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Title **The Relevance of the Neonatal Urine Screening for Inborn Errors of Metabolism Performed in Québec**

Agency **AETMIS, Agence d'évaluation des technologies et des modes d'intervention en santé**
2021 avenue Union, suite 10.083, Montréal, Québec H3A 2S9, Canada;
Tel: +1 514 873 2563, Fax: +1 514 873 1369; aetmis@aetmis.gouv.qc.ca,
www.aetmis.gouv.qc.ca

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Aim

To assess the scientific relevance of screening for 18 diseases that has been detected in at least one child in Québec since 1973 under the Québec Newborn Urine Screening Program (QNUSP), to weigh its benefits and drawbacks, and to evaluate the efficacy and efficiency of screening techniques.

Conclusions and results

The lack of relevant evidence to address screening criteria for rare diseases makes it difficult to determine the full range of inborn errors of metabolism (IEMs) that should be screened for. Only those tested for under the QNUSP were examined. For these diseases, mass neonatal screening using tandem mass spectrometry (MS/MS) on blood samples seems more effective than multiplex thin-layer chromatography (TLC) on urine samples for: urea cycle disorders, triple H syndrome, methylmalonic aciduria, propionic aciduria, 3-methylcrotonylglycinuria I, and glutaric aciduria I. Cystathioninuria, hypersarcosinemia, hyperhistidinemia, and Hartnup disorder, generally benign conditions, should not be screened for. The debatable benefits of early screening for cystinuria, dicarboxylicamino aciduria, Fanconi-Bickel syndrome, prolidase deficiency, and pyroglutamic aciduria remain unresolved because of a lack of evidence. Waiting until the 21st day of life to obtain a urine sample (presently the case) can considerably affect screening performance. Hence, performing MS/MS on blood samples during the first few days of life appears to be more advantageous. MS/MS has an excellent level of diagnostic accuracy and is a quantitative method that is easier to standardize than the semi-quantitative TLC method, which depends on the interpreter's expertise. The relevance of adding other IEMs for neonatal screening should be assessed in a planned manner based on available scientific evidence.

Methods

A list of 14 screening criteria based on UK National Screening Committee criteria, and used for a report on neonatal blood screening done at the *Institut national de santé publique du Québec* to determine screening relevance, served as a basis for this assessment. Sources of information for evaluating clinical relevance included specialized manuals, recent literature reviews, and evidence based assessment reports from 1995 to August 2008. A systematic review (SR) of the literature with no time limit was carried out for neonatal urine screening by TLC. Primary study quality was assessed using the QUADAS checklist. SR of economic studies published since 1975 on urine screening with TLC was carried out, and the SR from a previous AETMIS report on MS/MS was updated. A SR updating the previous reports on ethical, psychosocial and organizational issues related to TLC and urine screening programs was carried out with no backward time limit, up to August 2008. Interviews with pediatricians were conducted to better understand specific issues related to clinical and organizational aspects of the program.

Further research/reviews required

The performance and viability of the QNUSP should be evaluated with regard to metabolite transport disorders that cannot be detected by blood sampling: cystinuria, Fanconi-Bickel syndrome, and dicarboxylicamino aciduria. Screening methods for these renal disorders should be reviewed, although the relevance of such screening remains controversial due to a lack of evidence on efficacy.

Written by Jolianne Renaud and Pierre Dagenais, AETMIS, Canada

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