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Title Clinical effectiveness of newborn errors of metabolism using mass spectrometry. Part II: mehylmalonic academia, propionic academia, tyrosinemia type I

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Reference avalia-t 201402, http://www.sergas.es/docs/Avalia-t/avalia-t201402Cribado-ECM-II.pdf

Aim

To assess the clinical effectiveness of newborn screening of the following diseases, i.e., methylmalonic acidemia, propionic acidemia and tyrosinaemia type 1.

Conclusions and results

- The evidence of the effectiveness of screening programmes of inborn errors of metabolism evaluated in this review is of low quality and is based on observational studies –fundamentally longitudinal or comparative case series and cross-sectional studies without a control group- with direct evidence being furnished in only some cases.
- Neither methylmalonic nor propionic acidemia would meet the requirement of having a sufficiently long latency period to ensure that the screening programme could yield the expected benefit, if there were no way of guaranteeing that results could be obtained before symptom onset. Although screening seems to reduce immediate mortality in MMA, there is no direct evidence that would enable conclusions to be drawn about its effects on short- and long-term morbidity and mortality. In the case of PA, screening does not seem to prevent the number of metabolic decompensations or alterations in the cognitive development of such patients. A comparative study reported that mortality was lower among patients diagnosed through newborn screening than among those diagnosed on the basis of clinical signs and symptoms, though without this proving statistically significant.
- Tyrosinaemia type 1 has a sufficiently long latency period to ensure that the screening programme could achieve the benefit expected from the intervention, since newborns do not present with the disease until the first weeks or months of life. With respect to the screening test, exclusive quantification of tyrosine levels has been shown to have negligible value as a marker, displaying little sensitivity and specificity. Accumulation of plasma SUAC is pathognomonic, so that the development of MS/MS screening methods for determination of its concentration increases specificity and reduces the risk of FPs, FNs and the recall rate. One of the chief contributions of screening is the early detection of a cause of acute liver failure, leading to the prevention of liver disease mortality and the possible development of hepatocellular carcinoma in chronic forms.
- Thanks to the efficacy of the treatment and the existence of a specific test for detection of tyrosinaemia type 1 in a dried blood spot sample (SUAC), this inborn error of metabolism meets the criteria for benefiting from the advantages of newborn screening.
- Before implementing a screening programme, a suitable protocol must be drawn up to maximise the test's sensitivity and specificity, stipulating the analytes to be used, the specific cut-off points for each population and laboratory and, where applicable, the need for second-tier testing.
- Lastly, it is essential to set up information systems based on pertinent, relevant and reliable results, which would make it possible to assess whether the activities or processes developed within the context of a given screening programme were in line with health needs, from the standpoint of both the population and the health-care system. Furthermore, such information would serve as an aid for measuring goal achievement, establishing priorities and making decisions.

Methods

Systematic literature review of the principal biomedical databases (Medline, Embase, Cochrane Library Plus, Health Technology Assessment, Database of Abstracts of Reviews of Effects, National Health Service Economic Evaluation Database, ISI Web of Science and *Índice Médico Español*, among others). Two search strategies were used, one centred on epidemiology, natural history, morbidity, mortality, diagnosis and treatment, and the other centred on the screening of the disease. To retrieve all existing systematic reviews and assessment reports on screening programmes, we updated the bibliographic search of the *avalia-t* report from 1 January 2006 to June 2013. Studies were selected on the basis of a series of inclusion/exclusion criteria.

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