

Title Management of haemophilia

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Aim

To assess the safety, efficacy and resource implications of; prophylaxis treatment when compared to on-demand treatment, recombinant factors compared to plasma derived factors, recombinant factor VIIa (rFVIIa) when compared to activated prothrombin complex concentrate (aPCC), and non-pharmacological management for patients with haemophilia.

Conclusions and results

Fifty-one studies met the inclusion and exclusion criteria. There was good level evidence from systematic reviews of randomised controlled trials and observational studies that a prophylaxis approach in the treatment of haemophilia was effective in decreasing the frequency of joint bleeds and preventing or slowing down the development of haemophilic arthropathy. The prophylaxis approach not increase the risk of inhibitor development and there was no increased risk of infection. However, the evidence showed that the cost of treatment was high which was attributed to the cost of factor concentrates. There was insufficient evidence on the efficacy and safety of the recombinant factor compared to plasma-derived factor concentrates. Only fair level evidence with high risk of bias was available for Haemophilia A. The evidence showed inconsistent results for recovery of recombinant factor IX (rFIX) and plasma-derived factor IX (pdFIX). Limited good level of evidence showed that recovery of rFIX was lower compared to pdFIX.

As for safety, it cannot be concluded that plasma-derived factors have a lower risk of inhibitor development due to the inconsistency of the results. Good level of evidence showed that rFVIIa and aPCC had similar efficacy and both can be administered as a single intravenous bolus (270 µg/kg of rFVIIa, 75-100 IU/kg of aPCC). There was no higher risk of adverse events reported in rFVIIa compared to aPCC. Fair level evidence suggested that rFVIIa is more cost-effective compared to aPCC in haemophilia patients with inhibitors. Fair level evidence showed that comprehensive care reduced the mortality rate, hospitalisation days and number of days lost from school or work in haemophilia patients. There was insufficient evidence on cost effectiveness however, the evidence suggested that comprehensive care leads to cost savings.

Recommendations

Prophylaxis therapy is recommended in haemophilia patients to improve their quality of life and prevent complications. Since the cost of factor concentrates is high, a low or intermediate dose prophylaxis may be considered. The use of bypassing agents either rFVIIa or aPCC, is recommended for the treatment of any kind of bleeds in haemophilia patients with inhibitors since a good level of evidence showed that both bypassing agents had similar efficacy. A national haemophilia program should be introduced in Malaysia to address issues pertaining to the management of haemophilia patients such as care delivery, medical expertise and treatment products. As an important component of comprehensive care a registry should be incorporated into the national program. This will enable centres to monitor their performance and use of resources both at a local and national level.

Methods

Electronic databases such as MEDLINE, PubMed, EBM Reviews-Cochrane of Systematic Reviews, EBM Reviews-Cochrane Central Register of Controlled Trials, EBM Reviews-Health Technology Assessment, EBM Reviews-Cochrane Methodology Register, EBM Reviews-NHS Economic Evaluation, Database of Abstracts of Reviews of Effects (DARE), Horizon Scanning, INAHTA, HTA and FDA were searched. No limits were applied to the search. Additional articles were identified from bibliographies of retrieved articles and hand-searching of journals. All relevant literature was appraised using the Critical Appraisal Skills Programme (CASP) and evidence was graded based on the U.S./Canadian Preventive Services Task Force guidelines.

Further research/reviews required

Further well designed, high quality research is needed to study the relative effectiveness of rFVIIa compared to plasma-derived aPCC. A study of the Malaysian population is strongly encouraged to provide better insight into the response to aforementioned bypassing agents. A local economic evaluation should be conducted to assess the best model of treatment for haemophilia patients in Malaysia that will not only improve the outcome of the patients but also be cost effective.

Written by

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