Newborn screening for inborn errors of metabolism

This is an excerpt from the full technical report, which is written in Norwegian.

The excerpt provides the report's main messages in English.

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Norwegian Knowledge Centre for the Health Services summarizes and disseminates evidence concerning the effect of treatments, methods, and interventions in health services, in addition to monitoring health service quality. Our goal is to support good decision making in order to provide patients in Norway with the best possible care. The Centre is organized under The Norwegian Directorate for Health, but is scientifically and professionally independent. The Centre has no authority to develop health policy or responsibility to implement policies.

We would like to thank all contributers for their expertise in this project. Norwegian Knowledge Centre for the Health Services assumes final responsibility for the content of this report.

Norwegian Knowledge Centre for the Health Services
Oslo, December 2007

Key messages

Newborn screening for inborn errors of metabolism
Currently in Norway, we screen our newborn for two inherited metabolic disorders: Congenital hypothyroidism (CH) and Phenylketonuria (PKU).

There is now a proposal to expand the newborn screening program with an additional 19 inherited metabolic disorders:

- Maple syrup urine disease, MSUD
- Tyrosinemia type 1 and 2, TH1 and 2
- Homocystinuria, HCU
- Propionic acidaemia, PA
- Methylmalonyl- CoA mutase deficiency, MMA
- Multiple carboxylase deficiency, MCD/ BIOT
- Glutaryl-CoA dehydrogenase deficiency, GA1
- Hydroxymethylglutaryl-CoA lyase deficiency, HMG/ 3MGA
- 3-Methylcrotonyl-CoA carboxylase deficiency, 3-MCC
- 3-Ketothiolase deficiency, BKT
- Isovaleric acidaemia, IVA
- Medium-chain acyl-CoA dehydrogenase deficiency, MCAD
- Very long-chain acyl-CoA dehydrogenase deficiency, VLCAD
- Long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency, LCHAD
- Multiple acyl-CoA dehydrogenase deficiency, GA2
- Carnitine transporter defect, CTD
- Carnitine palmitoyl transferase deficiency 1 and 2, CPT1 and 2
- Carnitine acylcarnitine translocase deficiency, CACT
- Congenial adrenal hyperplasia, CAH

These are rare diseases in Norway. The proposed disorders can cause serious morbidity including mortality if left untreated. The majority of these diseases can be treated by customized diets.

For 17 of the inherited metabolic disorders, we did not find summarized documentation describing the effect of newborn screening.

We found systematic reviews regarding newborn screening for four of the inherited metabolic diseases; PKU, tyrosenemia, MCAD and CAH. Mortality was reported only for MCAD and CAH. The overall quality of the evidence is very low.

We do not know what effect to expect from newborn screening for inherited metabolic disorders.

Executive summary

English

Newborn screening for inborn errors of metabolism

BACKGROUND

Currently in Norway, we screen our newborn for two inherited metabolic disorders: Congenital hypothyroidism and Phenylketonuria.

There is now a proposal to expand the newborn screening program with an additional 19 inherited metabolic disorders. These are rare diseases in Norway. The proposed disorders can cause serious morbidity including mortality if left untreated. The majority of these diseases can be treated by customized diets.

A blood sample is collected between 60 and 72 hours after birth by the heel prick method. An expanded newborn screening program will require the same blood sample as during current practice. Using tandem mass spectrometry (MS/MS) a metabolic profile of amino acids and acylcarnitines is available in two minutes.

The main aim of newborn screening is to detect children with the disease, the 'true positive'. But screening tests may also find 'false positive', which means that sometimes the test gives the wrong answer and is positive for a healthy person. 'True negative' are those who are well and the test say are well. It is also possible that the test gives the wrong answer to someone who has the disease, this is called 'false negative'.

The Norwegian Knowledge Centre for the Health Services was requested by the Directorate for Health and Social Affairs to summarise the available systematic reviews on the effect of newborn screening for inherited metabolic diseases.

METHOD

In July 2007 we searched in six databases for systematic reviews on newborn screening for the two inborn metabolic diseases we currently screen for and for the 19 disorders that are proposed in the extended screening program.

Currently in Norway, we screen our newborn for two inherited metabolic disorders: Congenital hypothyroidism (CH) and Phenylketonuria (PKU).

There is now a proposal to expand the newborn screening program with an additional 19 inherited metabolic disorders:

- Maple syrup urine disease, MSUD
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The main outcomes we included were mortality, up to three critical clinical outcomes (specific to each disease), quality of life, proportion of false positive tests measured against a reference standard, proportion of false negative tests measured against a reference standard, sensitivity and specificity.

We critically appraised the identified systematic reviews using our check lists. We included systematic reviews of high quality. We assessed the overall quality of the evidence for each of the main outcomes using GRADE.

RESULTS

We assessed 170 articles based on titles and abstract, and included eight systematic reviews.

For 17 of the inherited metabolic disorders, we did not find summarized documentation describing the effect of newborn screening.

We found systematic reviews regarding newborn screening for four of the inherited metabolic diseases; PKU, tyrosenemia, MCAD and CAH. All the results were from

observational studies, the available information about the effect of newborn screening is sparse, and of very low quality of evidence for all of these four inherited metabolic diseases.

Mortality was reported only for MCAD and CAH. The results are difficult to interpret because of the sparseness of information.

Quality of life was not reported in any of the included systematic reviews.

The test qualities that are reported are difficult to interpret because of variation in the timing of the studies, differences in test populations, control groups, cut off limits and test combinations.

DISCUSSION

In this overview of systematic reviews we only found sparse amounts of summarised information about newborn screening for inherited metabolic diseases. The information that we did find was of very low quality.

Overviews of reviews are prone to quickly go out of date as new studies are published continuously.

The information on the four inherited metabolic diseases for which summarised documentation was found, was summarised in systematic reviews published in 2007. However, the included evidence, the results from the studies included in the systematic reviews was sparse and of very low quality.

CONCLUSION

We do not know what effect to expect from newborn screening for inherited metabolic disorders.

NEED FOR FURTHER RESEARCH

There is a lack of systematic reviews on the effect of newborn screening for the majority of the inherited metabolic diseases.

If the newborn screening program is expanded, its effectiveness should be evaluated.

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