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Drug use patterns for the prevention of paediatric low cardiac output syndrome in Europe

Accepted: 8 May 2011
Published online: 7 June 2011
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These results were presented in part at the
12th biannual congress of the European
Society for Developmental Perinatal &
Paediatric Pharmacology, in Chamonix,
France in 2009.

Dear Editor,
Low cardiac output syndrome
(LCOS) affects approximately 25%
of children undergoing open heart
surgery (OHS) and is associated with
increased morbidity and mortality [1].
Evidence for preventive drug therapy
for LCOS is derived primarily from

the PRIMACORP study [1], which
reported a reduction in LCOS risk
after administration of high-dose
milrinone, using a bolus of 75 µg/kg,
followed by a maintenance infusion
of 0.75 µg kg⁻¹ min⁻¹ over 35 h.
Low-dose milrinone (25 µg/kg bolus
and 0.25 µg kg⁻¹ min⁻¹ infusion)
was not more effective than placebo.
Other drugs may be also used but are
not supported by safety and efficacy
data [2, 3]. Data on drug use for
LCOS prevention in children with
OHS is not available for Europe.
Therefore, the aim of this study was
to characterise hospital practices
related to preventive drug therapy for
LCOS in children undergoing OHS as
a basis for improving the standard of
care in this setting.

A Web-based questionnaire was
developed to survey 125 specialised
hospitals from 36 European countries
between January and August 2009. It
included 15 questions allocated to 4
sections: prescribing resources and
LCOS treatment (data not shown),
LCOS prevention, and participant
characteristics and comments. The
questions on LCOS prevention
enquired about the target patient
group (all, at risk, none) and mode of
drug administration, which was not

further stratified. The hospitals were
notified by email; of those, 90 hos-
pitals from 31 countries responded
(72.0% response rate). Respondents
included clinicians (98.9%) and
pharmacists (1.1%), specialising pri-
marily in paediatric intensive care,
anaesthesiology, cardiology, and car-
diothoracic surgery. Nearly all
respondents (94.4%) had at least
5 years of experience in caring for
children undergoing OHS.

Most European hospitals (70 out of
90) reported preventive drug therapy
for LCOS, from which the majority
(57 hospitals) selectively targeted
patients at risk. However, the drug
use was highly variable. In total, 24
different drug regimens were repor-
ted, including 17 drugs from 7
therapeutic drug classes. Overall,
70.7% of the drug regimen reports
included milrinone, making this the
most commonly used drug. Dopa-
mine, dobutamine, epinephrine, and
levosimendan were reported signifi-
cantly less often (Table 1). The
dosage and duration of drug admin-
istration differed substantially among
hospitals.

The results of this survey present
the current pattern of drug use for
LCOS prevention in children with

Table 1 Summary characteristics of the drugs commonly reported for LCOS prevention

Drug ^a	Frequency of drug use			Drug administration		
	N	%	95% CI	Bolus ^b (µg/kg)	Maintenance infusion ^b (µg kg ⁻¹ min ⁻¹)	Duration ^b (h)
Milrinone	53	70.7	59.6–79.8	50 (20–300)	0.5 (0.2–1.5)	39 (6–168)
Dopamine	14	18.7	11.5–28.9	– ^c	5 (0–15)	36 (8–72)
Dobutamine	12	16	9.4–25.9	7 ^d (6–8)	5 (2–14)	36 (6–48)
Epinephrine	12	16	9.4–25.9	1 (1–1)	0.065 (0.003–0.3)	9 (6–12)
Levosimendan	12	16	9.4–25.9	12 (12–12)	0.15 (0.1–0.2)	24 (24–48)
Methylprednisolone	4	5.3	2.1–12.9	25 ^e (10–35)	–	–

The analysis was based on 75 drug regimens reported from 69
hospitals. Two hospitals provided three different drug regimens and
another two hospitals provided two drug regimens based on the
clinical condition of the patient and the type of open heart surgery.
One hospital did not fill in the information on drug dosing

^a Only 6 out of 17 drugs were reported more than twice and are
listed in the table. The following drugs were reported once or twice:
alprostadil, bosentan, calcium, enoximone, glyceryl trinitrate,

inhaled nitric oxide, norepinephrine, phenoxybenzamine, phenyl-
ephrine, nitroprusside, and thiopental

^b Data are median with range in parenthesis

^c Not reported

^d Bolus dose in µg kg⁻¹ min⁻¹

^e Bolus dose in mg/kg

OHS across Europe, which is characterised by a marked variability. In addition, the dose of milrinone appears to be lower than that supported by PRIMACORP. Although our survey shows that milrinone is the most frequently used drug in Europe, neither the dosing nor the duration of drug administration coincide with those demonstrating efficacy in PRIMACORP (Table 1). Reasons for the reduced dose of milrinone may be attributable to concerns about potential side effects, especially hypotension [4], and the role of age-specific pharmacokinetic differences in the elimination of milrinone [5]. Nonetheless, these factors cannot explain the generally lower dose of milrinone used across all paediatric age groups, which needs to be addressed in future clinical research.

In summary, preventive drug therapy for LCOS in children undergoing OHS is highly variable across Europe, and the data available to support current hospital practices are insufficient. Given the importance of balancing benefits and risks with preventive drug therapy, this survey emphasises the need for further studies that will substantiate effective and safe LCOS prevention.

Acknowledgments The results presented in this Letter to the Editor are part of the PhD work of Ms Vogt, carried out at Heinrich Heine University of Düsseldorf. The authors would like to thank all of the members of the expert panel in the field of paediatric cardiology, anaesthesiology, intensive care, cardiac surgery, general medicine, and psychology for their support during the questionnaire development, the survey participants for taking the time to complete the questionnaire, and the European Congenital Heart Disease Organisation members for establishing contact with various hospitals. We would also like to thank Dr. Lechner for review and comments on the manuscript.

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