Newborn screening for tyrosinaemia type 1: Benefit unclear

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Tyrosinaemia type 1 is a rare, hereditary metabolic disease that, if left untreated, can already lead to serious liver and kidney damage in infancy. The German Institute for Quality and Efficiency in Health Care (IQWiG) investigated the benefit and harm of tandem mass spectrometry screening for tyrosinaemia type 1 in newborns.

In its report published on 27 September 2016 the Institute concludes that the benefit and harm of this type of screening remain unclear due to a lack of informative studies. However, unnecessary treatments through screening seem to be unlikely, as positive test results can be verified by subsequent gene analysis.

Untreated children are at risk of serious liver and kidney damage

Tyrosine is an amino acid contained in dietary proteins. In patients with tyrosinaemia type 1, a gene mutation leads to a defect in an enzyme that contributes to breaking down tyrosine. This results in the formation of toxic metabolites that can seriously damage organs such as the liver, the kidneys as well as the brain and peripheral nerves. Currently, tyrosinaemia type 1 is routinely treated with drugs (NTBC, nitisinone) and a low-protein diet. Medical professionals assume that treating the condition as early as possible increases the chances of preventing organ damage.

Tyrosinaemia type 1 not yet included in the German routine screening programme

Germany is conducting the so-called expanded newborn screening programme; participation in these screening tests is voluntary. The aim is the early detection of diseases that could jeopardize physical or mental development. Which diseases are included and which tests are used is specified by the Federal Joint Committee (G-BA) in the so-called Paediatric Directives. Tyrosinaemia type 1 is not yet included there.

The G-BA commissioned IQWiG to assess the benefit and harm of tandem mass spectrometry screening for tyrosinaemia type 1 in newborns. This is a procedure with which, among other things, dried blood is analysed.

Studies with a lower evidence level also searched for

The certainty of conclusions of cohort studies is considerably lower than that of randomized controlled trials (RCTs); their results are thus less robust. Nevertheless, IQWiG searched not only for RCTs but also for controlled cohort studies, including those with retrospective and historical comparisons. This is because due to the rarity of the disease, it was to be expected that only relatively few study data would be available. Worldwide, tyrosinaemia type 1 only affects about 1 in 100,000 children; a total of 25 children were treated in hospital in Germany in 2013.

Studies compared an earlier versus a later start of treatment

The IQWiG researchers found no study comparing the health advantages and disadvantages in a group with screening versus a group without

screening.

However, they identified a few intervention studies comparing an earlier with a later start of treatment and reporting patient-relevant outcomes such as mortality, liver failure or hospital stays. IQWiG could also include a study on diagnostic accuracy in the assessment; this study verified positive test results from tandem mass spectrometry by means of subsequent gene analysis.

No dramatic effects

Due to the design of the studies, differences between the study groups would have had to have been very large in order to derive an advantage or disadvantage of screening from them. If a "dramatic effect" is shown, the benefit or harm of medical interventions can also be proven with non-RCTs.

However, this was not the case in any of the studies included, as the differences measured were not large enough. It could not be reliably determined from these studies that treatment starting only after first symptoms occur more often leads to serious organ damage in affected children.

Likewise, the study on diagnostic accuracy showed only limited robustness, as, among other things, information on the selection of patients and on the study schedule was missing.

Potential harm is limited

Consequently, suitable data are lacking to be able to weigh the benefit and harm of an earlier versus a later start of treatment or to assess the diagnostic quality of the test. As positive test results can be verified by

subsequent gene analysis, unnecessary treatments through screening seem to be unlikely. At most, potential harm could affect parents: following a positive test result, they may experience strong psychological stress, even if the genetic test ultimately yields an "all clear".

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