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Cardiovascular drug therapy for human newborn: review of pharmacodynamic data

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Table 2 - Characteristics of included studies investigating the use of dobutamine (DOB).

Reference	Study Type	Level of Evidence	Study Population	Dobutamine infusion dose range
Subhedar <i>et al</i> 2013. [13]	Systematic review	I	Included 5 RCTs (209 patients in total) with neonates born before 37 weeks gestation and less than 28 days of age. No specific definition of hypotension was used.	As in studies [11,18,10,12]
Klarr <i>et al.</i> 1994 [10]	Randomised controlled trial	II	63 neonates (GA \leq 34 weeks) with hypotension and RDS.	5-20 mcg/ kg/min
Greenough <i>et al.</i> 1993 [11]	Randomised controlled trial	II	40 neonates (median GA = 27 weeks) with hypotension	5-15 mcg /kg/min
Roze <i>et al.</i> 1993 [12]	Randomised controlled trial	II	20 neonates (GA \leq 32 weeks) with hypotension	5-20 mcg/ kg/min
Filippi <i>et al.</i> 2007 [14]	Non-blind randomised controlled trial	II	35 neonates with BW <1500grams with hypotension	4-20 mcg/ kg per min
Bravo <i>et al.</i> 2015 [15]	Randomised controlled trial	II	28 neonates (GA \leq 32 weeks) with low superior vena cava flow in the first 24 h of life	5-20 mcg/ kg/min
Osborn <i>et al.</i> 2007 [16]	Randomised controlled trial	II	37 neonates (GA \leq 30 weeks) with low superior vena cava flow in the first 24 h of life	10-20 mcg/ kg/min
Osborn <i>et al.</i> 2002 [17]	Randomised controlled trial	II	42 neonates (GA \leq 30 weeks) with low superior vena cava flow in the first 24 h of life	10-20 mcg/ kg/min

Table 3 - Characteristics of included studies investigating the use of dopamine (DA).

Reference	Study Type	Level of Evidence	Study Population	Dopamine infusion dose range
Subhedar <i>et al.</i> [13]	Systematic review	I	Included 5 RCTs (209 patients in total) with neonates born before 37 weeks gestation and less than 28 days of age. No specific definition of hypotension was used.	As in studies [11,18,10,12]
Greenough <i>et al.</i> 1993 [11]	RCT	II	40 neonates with median GA 27 weeks (range 23-33) randomized to dopamine or dobutamine infusion. Hypotension: systolic BP < 40 mmHg despite receiving a colloid infusion.	5-15 mcg/ kg/min
Hentschel, R. <i>et al.</i> 1995 [18]	RCT	II	20 neonates with GA 25-36 weeks and BW 830 - 2610 g randomized to dopamine or dobutamine infusion. Hypotension: Mean BP < 10th percentile of GA-dependent normal values	10 mcg/kg/min
Klarr <i>et al.</i> 1994 [10]	RCT	II	63 neonates < 34 weeks gestation randomized to dopamine or dobutamine infusion after volume expansion with 20 ml/kg . Hypotension: mean arterial blood pressure <30mm Hg persisting for >30min.	5-20 mcg/ kg/min
Roze <i>et al.</i> 1993 [12]	RCT	II	20 neonates with GA 26 -31 weeks and BW 670 - 1800 g randomized to dopamine or dobutamine infusion. Hypotension: Mean BP < 30 mmHg	5-20 mcg/ kg/min
Pellicer, A. <i>et al.</i> [20] (same study as [38])	RCT	II	59 neonates with BW <1501 g or GA <32 weeks' were randomized to dopamine or epinephrine Hypotension: mean BP < GA in the first 24 hours of life	2.5-10 mcg/ kg/min
Valverde <i>et al.</i> 2006 [38] (same study as [20])	RCT	II	60 neonates of BW<1501g or GA<32 weeks with a, randomized to dopamine or epinephrine Hypotension: mean BP lower than GA in the first 24 hours of life	2.5 -10mcg/ kg/min

Reference	Study Type	Level of Evidence	Study Population	Dopamine infusion dose range
Lundstrom, K. et al. [21]	RCT	II	36 neonates with GA < 33 weeks, with mean BP between 29 and 40 mm were randomised to receive either dopamine, volume expansion with albumin or no treatment. Normotensive preterm neonates	5 mcg/ kg/min
Osborn, D.A. [16]	RCT	II	42 neonates with low SVC flow (<41 mL/kg/min) were randomized to volume and dobutamine versus volume and dopamine.	10-20 mcg/ kg/min
Seri, I. et al [24]	Observational study	IV	20 indomethacin-treated normotensive preterm neonates with patent ductus arteriosus and mean GA 27.2+/-1.5 weeks were treated with dopamine	5 mcg/ kg/min
Bouissou, A. et al. [26]	Prospective observational study	IV	17 neonates with patent ductus arteriosus and systemic hypotension and mean GA 28+/-2 weeks and BW 1030 +/- 400 g. Hypotension: mean BP < GA during the first 2 days after birth, or mean BP < 10th percentile of GA-dependent normal values.	Mean rate 8 +/- 2 mcg/ kg/min
Seri, I. et al. [28]	Prospective observational study	IV	6 neonates with BW< 2500 g and GA<36 weeks were given dopamine for oedema, moderate oliguria, poor peripheral perfusion and/or mild systemic hypotension and matched with controls.	2 mcg/ kg/min
Ishiguro, A. et al. [31]	Prospective observational study	IV	29 neonates with median GA 27.1 (23.8–29.7) weeks and BW (g) 790 (388–1,292) were treated with dopamine Hypotension: mean BP< 10th percentile of GA-dependent normal values	5-20 mcg/ kg/min
Saini, S.S. et al. [25]	Prospective observational study	IV	52 neonates with septic shock (shock group) with mean GA 31.1±2.8 and BW 31.2±2.3 (g) and matched healthy control group. Hypotension: systolic BP or diastolic BP less than fifth percentile for the postmenstrual age	10-20 mcg/ kg/min

Reference	Study Type	Level of Evidence	Study Population	Dopamine infusion dose range
Zhang, J. et al. [22]	Prospective observational study	IV	50 hypotensive preterm neonates in whom cardiac output increased or decreased after dopamine treatment. Hypotension: mean BP < 10th percentile of the normal range, taking account of BW and postnatal age	5-10 mcg/ kg/min
Liet, J.M. et al.[27]	Prospective observational study	IV	14 neonates with GA < 32 weeks (range 24 to 31 weeks), with BW ranging from 480 to 1482 g were treated with dopamine for hypotension after initial volume expansion Hypotension: mean BP ≤ 10th percentile of the normal range	5-10 mcg/ kg/min
Seri, I. et al. [30]	Prospective observational study	IV	61 neonates with variable characteristics analysed in different substudies (control-normotensive, hypotensive and oliguric) Hypotension: systolic BP > 15 mm Hg below the predicted normal the time of the studies	2-4 mcg/ kg/min
Lynch, S.K. et al. [29]	Prospective observational study	IV	15 neonates with mean GA 34+/-2 weeks and mean BW 2.43+/-0.6 kg) who had respiratory distress, were normotensive, and had a low urine output (0.9+/-0.1 ml/kg per hour)	0.5-7.5 mcg/ kg/min

Table 4 - Characteristics of included studies investigating the use of epinephrine (EPI).

Reference	Study Type	Level of Evidence	Study Population	Epinephrine infusion dose range
Buijs <i>et al</i> 2014 [23]	Prospective observational cohort study	IV	70 neonates with median BW 3125 grams and GA 38.6 weeks. (28 controls)	0.02-0.22 mcg/ kg/min
Heckmann <i>et al</i> 2002 [40]	Retrospective cohort study	IV	31 neonates with BW 390-1310 grams and GA 23-30 weeks	0.05-2.6 mcg/kg per min
Pellicer <i>et al</i> 2005 [20]	Randomised controlled trial	II	60 neonates with BW <1501grams, GA <32 weeks and <24 hours post-natal age.	0.125-0.5 mcg/kg per min
Phillipos <i>et al</i> 1996 [37]	Randomised controlled trial	II	20 neonates with BW >1750grams and <24 post-natal age.	0.125-0.5 mcg/kg per min
Rai <i>et al</i> 2010 [39]	Case series	IV	20 neonates with BW 1400-3400 grams, GA 30-39 weeks and 20-32 hours post-natal age.	0.3-1.5 mcg/kg per min
Valverde <i>et al</i> 2006 [38]	Randomised controlled trial	II	60 infants with BWs <1501g, GA <32 weeks and <24 hours post-natal age.	0.125-0.5 mcg/kg per min

Table 5 - Characteristics of included studies investigating the use of hydrocortisone (HC).

Reference	Study Type	Level of Evidence	Study Population	Hydrocortisone infusion dose range
Dempsey <i>et al.</i> 2007 [52]	Systematic review	I	Preterm hypotensive newborns 15 studies included	
Higgins <i>et al.</i> 2010 [53]	Meta-analysis	I	7 studies 147 preterm newborn included	
Ibrahim <i>et al.</i> 2011 [54]	Cochrane review	I	4 studies 123 newborns included	

Table 6 - Characteristics of included studies investigating the use of levosimendan (LS).

Reference	Study Type	Level of Evidence	Study Population	Levosimendan infusion dose range
Ricci, <i>et al</i> 2012 [61]	Randomised controlled trial	II	63 neonates (< 30 days of age) undergoing corrective open-heart surgery	0.1 mcg/ kg/min
Lechner <i>et al</i> 2012 [62]	Randomised controlled trial	II	40 infants <1 year of life undergoing corrective open-heart surgery	0.1 mcg/ kg/min
Pellicer <i>et al</i> 2013 [63]	Randomised controlled trial	II	20 neonates (6-34 days of age) undergoing corrective open-heart surgery	0.1-0.2 mcg /kg/min

Table 7 - Characteristics of included studies investigating the use of milrinone (MIL).

Reference	Study Type	Level of Evidence	Study Population	Milrinone infusion dose range
Lechner <i>et al</i> 2012 [62]	Randomised controlled trial	II	40 infants <1 year of life undergoing corrective open-heart surgery	0.5 mcg/ kg/min
Pellicer <i>et al</i> 2013 [63]	Randomised controlled trial	II	20 neonates (6-34 days of age) undergoing corrective open-heart surgery	0.5-1 mcg /kg/min
Paradisis <i>et al</i> 2009 [68]	Randomised controlled trial	II	90 neonates (GA \leq 30 weeks) < 6 hours of age	Loading dose 0.75 mcg /kg/min for 3 hours then maintenance 0.2 mcg/kg/min until 18 hours after birth
Jain <i>et al</i> 2012 [69]	Retrospective cohort study	IV	52 neonates (mean GA 25 weeks) undergoing PDA ligation	0.33 mcg /kg/min for 24 hours

Table 8. Characteristics of included studies investigating the use of norepinephrine (NE).

Reference	Study Type	Level of Evidence	Study Population	Norepinephrine infusion dose range
Buijs <i>et al</i> 2014 [23]	Prospective observational cohort study	IV	28 neonates with CDH with median BW 3125 grams and GA 38.6 weeks. (28 controls)	0.11 mcg/ kg/min (median)
Rowcliff <i>et al</i> 2016 [80]	Retrospective cohort study	IV	48 neonates with BW 390-1310 grams and GA 26-30 weeks, BW 726-1450 grams	0.2-1 mcg/kg per min

Table 9. Characteristics of included studies investigating the use of vasopressin (VAS).

Reference	Study Type	Level of Evidence	Study Population	Vasopressin infusion dose range
Buijs <i>et al.</i> 2014 [23]	Prospective observational cohort study	IV	28 neonates with CDH with median BW 3125 grams and GA 38.6 weeks. (28 controls)	0.11 mcg/ kg/min (median)
Masarwa <i>et al.</i> 2017 [89]	SR-MA-Trial Sequential analysis	I	35 newborns out of 248 children	TP 4-20-mcg/kg/h AVP 0.01-0.04 u/kg/h
Rodriguez-Nunez <i>et al.</i> 2010 [87]			2 term newborn	TP 20mcg/kg Q 6 h AVP 0.01-0.04 u/kg/h
Bidegain <i>et al.</i> 2010 [100]			20 ELBW (23-27 weeks, 400-980 g)	
Matok <i>et al.</i> 2005 [85]			3 term newborns	