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CLINICAL RESEARCH

Single-centred experience with levosimendan in paediatric decompensated dilated cardiomyopathy

Expérience monocentrique du levosimendan dans les myocardiopathies dilatées pédiatriques en insuffisance cardiaque terminale

Pierre-Emmanuel Séguéla[a,*], Philippe Mauriat[b], Jean-Baptiste Mouton[a], Nadir Tafer[b], Jana Assy[b], Géraldine Poncelet[a], Karine Nubret[b], Xavier Iriart[a], Jean-Benoit Thambo[a]

[a] *Paediatric Cardiology Unit, Bordeaux University Hospital, Bordeaux, France*
[b] *Department of Paediatric Cardiac Anaesthesiology, Bordeaux University Hospital, Bordeaux, France*

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KEYWORDS
Levosimendan;
Dilated cardiomyopathy;
Paediatric heart failure;
Brain natriuretic peptide;
Paediatric heart transplantation

Summary
Background. — Children with dilated cardiomyopathy in advanced heart failure may spend a long time awaiting heart transplantation. Consequently, mechanical circulatory support is sometimes required as a bridge to transplantation. Levosimendan, a positive inotropic agent, has been reported to be safe and efficient for the treatment of paediatric heart failure.
Aims. — To report our experience with levosimendan in children with decompensated dilated cardiomyopathy.
Methods. — Paediatric patients with dilated cardiomyopathy on the transplant waiting list and with criteria for mechanical support were included in this single-centred retrospective study. Each patient received at least one 24-hour infusion of levosimendan before mechanical circulatory support was considered. Biological and echocardiographic data were analysed.

Abbreviations: BNP, B-type natriuretic peptide; DCM, dilated cardiomyopathy; ECMO, extracorporeal membrane oxygenation; LVEF, left ventricular ejection fraction; MCS, mechanical circulatory support; VAD, ventricular assist device.

* Corresponding author. Paediatric Cardiology Unit, hôpital Haut Lévèque, CHU de Bordeaux, avenue de Magellan, 33604 Pessac cedex, France.
E-mail address: peseguela@yahoo.fr (P.-E. Séguéla).

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Results. — Six patients were included over a 24-month period. The median age was 25.5 months (7.7—34.2 months); 82 infusions were performed. Median B-type natriuretic peptide concentration decreased significantly between days 0 and 2 (2443 ng/L [1458—3819 ng/L] vs 1358 ng/L [1025—2534 ng/L]; $P = 0.003$). While only a trend was noted in left ventricular ejection fraction improvement ($P = 0.054$ by Simpson's method and $P = 0.068$ by the Teicholz method), the subaortic velocity time integral rose significantly between days 0 and 8 (12.8 cm/s [10—14.5 cm/s] vs 15.3 cm/s [14.3—16.9 cm/s]; $P = 0.041$).
Conclusions. — Levosimendan seems to improve haemodynamics in children with decompensated dilated cardiomyopathy; repeated infusions may delay the need for mechanical circulatory support while awaiting heart transplantation. This therapeutic agent should be systematically considered in this setting, in addition to conventional inotropic drugs.

MOTS CLÉS
Levosimendan ;
Cardiomyopathie dilatée ;
Insuffisance cardiaque pédiatrique ;
Brain natriurétique peptide ;
Transplantation cardiaque pédiatrique

Résumé
Contexte. — Les enfants qui ont une cardiomyopathie dilatée en insuffisance cardiaque terminale et qui sont sur liste de transplantation cardiaque sont susceptibles d'attendre longtemps un greffon. Ainsi, le recours à une assistance mécanique circulatoire est parfois nécessaire lorsque l'état du patient ne lui permet plus d'attendre. Le levosimendan, inotrope positif, a précédemment été rapporté sûr et efficace pour le traitement de l'insuffisance cardiaque de l'enfant.
Objectifs. — Rapporter notre expérience du levosimendan chez des enfants avec cardiomyopathie dilatée en insuffisance cardiaque terminale.
Méthodes. — Ont été inclus, dans une étude rétrospective monocentrique, tous les enfants ayant une cardiomyopathie dilatée sur liste de transplantation cardiaque et avec des critères d'assistance circulatoire mécanique. Avant la mise sous assistance, chaque patient a au moins reçu une cure de levosimendan de 24 h. Les paramètres biologiques et échocardiographiques ont ensuite été analysés.
Résultats. — Six patients ont été inclus sur une période de 24 mois. L'âge médian était de 25,5 mois (7,7—34,2). Quatre-vingt-deux infusions ont été réalisées au total. Le taux médian de BNP diminuait significativement entre j0 et j2 (2443 ng/L [1458—3819 ng/L] contre 1358 ng/L [1025—2534 ng/L] ; $p = 0{,}003$). Alors que seule une tendance à l'amélioration était notée pour la fraction d'éjection ventriculaire gauche ($p = 0{,}054$ par la méthode de Simpson et $p = 0{,}068$ en Teicholz), l'ITV sous-aortique augmentait significativement entre j0 et j8 (12,8 cm/s [10—14,5 cm/s] contre 15,3 cm/s [14,3—16,9 cm/s] ; $p = 0{,}041$).
Conclusion. — En considérant la possibilité de perfusions itératives, le levosimendan semble améliorer l'état hémodynamique de ces patients. Afin d'attendre au mieux un greffon cardiaque, le levosimendan devrait être systématiquement considéré dans cette indication et en association avec les traitements habituels.

Background

Dilated cardiomyopathy (DCM), with an annual incidence of 0.57 to 0.72 per 100,000 children, is the most common form of paediatric cardiomyopathy [1,2]. Indeed, within the Pediatric Heart Transplant Study group, DCM accounts for 83% of all paediatric cardiomyopathy [3]. This disease is caused by a variety of conditions: idiopathic, familial, neuromuscular disorders, post-myocarditis, chemotherapeutic drugs, metabolic disorders and ventricular non-compaction. Despite the use of conventional therapies, the prognosis for DCM has not changed appreciably in recent decades [4]. DCM accounts for > 50% of indications for paediatric heart transplantation [5], which remains the gold standard therapy for end-stage heart failure. Because the wait for a transplant may be long, the use of mechanical circulatory support (MCS) is sometimes required as a bridge to transplantation, despite the use of conventional inotropic drugs.

Levosimendan, being a calcium sensitizer of cardiac troponin and an adenosine triphosphate-sensitive potassium agonist, improves myocardial contraction [6] and allows relaxation of the vascular smooth muscle cells [7], which are responsible for coronary vasodilatation. Maximal haemodynamic effects of levosimendan have been shown to occur 1—3 days after starting the infusion and are sustained for at least a week. Although this positive inotropic agent