Effectiveness and safety of the left ventricular assist device (LVAD) as destination therapy in paediatric patients

Spanish full text

Introduction: Heart failure (HF) is a rare condition in the paediatric population. It is mainly due to structural cardiac causes (congenital cardiopathies, CC) or non-structural (myocardiopathies or myocardial dysfunction associated with surgery) or non-cardiac causes. It is estimated that the main cause of HF is CC (52%), followed by primary and secondary cardiomyopathies (18-19%). Both the underlying causes of HF and the symptoms associated with it differ according to age. The incidence of HF in children and adolescents (<18 years) ranges from 0.87 to 7.4 per 100 000. According to data from the National Institute of Statistics (INE), the mortality rate associated with HF during 2017 was 0.858 deaths per 100 000 inhabitants in the paediatric population (<19 years). The highest rate was observed in children under 1 year of age (0.509 deaths per 100 000) and no data was recorded in the 5-9 year age range. Medical treatment of HF in children focuses on correction of the underlying cause if it is reversible, such as in sepsis or electrolyte imbalance; or on control of the symptoms and progression of the disease when the failure is due to CC or myocardiopathy. This includes the use of various general measures, pharmacological treatment, corrective surgical interventions in the first instance, and implantation of short or long term ventricular assist devices, or heart transplant when the previous therapeutic options are ineffective. In addition, there are cases in which the use of long-term support would be indicated due to the fact that improvement is not achieved with short-term support or that the heart transplant would be limited by various serious irreversible clinical situations. In these latter cases, the use of long-term support would be considered as a target therapy.

Aims: The main aims of this report are to assess the safety in terms of adverse events and effectiveness in terms of survival in paediatric population of VADs as target therapy compared to drug treatment or other ventricular assist devices. As secondary objectives it has been considered relevant to estimate the economic impact associated with the use of VADs as target therapy in paediatric age and to assess the organisational, social, ethical or legal aspects derived from the use of VADs as target therapy in this population group.

Methods: specific search strategies were designed to locate studies that assess the safety and/or effectiveness of VADs as a target therapy, their economic and organisational impact, patient acceptability and satisfaction, and ethical, social and legal aspects of their use. These strategies were implemented in April 2019 in the main medical literature databases. The main characteristics and results of the included studies were summarized in evidence tables. A qualitative synthesis of the evidence was made through the GRADE system for which 8 outcome variables were selected, all of them classified by clinicians as important or critical. Specific tools were used to assess the risk of bias of the studies according to the type of study. The quality of evidence was evaluated using the GRADE system for quantitative studies and the GRADE-CERQual version was used for qualitative studies. Both the extraction of data from the studies and the synthesis and appraisal of the evidence were carried out by two researchers independently and blindly.

Results: The bibliographic search of primary studies returned 1410 references. Twenty-eight primary studies were selected for full-text reading. In addition, 6 other primary studies were located by manual search. According to the inclusion criteria defined in the methodology, 8 primary studies were included. All of them evaluated left support devices (LVADs). In 5 of them the safety and/or effectiveness of LVADs as target therapy in paediatric population was assessed, 2 others explored the perspectives of family members/carers and/or health professionals and 1

study collected some of the main ethical and social aspects related to ventricular support in the paediatric population. The published evidence on the safety and effectiveness of LVADs in paediatric target therapy was evaluated, according to the GRADE system, with a very low level of quality and refers to a total of 17 patients aged between 14-23.4 years, in whom the underlying cause of HF was dystrophy. Regarding adverse events, a number of cases recorded a high percentage of adverse events such as heart failure (57% patients), infections (13 events in 7 patients), pump thrombosis (85.7% patients), or device dysfunction (57% patients) (assessed during a mean follow-up of 292 [71-1437] days). Another series observed long-term (>10 months), 14% (1/7) of cases of infection and osteolysis and 14% of stroke (1/7), while two patients presented no short- and long-term adverse events. With regard to effectiveness results, the main variable of interest was survival. The two case series included (total n=14 patients) in the present review reported a survival rate during an approximate 4-year follow-up ranging from 33-57%. As regards the perspectives of carer-family members, the qualitative study identified 7 main issues focused mainly on the challenge of remaining physically connected to a device, related to activities of daily living, relationship with other children, future prospects, etc. The vision of the medical professionals focused on 4 themes related to clinical aspects such as pre-implant evaluation, adequate selection of candidates, etc. Finally, in the review which included ethical-legal aspects related to the deactivation of LVADs, the authors highlighted that there are no documents available with 17 recommendations both on the deactivation process and on the indication of LVADs carried out from an ethical, legal and social perspective, and taking into account the perspectives of all the agents involved.

Conclusions: The available evidence on LVADs as target therapy in patients with dystrophy does not allow conclusions to be drawn regarding their effectiveness and safety in this group, and limits their applicability to other possible indications of LVADs as a target therapy in the paediatric population. The main limitations of the literature reviewed are due to the fact that adverse events were not collected homogeneously across the studies analysed, and they did not assess the improvement in clinical terms or with regard to quality of life associated with the use of LVADs as target therapy in a group of patients characterised by a significant rate of adverse events and readmissions. Nor were any studies identified that assessed the organisational and economic impact that the use of LVADs as target therapy could have on the paediatric population.