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Title **Clinical Effectiveness of Newborn Screening for Inborn Errors of Metabolism Using Tandem Mass Spectrometry. Systematic Review**

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www.sergas.es/MostrarContidos_N3_T02.aspx?IdPaxina=60056&uri=http://www.sergas.es/Docs/Avalia-t/InfTandem.pdf&hifr=900&seccion=0&seccion=0

Aim

To analyze the state of knowledge on the efficacy/effectiveness of neonatal screening of hereditary metabolic diseases, using tandem mass spectrometry; and to compare the neonatal screening services offered in Spain's various Autonomous Regions (ARs).

Conclusions and results

Of 305 studies retrieved in the second search, 9 were included. Many were lacking in quality, and outcome variables and study populations were heterogeneous. MS/MS sensitivity, specificity, and PPV values varied depending on the inborn errors of metabolism (IEM) (sensitivity 91.7%-100%; specificity 99.3%-99.9%; and PPV 2.0%-53%). While the introduction of screening for phenylketonuria (PKU) and medium chain acyl coenzyme A dehydrogenase (MCAD) deficiency yielded benefits in morbidity-mortality, the evidence was unclear for glutaric acidemia type I and tyrosinemia type I. Current knowledge does not support inclusion of the remaining IEM in neonatal screening programs. In Spain, 21 laboratories serve the neonatal screening programs in the ARs.

- The quality and heterogeneity of existing studies on MS/MS-based detection of IEM render comparison difficult and prevent definitive and categorical conclusions on the different aspects assessed.
- MS/MS has a potential for simultaneous detection of a wide range of IEM. It is a rapid and highly sensitive and specific technology for detecting MCAD deficiency and PKU, with these being the best candidates for inclusion in a MS/MS-expanded screening program. Doubts exist as to glutaric acidemia type I and tyrosinemia type I, and no evidence supports the inclusion of the remaining IEM.

Recommendations

- Any decision to include a given disorder in a neonatal screening program must be based on screening's ability to favorably alter the prognosis following early detection and intervention.
- As a priority, it is necessary to draw a portfolio of services in the context of early detection of IEM, based on systematic assessment of their effectiveness and social efficiency. Different aspects of the screening programs in Spain must be standardized by defining common criteria for outcome variables, quality control indices, specimen storage, and incorporating new disorders into screening.
- It is advisable to establish a case registry to enable active and regular follow-up of patients with confirmed diagnoses of IEM which, for healthcare, teaching, and research purposes, would pool information on incidence, trends, survival, etc linked to neonatal screening of metabolic diseases.

Methods

A systematic literature review covered the main biomedical databases. An initial bibliographic search retrieved 6 systematic reviews, whereof the 2004 *NHS R&D Health Technology Assessment Programme* best suited our objectives and was updated accordingly. In the second search, we selected papers using inclusion and exclusion criteria on study design, patient characteristics, and outcome variables analyzed. Data sources included MEDLINE, EMBASE, Cochrane Library Plus, NHS Centre for Reviews and Dissemination, Health Technology Assessment (HTA), and DARE.

Further research/reviews required

Further studies must ascertain the sensitivity and specificity of tandem mass spectrometry in detecting other IEM by assessing the long-term effectiveness of diagnostic strategies and conventional treatment, and the potential impact of early diagnosis using MS/MS.

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