European Journal of Pediatrics (2022) 181:423
https://doi.org/10.1007/s00431-021-04226-5

CORRESPONDENCE

Life-threatening PPHN refractory to NO: therapeutic algorithm

Dietmar Schranz[1] · Roland Schrewe[2] · Anoosh Esmaeili[2]

Received: 19 July 2021 / Revised: 19 July 2021 / Accepted: 27 July 2021 / Published online: 26 August 2021

We read with great interest the excellent review of Feriel Fortas et al. [1], which summarizes the treatment modalities of NO-refractory PPHN. However, when describing the available weaponry and the consecutive therapeutic algorithm with a focus on PPHN as a precapillary pulmonary hypertension without reference to a left heart disease or pulmonary parenchyma disease, a few questions and recommendations arose. First, with the exception of NO (maximal 20 ppm), there are no dose recommendations for the other recommended drugs, especially not for adenosine. Adenosine, recommended as a drug for add-on therapy, requires instructions for use and dosage, particularly because of the potential for unpredictable cardiac arrhythmias as bradycardia, AV-block, etc. Further questions arose with regard to NO-refractory PPHN and the use of bosentan, a dual endothelin, ET-A, and ET-B receptor blocker and, in turn, adenosine as an endothelial-dependent vasodilator. Either there is still residual function of the endothelium, in this case, a dual endothelin blocker is not indicated [2], but instead a selective ET-A receptor blocker or the presence of an endothelial dysfunction contraindicated the use of adenosine due to its risk of vasoconstriction (and bronchospasm) combined with an increased arrhythmic side effects. Furthermore, should alprostadil, a PGE2-prostaglandin, be considered in place of PGE1 for reopening an arterial duct in a newborn with PPHN and right heart failure? When weighing the risk/benefit ratio of PGE2 versus PGE1, the proinflammatory and other more pronounced side effects together with less predictable pulmonary vasodilative effects advocate against PGE2 and favor PGE1.

Communicated by Peter de Winter

✉ Dietmar Schranz
dietmar.schranz@kgu.de;
dietmar.schranz@paediat.med.uni-giessen.de

[1] Pediatric Heart Center, Johann-Wolfgang Goethe University Clinic, Theodor-Stern-Kai 7, 60590 Frankfurt, Germany

[2] Johann-Wolfgang-Goethe University Clinic, Frankfurt, Germany

However, we appreciate one of your basic key measures in reducing the pulmonary-systemic pressure difference by preferably using norepinephrine as an i.v. infusion with simultaneous establishment of an adequate intravascular volume status. When using catecholamines (i.e., dobutamine), do the authors pay attention to an upper limit of the heart rate with regard to the general and especially myocardial oxygen consumption and the achievement of an adequate diastolic filling time of the left ventricle? In this context, and with regard to the neonatal myocardial calcium handling, should milrinone — regardless of iloprost — and possibly levosimendan not be used as first-line treatment for myocardial dysfunction in newborns with PPH, quite apart from the likely beneficial effects on the pulmonary circulation?

Declarations

Conflict of interest The authors declare no competing interests.

References

1. Fortas F, Di Nardo M, Yousef N, Humbert M, De Luca D (2021) Life-threatening PPHN refractory to nitric oxide: proposal for a rational therapeutic algorithm. Eur J Pediatr 180:2379–2387. https://doi.org/10.1007/s00431-021-04138-4
2. Apitz C, Zimmermann R, Kreuder J, Jux C, Latus H, Pons-Kühnemann J, Kock I, Bride P, Kreymborg KG, Michel-Behnke I, Schranz D (2012) Assessment of pulmonary endothelial function during invasive testing in children and adolescents with idiopathic pulmonary arterial hypertension. J Am Coll Cardiol 10;60(2):157–64