IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Newborn screening for critical congenital heart defects using pulse oximetry[1]

Executive Summary

[1] Translation of the executive summary of the final report *Screening auf kritische angeborene Herzfehler mittels Pulsoxymetrie bei Neugeborenen* (Version 1.0; Status: 11 March 2015). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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This report was prepared in collaboration with external experts.

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According to §139 b (3) No. 2 of Social Code Book (SGB) V, Statutory Health Insurance, external experts who are involved in the Institute's research commissions must disclose "all connections to interest groups and contract organizations, particularly in the pharmaceutical and medical devices industries, including details on the type and amount of any remuneration received". The Institute received the completed *Form for disclosure of potential conflicts of interest* from each external expert. The information provided was reviewed by a Committee of the Institute specifically established to assess conflicts of interests. The information on conflicts of interest provided by the external experts is presented in Appendix H of the full report. No conflicts of interest were detected that could endanger professional independence with regard to the work on the present commission.

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IQWiG thanks the external experts for their collaboration in the project.

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Executive summary

With its letter of 26 June 2013, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess newborn screening for critical congenital heart defects (CCHD) using pulse oximetry.

Research question

The aim of the present investigation is the benefit assessment of pulse oximetry screening as an add-on test to the existing diagnostic standard (U1 and U2 screening or comparable clinical examinations) versus the existing diagnostic standard without pulse oximetry screening. Pulse oximetry screening as an add-on test versus the existing diagnostic standard with selective use of pulse oximetry was also to be investigated.

Methods

Comparative intervention studies were included that investigated pulse oximetry screening as an add-on test to existing screening (U1 and U2) or comparable clinical examinations, where applicable, with selective use of pulse oximetry, in respect of

- mortality
- morbidity (e.g. severe heart failure, severe hypoxia, cardiogenic shock, severe pulmonary hypertension)
- health-related quality of life of the child (measured, e.g., by proxy rating).
- psychosocial development (e.g. communication skills, social integration, development of self-concept)
- emotional development (e.g. behavioural disorders)
- gross and fine motor development
- cognitive and educational development (e.g. school performance, kindergarten / school placement / mode of schooling, training opportunities)
- inpatient treatment of any cause (e.g. number of operations, duration of stay)
- adverse events

In addition, studies were included on the diagnostic accuracy of pulse oximetry screening as an add-on test versus the existing diagnostic standard without pulse oximetry. The minimum follow-up period of the studies (in the case of follow-up as a reference test) was 6 months.

For this purpose, a systematic literature search was conducted in the following databases: MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (Clinical Trials). In addition, parallel to the search for relevant primary studies, a search for relevant systematic reviews was conducted in the MEDLINE and EMBASE databases, as well as in the Cochrane Database of Systematic Reviews (Cochrane Reviews), the Database of

Abstracts of Reviews of Effects (Other Reviews), and the Health Technology Assessment Database (Technology Assessments). The last search was conducted on 25 November 2014.

In addition, systematic reviews, reports from publicly available trial registries, documents transferred by the G-BA, and publications that had been provided in the hearing procedure for the preliminary report plan were screened. Furthermore, authors of the publications of relevant studies were contacted in writing to clarify important questions.

The selection of relevant studies from the results of the searches of bibliographic databases and publicly available trial registries, as well as the screening of documents transferred by the G-BA, was performed by 2 reviewers independently of each other. The selection of relevant studies from the other sources was conducted by 1 reviewer and checked by another.

Data were extracted into standardized tables. To evaluate the certainty of results, the risk of bias at study level was assessed, also at the outcome level in intervention studies, and in each case rated as low or high. For diagnostic accuracy studies, the category "unclear" was added following QUADAS 2. The results of the comparative intervention study were organized by outcomes and described. If the studies were comparable regarding the research question and relevant characteristics, the individual results were to be pooled quantitatively by means of meta-analyses.

Results

A total of 6 studies were identified as relevant for the research question of the present benefit assessment.

The studies investigated the benefit of pulse oximetry screening as an add-on test to the existing diagnostic standard for the detection of CCHD: 1 was a comparative intervention study and 5 were diagnostic accuracy studies. The latter were included in the benefit assessment as the underlying assumption of the report was that, due to the specific constellation of the clearly positive effects of treatment for CCHD, earlier versus later diagnosis and treatment are accompanied by a more favourable prognosis.

The result of the comparative intervention study supports the hypothesis that pulse oximetry screening as an add-on test to a routine clinical examination reduces disease-specific morbidity in newborns with CCHD (odds ratio [OR]: 0.268 [0.110; 0.654], p = 0.003 for the outcome "severe preoperative acidosis"). An added benefit of pulse oximetry screening cannot be inferred from this study alone, which is largely due to the low qualitative certainty of results, the different prevalence in the study groups, and the incomplete follow-up of newborns included towards the end of the study.

The results of the 5 diagnostic accuracy studies included should be viewed against this background. From these studies it can be derived that pulse oximetry screening detected additional newborns with CCHD whose findings were initially inconspicuous in the routine clinical examination.

Due to an insufficient evidence base the results of the studies could not be pooled, so that the individual studies were drawn upon to present results. In all studies, additional children with CCHD were identified by pulse oximetry screening. In 2 studies, information on prevalence was also available. These studies show that between 60% and 78% of children with CCHD are additionally detected by pulse oximetry screening. In relation to the newborns examined, this means a number needed to screen (NNS) of between 421 and 7100, that is, in order to find 1 additional newborn with CCHD, between 421 and 7100 asymptomatic newborns in the studies had to undergo pulse oximetry screening as an add-on test to a routine clinical examination.

The predictive positive value (PPV) lay between 25.9% und 75%. A quarter to three-quarters of newborns with conspicuous findings in pulse oximetry screening actually suffered from CCHD. Conversely, it can be derived from the PPV that likewise, a quarter to three-quarters of newborns with conspicuous findings in pulse oximetry screening did not suffer from CCHD. In these cases of false-positive findings, unnecessary treatment might be initiated. The study data show that in relation to CCHD, in 70% to 100% of cases false-positive findings could be ascribed to other largely neonatal diseases. These unintended findings were classified as false-positive within the present assessment; nevertheless, they are often considered to be in urgent need of treatment. This means that for 1 identified newborn with CCHD, pulse oximetry screening identifies between 2 and 8 newborns with such unintended findings who can already be referred to further diagnostic procedures and treatment in an asymptomatic stage of disease. However, the advantages and disadvantages of earlier detection and treatment of these diseases cannot be assessed on the basis of the studies included.

Conclusion

Pulse oximetry screening shows a hint of a benefit as an add-on screening test to the existing diagnostic standard (U1 and U2 screening or comparable clinical examinations) for the detection of CCHD in asymptomatic newborns. This result is based on 1 comparative intervention study and 5 diagnostic accuracy studies. The latter consistently show that pulse oximetry screening detects additional newborns with CCHD whose findings were initially inconspicuous in the routine clinical examination. The result of the comparative intervention study supports the hypothesis that disease-specific morbidity in newborns with CCHD can be reduced by additional pulse oximetry screening. A statistically significant difference in favour of pulse oximetry screening was shown for the outcome “severe preoperative acidosis” in newborns with CCHD. There is an insufficient evidence base to weigh benefit and harm with regard to the unintended findings additionally detected by pulse oximetry screening.

Keywords: oximetry, heart defects – congenital, benefit assessment, systematic review

The full report (German version) is published under

https://www.iqwig.de/de/projekte-ergebnisse/projekte/nichtmedikamentoese-verfahren/s13-01-screening-auf-kritische-angeborene-herzfehler-mittels-pulsoxymetrie-bei-neugeborenen.3681.html.