VII CONGRESSO CATARINENSE DE OBSTETRÍCIA E GINECOLOGIA

II Congresso Catarinense de Perinatologia

25 a 27 de junho de 2015 | Expoville | Joinville | SC

Maria Elisabeth Lopes Moreira

Declaração de conflito de interesse

Nestlé, Mead Jonhson e Danone nos anos 2014-2015

Hipotensão e prematuridade

Tratamento

Diagnóstico

perda da auto-regulação do fluxo sanguíneo

- Definição estatística – média e mediana por idade gestacional – critica poucos incluidos
- MAP menor que 30 mm Hg – informação NIRS
- Eco funcional –fluxo da cava superior
- MAP associada a debito urinário, perfusão e níveis séricos de lactato

Diagnostico

Figure 1.

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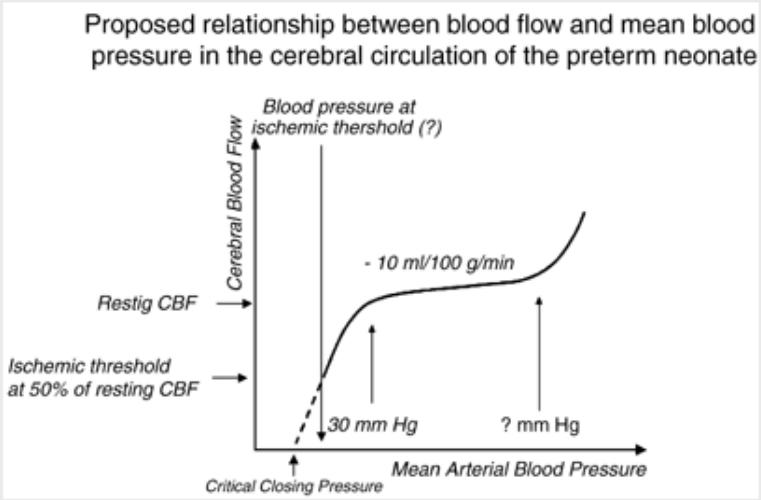

The flat portion of the curve represents the autoregulatory plateau. The upper threshold is not known. Below the lower threshold, which is thought to be around 30 mm Hg, blood flow falls more in proportion to blood pressure. The critical closing pressure (CrCP) depends on arterial elasticity and intracranial pressure. The ischemic threshold is assumed to be around 50% of resting blood flow but the blood pressure at the ischemic threshold is not known. Adapted with permission, Early Human Development[4].

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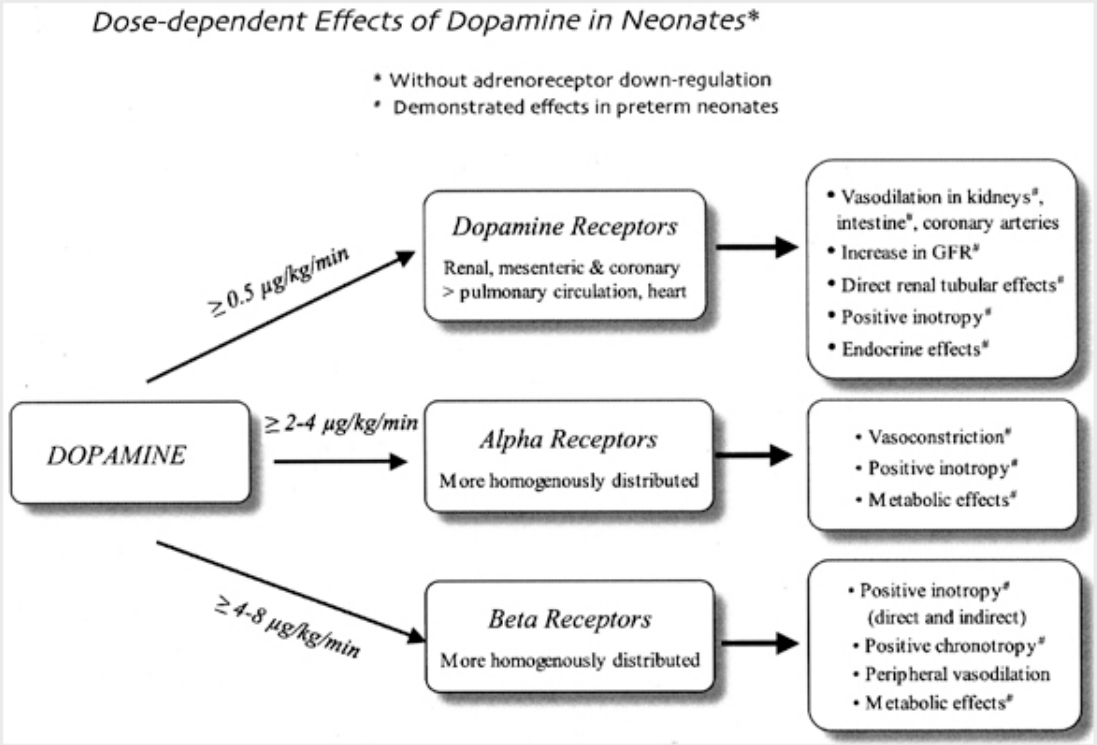
Circulação no pré-termo

- Preload-
- Afterload
- Contratilidade
- Frequencia cardiaca maior
- Shunts forame oval e canal arterial

Dopamina



In the preterm neonate, low doses of dopamine stimulate the dopaminergic receptors. At low-to-medium doses, effects of alpha-adrenergic receptor stimulation also appear. At medium-to-high doses (>8–10 µg/kg/min), effects of both beta- and alpha-receptor stimulation dominate the hemodynamic response to the drug.[21] However, this response is influenced by several factors (state of cardiovascular adrenergic receptor expression, etc) regulated by the level of maturity and disease severity.[1]

Dobutamina

Figure 4.

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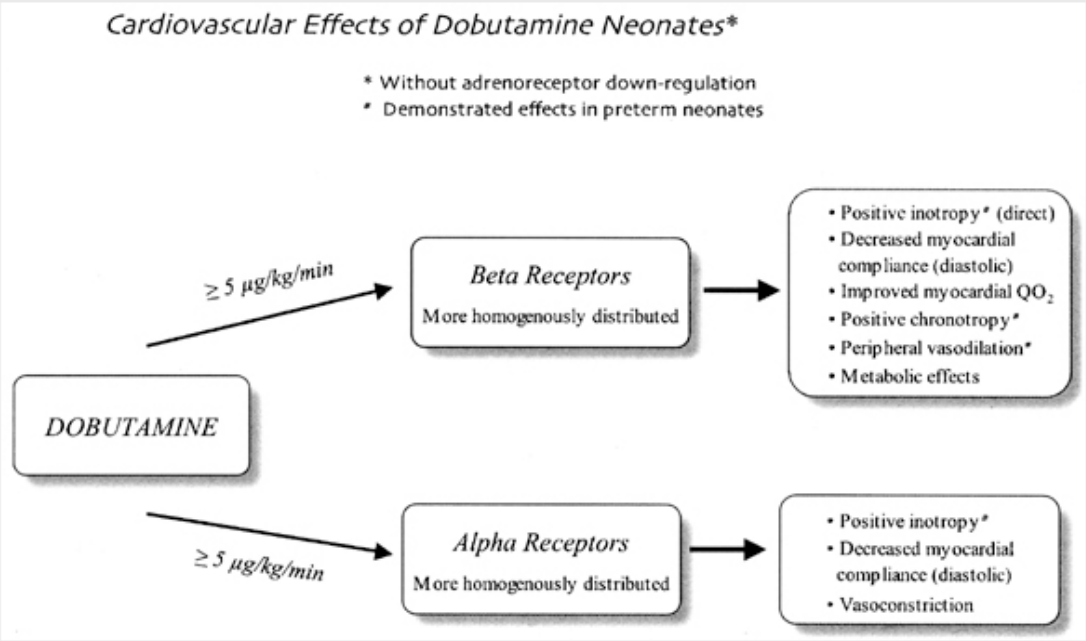

In the preterm neonate, dobutamine increases cardiac output and exerts a variable degree of a peripheral vasodilatory effect.[23, 24] The cardiovascular response is influenced by several factors (state of cardiovascular adrenergic receptor expression, etc) regulated by the level of maturity and disease severity.[1]

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Epinefrina

Figure 3.

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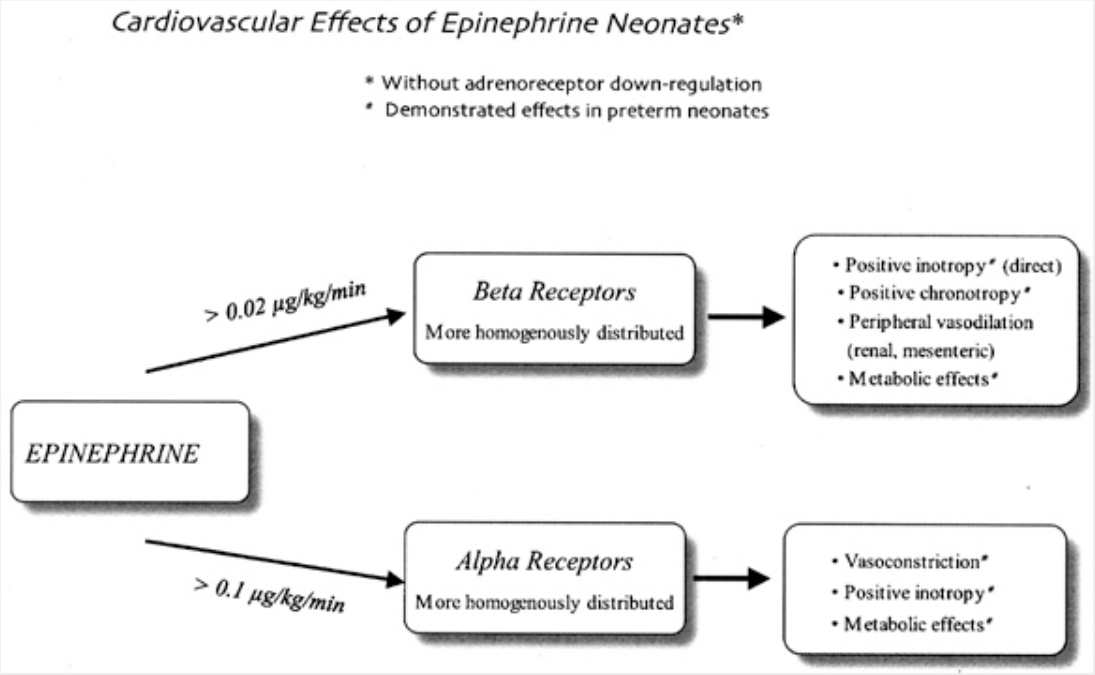

In the preterm neonate, at low-to medium doses of epinephrine administration, effects of beta- and alpha-adrenergic receptor stimulation become apparent.[22] The cardiovascular response is influenced by several factors (state of cardiovascular adrenergic receptor expression, etc) regulated by the level of maturity and disease severity.[1]

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Drogas vasoativas

Table 2
Estimated relative cardiovascular receptor stimulatory effects of inotropes, lusitropes, and vasopressors

	Adrenergic, Dopaminergic, and Vasopressin Receptors					
	α_1/α_2	β_2	α_1	β_1/β_2	DA_1/DA_2	V_{1a}
	Vascular	Vascular	Cardiac	Cardiac	Vascular/Cardiac	Vascular
Phenylephrine	++++	0	+	0	0	0
Norepinephrine	++++	0/+	++	++++	0	0
Epinephrine	++++	++++	++	++++	0	0
Dopamine[a]	++++	++	++	+++	++++	0
Dobutamine[b]	+/0	++	++	++++	0	0
Isoprenaline	0	+++	0	++++	0	0
Vasopressin	0	0	0	0	0	++++
PDE-III inhibitors	0	0	0	0	0	0
PDE-V inhibitors	0	0	0	0	0	0

Abbreviations: $\alpha_1/\alpha_2/\beta_1/\beta_2$, subtypes of α- and β-adrenoreceptors; DA, dopamine; DOB, dobutamine; PDE, phosphodiesterase enzyme; PDE-III inhibitors used in neonates, amrinone, milrinone; PDE-V inhibitors used in neonates, sildenafil; V_{1a}, vasopressin receptor expressed in the vasculature.

[a] Dopamine also has serotoninergic actions.

[b] Efficacy of dobutamine is independent of its affinity for adrenoreceptors.

Rating System for the Hierarchy of Evidence

Level I: Evidence from a systematic review or meta-analysis of all relevant randomized controlled trials (RCTs) or evidence-based clinical practice guidelines based on systematic reviews of RCTs

Level II: Evidence obtained from at least one well-designed RCT

Level III: Evidence obtained from well-designed controlled trials without randomization

Level IV: Evidence from well-designed case-control and cohort studies

Level V: Evidence from systematic reviews of descriptive and qualitative studies

Level VI: Evidence from a single descriptive or qualitative study

Level VII: Evidence from the opinion of authorities or reports of expert committees

Princípios gerais para tratamento

New NANN Practice Guideline: The Management of Hypotension in the Very-Low-Birth-Weight Infant.
Vargo, Lyn; PhD, RN; Seri, Istvan; MD, PhD

Advances in Neonatal Care. 11(4):272-278, August 201
DOI: 10.1097/ANC.0b013e318229263c

1- Hipotensão em recem-nascidos deve ser tratada baseada na etiologia da hipotensão – Nível de evidência VII
2- Em geral, não está indicado expansão de volume em recem-nascidos em choque. Na maioria das vezes estes RN não são hipovolemcimos . Nível de evidencia I
3- RN com DPP ou outras perdas de volume irao necessitar de volume e soro fisiologico, ringer, sangue O negativo pode ser usado e admisntrado em 5 a 10 minutos- 10 ml/Kg. Albumina não é recomendada para expansão – Nível de evidencia V
3- Dopamina deve ser considerada a primeira droga a ser utilizada quando a causa da hipotensão é desconhecida. Nível de evidencia I
4- Dobutamina deve ser considerda como primeira escolha quando houver evidencais de disfunção miocárdica – Nível de evidencia I

Practice Recommendation	Level of Evidence	Referen
1. Hypotension in VLBW infants should be treated on the basis of the etiology of the hypotension whenever an etiology is known. **Rationale**: It is generally agreed by experts that adequate treatment of blood pressure requires identification of the primary factor leading to the hypotension.	VII	15, 16, 17
2. In general, the early use of volume expansion with normal saline, fresh frozen plasma, albumin, plasma substitute, or blood in VLBW infants with hypotension is not recommended. **Rationale**: Evidence that VLBW infants with hypotension benefit from volume expansion is insufficent, as is evidence to determine what type of volume expansion should be used in VLBW infants.[18,19] The majority of VLBW infants who are hypotensive are not hypovolemic and have normal circulating blood volume.[15,16]	I VII	18, 19 15, 16
3. In VLBW infants with evidence of placenta previa, abruption, blood loss from the umbilical cord, fetal anemia, or evidence of fetal-maternal transfusion, the administration of a volume expander such as normal saline, ringers lactate, or O Rh-negative blood may be used as an initial dose of 10 ml/kg given over 5–10 minutes. This dose may be repeated.[20] Albumin is not generally recommended for use as a volume expander in VLBW infants. **Rationale**: In VLBW infants with evidence of blood loss, the effective circulating blood volume may be decreased, which can result in hypotension. Volume expansion will restore normal intravascular volume, increase preload, and thus increase cardiac output in a hypovolemic baby.[20,21,22] Use of albumin is not generally recommended because of the increased risk of infection (it is a blood product); also, the cost of isotonic saline is approximately one-fifth the cost of 4.5% human albumin.[23]	VII	20, 21, 22
4. Dopamine, carefully titrated to the optimum hemodynamic response, should be considered prior to dobutamine for treatment of hypotension alone in VLBW infants when the cause of hypotension is unknown. **Rationale**: Dopamine is more effective than dobutamine for treating hypotension in premature infants. Dopamine does not appear to affect the incidence of severe periventricular hemorrhage, periventricular leukomalacia, or tachycardia. *Cautious stepwise increases* in dopamine in hypotensive VLBW infants are not associated with an abnormal neurologic picture, combined adverse outcomes (death, cerebral palsy, or profound neurodevelopmental delay), or developmental delay.	I III	24 25, 26
5. In VLBW infants with hypotension and LSBF during the *first postnatal day* caused by the immature myocardium's inability to pump against the sudden increased peripheral resistance that occurs with the removal of the placenta (myocardial dysfunction is caused by the VLBW infant's decrease in cardiac output when faced with an increase in peripheral resistance) and vasoconstriction of the immature forebrain vasculature, dobutamine may be considered the initial treatment choice in improving blood pressure. If blood pressure decreases after beginning dobutamine, low-dose dopamine can be added to the treatment regimen. **Rationale**: Dobutamine has a direct positive inotropic effect and has a variable degree of peripheral vasodilatory response. Thus, in situations where the VLBW infant's cardiac output has been compromised by the sudden increased peripheral resistance caused by removal of the low resistance placenta, as happens after birth, experts believe that *cautious stepwise increases* in dobutamine may increase cardiac output by promoting systemic vasodilation and improving LSBF. However, *no evidence* that dobutamine promotes vasodilation in the 1-day-old VLBW infant exists. Use of dopamine, primarily at high doses, in these patients may further increase vasoconstriction and decrease systemic blood flow and thus decrease cardiac output.[28]	I VII	27 28

Princípios gerais para tratamento Table. No

6- Se a causa presumida do choque for infecçnao dopamina é a primeira droga de escolha e se ela não funcionar epinefrina deve ser considerada. Nivel VII

7- Epinefrina pode ser tão efetiva quanto a dopmaina mas os conhecimentos sobre sua ação em pretermos sao escassos – Nível de evidencia II

8- O uso de hidrocortisona deve ser reservado para choque refratário . De preerencia deveria ser obtido um nível de cortisol antes do uso. Nivel de evidencia I e II

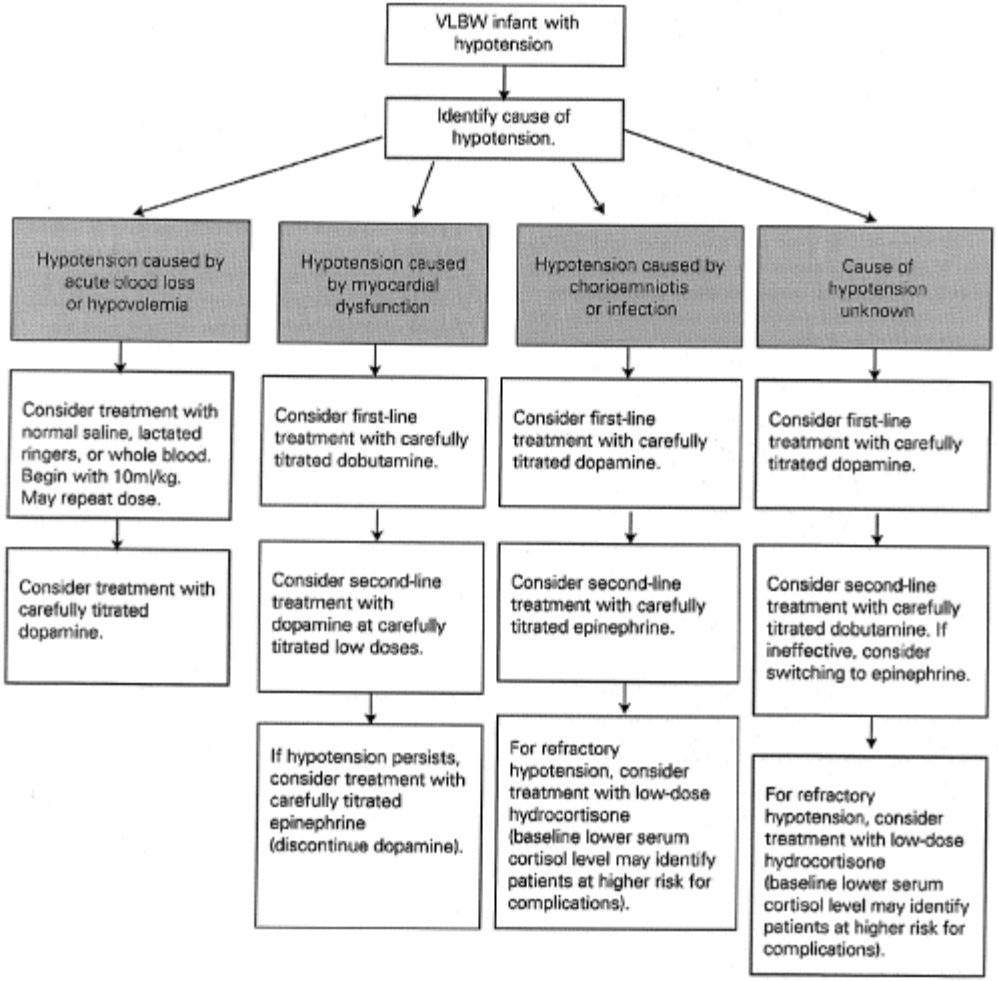
9- Dexametadona esta associada a paralisia cerebral e seu uso deve ser reservado Nivel I

New NANN Practice Guideline: The Management of Hypotension in the Very-Low-Birth-Weight Infant.
Vargo, Lyn; PhD, RN; Seri, Istvan; MD, PhD

Advances in Neonatal Care. 11(4):272-278, August 2011.
DOI: 10.1097/ANC.0b013e318229263c

Practice Recommendation	Level of Evidence	Reference(s)
6. If hypotension in the VLBW infant is related to evidence of infection, dopamine should be considered as the first-line treatment. If dopamine is not effective, treatment with epinephrine should be considered. **Rationale**: Hypotension related to infection is primarily caused by systemic vasodilation. Only in the late phase of sepsis is hypotension related to myocardial dysfunction. Therefore, hypotension in VLBW infants with probable infection should be treated with a vasopressor or intropic agent such as dopamine or epinephrine that will promote vasoconstriction as well as myocardial function.	VII	28, 29, 30
7. Epinephrine can be as effective as dopamine in increasing blood pressure in hypotensive VLBW infants, but knowledge about epinephrine's effect on systemic blood flow is limited. **Rationale**: Low-dose epinephrine has strong beta- and somewhat weaker alpha-adrenergic effects and produces an increase in cardiac output and blood pressure. *Cautious stepwise increases* in epinephrine in hypotensive VLBW infants are not associated with an abnormal neurologic picture, combined adverse outcomes (death, cerebral palsy, or profound neurodevelopmental delay), or developmental delay.	II	25, 28, 31, 32, 33
8. The use of hydrocortisone is as effective as dopamine in improving hypotension in VLBW infants, but data on the long-term safety of corticosteroids for this use are insufficient. Thus, its use should be reserved for infants with refractory hypotension. Hydrocortisone should *not* be used concurrently with indomethacin. When one is considering the use of hydrocortisone for treatment, it may be useful to obtain a baseline serum cortisol level; this may identify infants with low levels who will benefit from hydrocortisone treatment. **Rationale**: Hydrocortisone has been shown to improve hypotension, increase tissue perfusion, and prevent ischemic tissue injury. However, hydrocortisone's neurodevelopmental effects and long-term effects are unclear. Nor is it clear whether longer-term clinical outcomes are improved with the use of hydrocortisone. Low baseline serum cortisol levels may identify infants who will benefit from hydrocortisone treatment; one study demonstrated that infants with serum cortisol levels below the median who were treated with hydrocortisone had increased survival without bronchopulmonary dysplasia when compared to those who did not receive hydrocortisone.	I II V VI VII	34 35, 36, 37, 38 39 40 41, 42
9. A single dose of dexamethasone may increase blood pressure in hypotensive VLBW infants, but dexamethasone cannot be recommended because of its documented negative effect on neurodevelopmental outcomes if given during the first postnatal days. **Rationale**: Several studies using both long and short courses of dexamethasone with relatively high doses have demonstrated significant effects on central nervous system development. Because of these findings and the lack of information on the safety of a short-course, lower-dose dexamethasone for treatment of hypotension, it cannot be recommended for use at this time.	I II VII	34 43, 44, 45, 46 15
10. At present, no evidence supports the use of milrinone for the treatment of hypotension in VLBW infants. **Rationale**: A double-blinded randomized controlled trial comparing the effectiveness of milrinone versus placebo on LSBF in VLBW infants demonstrated that milrinone did not prevent LSBF in these infants. No adverse effects were demonstrated with milrinone.	II	47
11. Research to recommend the use of dopamine (or other vasopressor-inotropes) for the treatment of hypotension related to a patent ductus arteriosus (PDA) in VLBW infants is scant. **Rationale**: Only one observational prospective study has been conducted that suggested that dopamine increased pulmonary vascular resistance in VLBW infants with hypotension and PDA and thus increased blood pressure and systemic blood flow (SVC flow) by decreasing the left-to-right shunt.	VI VII	48 49

Algorithm for Treatment of Hypotension in the VLBW Infant During the First 3 Days of Postnatal Life



Outras drogas

- Milrinona
- Vasopressina
- Noradrenalina

Vasopressina

J Pediatr. 2015 Apr;166(4):850-5. doi: 10.1016/j.jpeds.2014.12.027. Epub 2015 Jan 29.

Vasopressin versus dopamine for treatment of hypotension in extremely low birth weight infants: a randomized, blinded pilot study.

Rios DR[1], Kaiser JR[2].

⊕ Author information

Abstract

OBJECTIVE: To evaluate vasopressin vs dopamine as initial therapy in extremely low birth weight (ELBW) infants with hypotension during the first 24 hours of life.

STUDY DESIGN: ELBW infants with hypertension ≤ 30 weeks' gestation and ≤ 24 hours old randomly received treatment with vasopressin or dopamine in a blinded fashion. Normotensive infants not receiving vasopressor support served as a comparison group.

RESULTS: Twenty ELBW infants with hypertension received vasopressin (n = 10) or dopamine (n = 10), and 50 were enrolled for comparison. Mean gestational age was 25.6 ± 1.4 weeks and birth weight 705 ± 154 g. Response to vasopressin paralleled that of dopamine in time to adequate mean blood pressure (Kaplan-Meier curve, P = .986); 90% of infants in each treatment group responded with adequate blood pressure. The vasopressin group received fewer doses of surfactant (P < .05), had lower PaCO2 values (P < .05), and were not tachycardic (P < .001) during vasopressin administration, compared with the dopamine group.

CONCLUSIONS: Vasopressin in ELBW infants as the initial agent for early hypotension appeared safe. This pilot study supports a larger randomized controlled trial of vasopressin vs dopamine therapy in ELBW infants with hypotension.

PMID: 25641242 [PubMed - in process] PMCID: PMC4380753 [Available on 2016-04-01]

Trial record **9 of 41** for: hypotension and newborn infant

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Study of Dopamine Versus Vasopressin for Treatment of Low Blood Pressure in Low Birth Weight Infants

This study has been completed.

Sponsor:
Baylor College of Medicine

Collaborator:
Thrasher Research Fund

Information provided by (Responsible Party):
Danielle Rios, Baylor College of Medicine

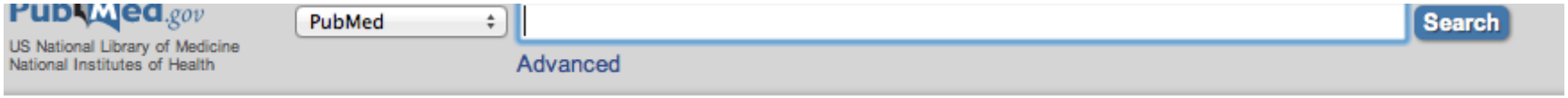
ClinicalTrials.gov Identifier:
NCT01318278

First received: March 16, 2011
Last updated: February 24, 2015
Last verified: February 2015
History of Changes

Full Text View | Tabular View | Study Results | Disclaimer | How to Read a Study Record

Arms	Assigned Interventions
Active Comparator: Dopamine treatment Dopamine treatment beginning at 5 mcg/kg/min and titrated by 5 mcg/kg/min to effect up to maximum of 20 mcg/kg/min	Drug: Dopamine dopamine at low/medium/and high dose (5, 10, 15, and 20 mcg/kg/min) given IV as a continuous infusion, titrated up for efficacy Other Name: Dopamine Hydrochloride
Active Comparator: Vasopressin treatment Arginine Vasopressin treatment beginning at 0.01 units/kg/hr and titrated up by 0.01 units/kg/hr to effect up to a maximum of 0.04 units/kg/hr	Drug: Arginine Vasopressin vasopressin at low/medium/and high dose (0.01, 0.02, 0.03, or 0.04 units/kg/hr) given IV as a continuous infusion, titrated up for efficacy Other Names: • Vasopressin • Antidiuretic Hormone (ADH) • Pitressin (US brand name) • Pressyn;Pressyn AR (Canadian brand names) • Argipressin

Milrinone



Abstract ▾ Send to: ▾

J Pediatr. 2009 Feb;154(2):189-95. doi: 10.1016/j.jpeds.2008.07.059. Epub 2008 Sep 25.

Randomized trial of milrinone versus placebo for prevention of low systemic blood flow in very preterm infants.

Paradisis M[1], Evans N, Kluckow M, Osborn D.

⊕ **Author information**

Abstract

OBJECTIVE: To assess the effectiveness of early prophylactic milrinone versus placebo for prevention of low systemic blood flow in high-risk preterm infants.

STUDY DESIGN: Double-blind randomized placebo controlled trial of milrinone (loading dose 0.75 microg/kg/min for 3 hours then maintenance 0.2 microg/kg/min until 18 hours after birth) versus placebo. Infants born <30 weeks gestational age and <6 hours of age were eligible and were monitored with serial echocardiography, head ultrasound scanning, and continuous invasive blood pressure. Primary outcome was maintenance of superior vena cava (SVC) flow > or =45 mL/kg/min through the first 24 hours. The exit criterion was hypotension unresponsive to volume and inotropes.

RESULTS: Ninety infants were enrolled, equal proportions maintained SVC flow > or =45 mL/kg/min after treatment commenced. No significant difference was observed in SVC flow, right ventricular output, and blood pressure during the first 24 hours; or grades 3 to 4 periventricular/intraventricular hemorrhage and death. Heart rate was higher and constriction of the ductus was slower in the infants randomized to milrinone.

CONCLUSIONS: Milrinone did not prevent low systemic blood flow during the first 24 hours in very preterm infants, and no adverse effects were attributable to milrinone. Use of a preventative treatment with rescue model allowed comparison of an inotrope with placebo in this high-risk group of infants.

PMID: [illegible] [PubMed - indexed for MEDLINE]