Report on treatment of patients with hemophilia published

July 13 2015

Numerous long-term randomized controlled trials (RCTs) have been conducted to investigate the long-term, factor concentrate-based treatment of patients with severe haemophilia A or B, despite the rareness of the diseases and the lack of incentives for pharmaceutical companies. These RCTs include three studies comparing prophylactic versus on-demand treatment (i.e. treatment initiated only in the event of bleeding). For patients with haemophilia A, both hints and an indication of an added benefit of prophylactic versus on-demand treatment can be inferred from these studies, but only for certain outcomes.

No evaluable data were available on the effects of the different treatment strategies on joint function. For children, the results for most outcomes are not interpretable due to inadequate data quality. However, the results support most current (clinical practice) guidelines and treatment algorithms with regard to recommendations on the prevention of severe bleeding.

These are the main conclusions of a rapid report published on 25 June 2015, which the German Institute for Quality and Efficiency in Health Care (IQWiG) prepared on behalf of the German Federal Ministry of Health (BMG).

Three research questions

The report had three aims: IQWiG was to map the available evidence on

the long-term, factor concentrate-based treatment of patients with severe haemophilia A or B in respect of different treatment strategies, factor concentrates, dosing regimens, and prophylactic treatment regimens. On this basis, the long-term benefit of prophylactic and on-demand treatment was to be compared with regard to patient-relevant outcomes analysed in controlled prospective studies. In addition, the Institute was to evaluate to what extent current guidelines and treatment algorithms are based on the evidence identified.

16 long-term studies identified

13 completed and three ongoing long-term RCTs were identified for the first research question. Only two studies included patients with haemophilia B. Important clinical questions remained unanswered for children. Likewise, it is still an open question as to whether differences exist between factor concentrates based on blood plasma and those based on biotechnology techniques.

This is partly due to the fact that manufacturers of factor concentrates have no incentive to conduct comparative long-term studies, as these are not required for approval. Even so, the mapping of evidence shows that RCTs are also feasible in relatively rare diseases such as haemophilia A or B.

No conclusion on added benefit possible for haemophilia B

A total of three of the studies were suitable for a comparison of the benefit of prophylactic versus on-demand factor concentrate-based treatment: one in adolescents and adults and two in children, all with severe haemophilia A. No conclusion on a greater or lesser patient-relevant benefit of prophylactic versus on-demand treatment is thus

possible for patients with haemophilia B.

For adolescents and adults with severe haemophilia A, the data provide hints of an added benefit of prophylactic treatment for the outcomes of health status and pain, as well as an indication of an added benefit for the outcome of severe bleeding. Both studies in children have such a high risk of bias that a hint of an added benefit of factor concentrate-based prophylactic treatment can only be inferred for severe bleeding. For children in particular, no added benefit of either of the two treatment strategies can therefore be inferred with regard to patient-relevant outcomes such as pain, joint function or quality of life.

Guidelines and treatment algorithms: few contradictions to available evidence

To identify guidelines and treatment algorithms, IQWiG wrote to German institutions specialized in the treatment of patients with haemophilia. Of the 13 potentially relevant guidelines and four treatment algorithms obtained, only three guidelines turned out to be evidence-based. Most of the guidelines and algorithms do not contradict the results of the benefit assessment.

However, for adult patients one of the clinics generally recommends on-demand treatment, which is not supported by the results of the benefit assessment. In addition, several recommendations contain statements on the preservation and functionality of joints that are not supported by the available evidence. This is because no evaluable data on these outcomes were reported in the studies.

Process of report production

The BMG commissioned IQWiG to prepare the report in an accelerated

process, known as a "rapid report". In contrast to the usual procedure, no preliminary reports are published here and no hearing takes place at which all interested parties can comment. The present rapid report was sent to the commissioning agency on 28 May 2015.

An overview of the background, methods and further results of the report is provided in the following German executive summary. An English executive summary will be available soon. If you would like to be informed when this document is available, please send an e-mail to " info@iqwig.de.

More information: www.iqwig.de/download/A13-07_K … philie-Patienten.pdf

Provided by Institute for Quality and Efficiency in Health Care