J Pediatr (Rio J). 2015;91(6):590–595

Jornal de Pediatria
www.jped.com.br

REVIEW ARTICLE

Sweat conductivity and coulometric quantitative test in neonatal cystic fibrosis screening☆

Mouseline Torquato Domingos[a,*], **Neiva Isabel Rodrigues Magdalena**[b], **Mônica Nunes Lima Cat**[b], **Alexandra Mitiru Watanabe**[a], **Nelson Augusto Rosário Filho**[b]

[a] *Serviço de Referência em Triagem Neonatal (SRTN), Fundação Ecumênica de Proteção ao Excepcional (FEPE), Curitiba, PR, Brazil*
[b] *Department of Pediatrics, Universidade Federal do Paraná (UFPR), Curitiba, PR, Brazil*

Received 12 September 2014; accepted 11 March 2015
Available online 16 June 2015

KEYWORDS
Cystic fibrosis;
Neonatal screening;
Sweat test;
Conductivity;
Pilocarpine;
Coulometric measurement

Abstract
Objective: To compare the results obtained with the sweat test using the conductivity method and coulometric measurement of sweat chloride in newborns (NBs) with suspected cystic fibrosis (CF) in the neonatal screening program.
Methods: The sweat test was performed simultaneously by both methods in children with and without CF. The cutoff values to confirm CF were >50 mmol/L in the conductivity and >60 mmol/L in the coulometric test.
Results: There were 444 infants without CF (185 males, 234 females, and 24 unreported) submitted to the sweat test through conductivity and coulometric measurement simultaneously, obtaining median results of 32 mmol/L and 12 mmol/L, respectively. For 90 infants with CF, the median values of conductivity and coulometric measurement were 108 mmol/L and 97 mmol/L, respectively. The false positive rate for conductivity was 16.7%, and was higher than 50 mmol/L in all patients with CF, which gives this method a sensitivity of 100% (95% CI: 93.8–97.8), specificity of 96.2% (95% CI: 93.8–97.8), positive predictive value of 83.3% (95% CI: 74.4–91.1), negative predictive value of 100% (95% CI: 90.5–109.4), and 9.8% accuracy. The correlation between the methods was $r = 0.97$ ($p > 0.001$). The best suggested cutoff value was 69.0 mmol/L, with a kappa coefficient = 0.89.
Conclusion: The conductivity test showed excellent correlation with the quantitative coulometric test, high sensitivity and specificity, and can be used in the diagnosis of CF in children detected through newborn screening.

☆ Please cite this article as: Domingos MT, Magdalena NI, Cat MN, Watanabe AM, Rosário Filho NA. Sweat conductivity and coulometric quantitative test in neonatal cystic fibrosis screening. J Pediatr (Rio J). 2015;91:590–5.

* Corresponding author.
E-mail: mussetd@hotmail.com (M.T. Domingos).

http://dx.doi.org/10.1016/j.jped.2015.03.003

PALAVRAS-CHAVE
Fibrose cística;
Triagem neonatal;
Teste do suor;
Condutividade;
Pilocarpina;
Dosagem coulométrica

Condutividade e teste quantitativo coulométrico na triagem neonatal para fibrose cística

Resumo

Objetivo: Comparar os resultados obtidos no teste do suor pelo método da condutividade e a dosagem coulométrica de cloreto no suor em recém nascidos (RN) suspeitos da triagem neonatal para fibrose cística (FC).

Métodos: O teste do suor foi realizado simultaneamente pelos dois métodos em crianças com e sem FC. Os valores de corte para confirmar FC foram na condutividade > 50 mmol/L e no teste coulométrico > 60 mmol/L.

Resultados: Quatrocentos e quarenta e quatro RN sem FC (185 do sexo masculino, 234 femininos e 24 não informado) realizaram o teste do suor por condutividade e dosagem coulométrica simultaneamente e obtiveram resultado mediano de 32 mmol/L e 12 mmol/L respectivamente. Para os noventa RN com FC os valores medianos de condutividade e dosagem coulométrica foram 108 mmol/L e 97 mmol/L respectivamente. O índice de falso positivo para condutividade foi de 16,7% e em todos os pacientes FC foi superior a 50 mmol/L conferindo ao método 100% de sensibilidade (IC 95% = 93,8 a 97,8), especificidade de 96,2% (IC 95% = 93,8 a 97,8), valor preditivo positivo 83,3 (IC 95% = 74,4 a 91,1), valor preditivo negativo 100% (IC 95% = 90,5 a 109,4) e acurácia 9,8%. A correlação entre os métodos foi de r = 0,97 (p > 0,001).O melhor valor de corte sugerido foi de 69,0 mmol/L, coeficiente de kappa = 0,89.

Conclusão: O teste da condutividade apresentou excelente correlação com o quantitativo coulométrico, alta sensibilidade e especificidade, podendo ser utilizado no diagnóstico da FC em crianças detectadas pela triagem neonatal.

Introduction

Cystic fibrosis (CF) is an autosomal recessive disease, resulting from mutations in the gene located in the long arm of chromosome 7, cystic fibrosis transmembrane conductance regulator (CFTR), with an incidence of about 1:10,000 in Brazil.[1,2] It is a multisystemic disease and pulmonary involvement accounts for the majority of patient morbimortality. The clinical signs and symptoms include chronic pulmonary disease, pancreatic failure, and abnormalities in the gastrointestinal tract and sweat gland secreting channels, with an increase of chloride concentration in the sweat.[3–5] Survival depends on early diagnosis confirmation and treatment initiation at the early stages of the disease. Identification is attained by the presence of signs or symptoms; family history; altered immunoreactive trypsin (IRT) in neonatal screening and confirmed by positive sweat test in two separate measurements, presence of two CF mutations, or altered nasal potential difference test. The latter test requires considerable skill, and is rarely used in Brazil.[6,7]

In Brazil, CF screening was introduced in the National Neonatal Screening Program (PNTN) in 2001 with the immunoreactive trypsin test (IRT) performed in blood collected from newborns and the sweat test.[2]

The confirmatory test, the gold standard, is the quantitative analysis of electrolytes in sweat, with an accuracy >90%.[8] Sweating is stimulated by pilocarpine, performed by iontophoresis; sweat is obtained using the Gibson and Cooke method. However, skill is necessary to prevent evaporation during collection and the subsequent determination of sweat weight on an analytical scale, followed by the accurate chemical composition of the sample. The sweat collection system with a capillary microtube Macroduct® (Wescor Inc., Logan, UT, USA) has been widely used due to its simplicity and efficiency. The microtube prevents evaporation, and the weighing and dilution steps are eliminated.

Sweat can have its ionic composition analyzed immediately or be submitted to a conductivity analyzer prior to chemical determination.[9] The test is positive if the chloride concentration is >60 mmol/L in at least two independent measurements.[8,10] For infants younger than 6 months, values between 30 mmol/L and 50 mmol/L are considered suspect.[9–11] The conductivity test also constitutes an alternative and valid method for the laboratory diagnosis of CF.[7,8,10] The system measures the capacity of the sweat to conduct electrical current in milliamperes (mAs), which depends on the concentration of Na^+ and Cl^-.[12]

The Sweat Check 3120® (Wescor Inc., Logan, UT, USA) conductivity analyzer, specifically designed for use with the Macroduct® (Wescor Inc., Logan, UT, USA) sweat collector, measures conductivity in a 6–10 μL sample. Values >80 mmol/L and a compatible clinical setting justify the start of treatment, whereas values between 50 mmol/L and 80 mmol/L indicate the need to perform the quantitative test, because conductivity is considered a screening method, as it is not selective to the chloride ion.[8–10] The aim of this study was to compare chloride levels in sweat by the quantitative coulometric test with conductivity values in newborns with and without CF, from the neonatal screening program of the state of Paraná.

Methods

This study was approved by the Ethics Committee of HC-UFPR, registered under No. 271EXT025/2008-06, CAAE 0117.0.208.000-08. This was a prospective, cross-sectional,