the occurrence of false-positive results in preterm or low-birth-weight newborns creates some diagnostic difficulties, with consequent therapeutic implications. This study aimed to report the results of a pilot project for neonatal CAH screening conducted in the state of Minas Gerais, Brazil from 09/2007 to 05/2008 with a three-year follow-up.
Methods: dried blood specimens were collected on filter paper cards three to seven days after birth of all newborns in the period. Samples were analyzed for 17-hydroxyprogesterone using an enzyme-linked immunosorbent assay (ELISA).
Results: a total of 159,415 children were screened. The apparent incidence of the classic variant of the disease was 1:9,963, based on initial diagnoses following newborn screening. During the follow-up period, eight of 16 children initially diagnosed with CAH were reclassified as unaffected, resulting in a revised incidence of 1:19,927. The false-positive rate was 0.31%, and the positive predictive value was 2.1%. Sensitivity and specificity were 100% and 99.7%, respectively.
Conclusions: newborn screening is an important public health policy in developing countries such as Brazil, where CAH remains underdiagnosed. It has great potential to identify children

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☆☆ Study conducted at the Núcleo de Ações e Pesquisa em Apoio Diagnóstico (NUPAD), Faculdade de Medicina/Hospital das Clínicas, Universidade Federal de Minas Gerais (UFMG), Minas Gerais, MG, Brazil.
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with the disease who otherwise cannot be diagnosed earlier. Long-term follow-up and monitoring of all children with positive screening results are crucial to ensure a correct diagnosis and to calculate a reliable incidence ratio of the disease.

PALAVRAS-CHAVE
Hiperplasia Adrenal Congênita;
Triagem Neonatal;
Diagnóstico Precoce;
17-hidroxiprogesterona

Um acompanhamento de três anos da triagem neonatal para hiperplasia adrenal congênita

Resumo

Objetivo: a triagem neonatal para hiperplasia adrenal congênita (HAC) pode evitar a morte de recém-nascidos com a forma perdedora de sal e o registro civil incorreto das meninas. Entretanto, a ocorrência de resultados falso-positivos em recém-nascidos pré-termos ou com baixo peso ao nascer gera dificuldades diagnósticas, com consequentes implicações terapêuticas. O objetivo do estudo foi avaliar os resultados do projeto piloto de triagem neonatal para HAC realizado no estado de Minas Gerais, Brasil, de setembro de 2007 a maio de 2008 com acompanhamento de três anos.

Métodos: A dosagem da 17-hidroxiprogesterona foi realizada por ensaio imunoenzimático (ELISA), em amostras de sangue seco coletadas em papel-filtro, três a sete dias após o nascimento de todos os recém-nascidos no período.

Resultados: Foram triadas 159.415 crianças. Observou-se incidência de 1:9.963 para a forma clássica da doença, baseando-se nos diagnósticos iniciais. Durante o período de acompanhamento, 8 de 16 crianças inicialmente diagnosticadas com HAC foram reclassificadas como não afetadas, resultando em uma incidência corrigida de 1:19.927. A taxa de falsos positivos foi de 0,31%, e o valor preditivo positivo foi de 2,1%. A sensibilidade e a especificidade foram 100% e 99,7%, respectivamente.

Conclusões: a triagem neonatal é uma importante política de saúde pública para países em desenvolvimento como o Brasil, onde a HAC continua subdiagnosticada. Ela possui grande potencial para identificar crianças que poderiam não ter a doença reconhecida precocemente. O acompanhamento em longo prazo e o monitoramento de todas as crianças com resultados positivos na triagem são cruciais para confirmação diagnóstica e para o correto cálculo da incidência da doença.

Introduction

Congenital adrenal hyperplasia (CAH) consists of a group of inborn autosomal recessive disorders that are characterized by the deficiency of one of the enzymes involved in cortisol synthesis in the adrenal cortex. Over 90% of CAH cases are due to 21-hydroxylase deficiency (21-OHD), which is one of the most common inborn errors of metabolism, with a variable incidence according to ethnicity and geography.[1–3]

The global incidence of the classic form of CAH is 1:15,000 live births, as determined by screening programs. Frequencies varying from 1:10,000 to 1:14,000 have been observed in Europe. In North America, the incidence varies from 1:15,000 to 1:16,000. The reported rates of CAH have been as high as 1:280 among the Yupik people of Alaska and 1:2,100 on the French island of Réunion in the Indian Ocean; both of these populations are geographically isolated.[4] The reported incidence of CAH in the two Brazilian states that have routinely included CAH in their public newborn screening programs is 1:11,655 in the South (Santa Catarina) and 1:10,325 in the Midwest (Goiás).[5,6]

Newborn screening for CAH, which is now performed in many countries, has reduced the number of deaths by enabling earlier diagnosis.[1] In females, the classic form of the disease can be diagnosed through the detection of ambiguous genitalia (AG) at birth. In males, however, the absence of overt physical signs at birth can lead to avoidable deaths caused by salt-losing crises.

The main goals of screening are to detect the severe, salt-wasting (SW) form of the disease; to prevent shock, brain damage or death, by implementing pre-symptomatic treatment; and to prevent or shorten the period of incorrect gender assignment that can occur in females.[7,8] However, the occurrence of false-positive results in sick children, preterm or low birth weight newborns creates some diagnostic difficulties, with consequent therapeutic implications.[9] Newborn screening for CAH also provides knowledge of the real incidence of the disease in the population.

The objective of this study was to provide the results of a pilot project for neonatal CAH screening developed in the state of Minas Gerais (MG), Brazil, aimed at establishing a routine program.

Methods

The pilot project for neonatal CAH screening was included in the newborn screening program of the State of Minas Gerais (PTN-MG) from September of 2007 to May of 2008.

This study was approved by the Research Ethics Committee of the Universidade Federal de Minas Gerais (UFMG), Brazil (ETIC 392/07) and by the Minas Gerais State Health