DOBUTamine
Newborn use only

2021

<table>
<tr><td>Alert</td><td>In conditions with low systemic vascular resistance (SVR) (e.g., septic shock) dobutamine is not the appropriate first drug of choice</td></tr>
<tr><td>Indication</td><td>Inotrope to increase cardiac output in neonates with myocardial dysfunction and unchanged or increased systemic vascular resistance.</td></tr>
<tr><td>Action</td><td>Catecholamine with beta-1 and beta-2 receptor actions which increases myocardial contractility, heart rate and conduction velocity and decreases SVR [1].
Dose dependent effects:
• Low dose, 2.5 microgram/kg/min – no significant hemodynamic effects in neonates with cardiovascular compromise
• Moderate dose, 5–7.5 microgram/kg/min – increases cardiac output
• Higher dose, 5–20 microgram/kg/min – increases cardiac output and blood pressure in hypotensive preterm infants
An additional effect of dobutamine on increasing cardiac output has been demonstrated in hypotensive preterm infants receiving dopamine.</td></tr>
<tr><td>Drug type</td><td>Inotropic agent</td></tr>
<tr><td>Trade name</td><td>Abbott Dobutamine Hydrochloride, Dobutamine Sandoz, Dobutamine Hydrochloride DBL, Dobutrex</td></tr>
<tr><td>Presentation</td><td>250 mg/20 mL solution for injection; 250mg powder for reconstitution (Dobutrex)</td></tr>
<tr><td>Dose</td><td>5−20 microgram/kg/minute</td></tr>
<tr><td>Dose adjustment</td><td></td></tr>
<tr><td>Maximum dose</td><td>Use of up to 20 microgram/kg/min reported in neonates</td></tr>
<tr><td>Total cumulative dose</td><td></td></tr>
<tr><td>Route</td><td>Continuous IV infusion</td></tr>
<tr><td>Preparation</td><td>SINGLE STRENGTH continuous IV infusion
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 10 microgram/kg/minute</td><td>30 mg/kg dobutamine and make up to 50 mL</td></tr>
</table>
Draw up 2.4 mL/kg (30 mg/kg of dobutamine) and add glucose 5% or sodium chloride 0.9% to make a final volume of 50 mL. Infusing at a rate of 1 mL/hour = 10 microgram/kg/minute.

DOUBLE STRENGTH continuous IV infusion - Can be used for infants up to 4200 g.*
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 20 microgram/kg/minute</td><td>60 mg/kg dobutamine and make up to 50 mL</td></tr>
</table>
Draw up 4.8 mL/kg (60 mg/kg of dobutamine) and add glucose 5% or sodium chloride 0.9% to make a final volume of 50 mL. Infusing at a rate of 1 mL/hour = 20 microgram/kg/minute.
* Maximum diluted concentration is 5 mg/mL.

QUARDRUPLE STRENGTH continuous IV infusion - Can be used for infants up to 2100 g.*
<table>
<tr><th>Infusion strength</th><th>Prescribed amount</th></tr>
<tr><td>1 mL/hour = 40 microgram/kg/minute</td><td>120 mg/kg dobutamine and make up to 50 mL</td></tr>
</table>
Draw up 9.6 mL/kg (120 mg/kg of dobutamine) and add glucose 5% or sodium chloride 0.9% to make a final volume of 50 mL. Infusing at a rate of 1 mL/hour = 40 microgram/kg/minute.
* Maximum diluted concentration is 5 mg/mL.</td></tr>
<tr><td>Administration</td><td>Continuous IV infusion preferably via a central line.
Do not flush line or suddenly stop infusion.
If Dobutrex brand is used reconstitute each vial with 20 mL WFI to make a concentration of 250 mg/20 mL.</td></tr>
<tr><td>Monitoring</td><td>Continuous heart rate, ECG and blood pressure monitoring preferable.
Assess urine output and peripheral perfusion frequently.</td></tr>
<tr><td>Contraindications</td><td>Contraindicated in patients with idiopathic hypertrophic sub aortic stenosis and previous hypersensitivity to dobutamine.</td></tr>
<tr><td>Precautions</td><td>May cause hypotension therefore ensure adequate circulating blood volume prior to commencement.</td></tr>
<tr><td>Drug interactions</td><td>No evidence of drug interactions demonstrated in clinical studies. Exert caution when co-administering with drugs which can cause hypertension or tachycardia.</td></tr>
<tr><td>Adverse reactions</td><td>The positive inotropic and chronotropic effects of dobutamine may cause hypertension, tachyarrhythmias, myocardial ischaemia and ventricular fibrillation.
Hypotension may result from vasodilation.</td></tr>
</table>

	May cause hypokalaemia. Phlebitis has been reported.
Compatibility	Fluids: Glucose 5%, glucose 10%, glucose in sodium chloride solutions, glucose 5% in Hartmann's, Hartmann's, sodium chloride 0.9%, sodium chloride 0.45% Y site:[10,11,12] Amino acid solutions, adrenaline hydrochloride, alfentanil, alprostadil, amiodarone (for amiodarone strength≤15 mg/mL)[10], amikacin, atenolol, atracurium besylate, atropine sulfate, azithromycin, aztreonam, calcium chloride, calcium gluconate, capreomycin, caspofungin, ceftizoxime, ciprofloxacin, clarithromycin, clindamycin phosphate, clonidine, dexmedetomidine, digoxin, diltiazem, dopamine, doxycycline, enalaprilat, ephedrine, epinephrine HCL, epoetin alfa, erythromycin lactobionate, fentanyl, fluconazole, gentamicin, glycopyrrolate, ketamine, labetolol, leucovorin, levofloxacin, lidocaine, linezolid, lorazepam, magnesium sulfate, methylprednisolone sodium succinate, metronidazole, milrinone, morphine sulfate, multiple vitamin injectins, naloxone, netilmicin, nitroglycerin, norepinephrine, octreotide, ondansetron, pamidronate, pancuronium, papaverine, pentoxifylline, potassium acetate and chloride (refer to special comments), procainamide, propranolol, protamine, pyridoxine, ranitidine, remifentanil, rocuronium, sodium acetate, streptokinase, succinylcholine, thiamine HCL, tobramycin, tolazoline, urokinase, vancomycin, vasopressin, vecuronium, verapamil, voriconazole, zidovudine.
Incompatibility	Fluids: Sodium bicarbonate, alkaline solutions, diluents that contain sodium bisulfite and ethanol. Y site:[10,11] Aciclovir, alteplase, aminophylline, amphotericin B cholesteryl sulfate complex, amphotericin B conventional colloidal, amphotericin B lipid complex, amphotericin B liposome, ampicillin, azathioprine, benzylpenicillin, cefalotin, cefazolin, cefotaxime, cefoxitin, ceftriaxone, cefuroxime, chloramphenicol sodium succinate, cloxacillin, dexamethasone, diazoxide, fluorouracil, folic acid (sodum salt), ganciclovir, heparin, hydrocortisone sodium succinate, ibuprofen lysine, indometacin, oxacillin, penicillin G potassium, penicillin G sodium, pentobarbital, phenobarbital, phenytoin, piperacillin, piperacillin-tazobactam, sodum bicarbonate, sugammadex, sulfamethoxazole-trimethoprim, ticarcillin, ticarcillin-clavulanate
Stability	Reconstituted solution − Dobutrex brand only: Stable for 6 hours at 25°C and 24 hours at 2 to 8°C. Diluted solution – other brands: Stable for 24 hours at 25°C. Solutions may turn pink and colour will increase with time but with no significant loss of potency. Discard solutions that are hazy or contain particles.
Storage	Vial: Store below 25°C. Protect from light. Discard remaining solution after use.
Excipients	
Special comments	Dobutamine should always have a dedicated line to prevent accidental bolus. A 1983 report by Kirschenbaum HL[12] observed change in colour when dobutamine was mixed with potassium chloride 20 meq/10 mL. However, Trissel's clinical pharmaceutical database on parenteral compatibility reports compatibility with potassium acetate and chloride.[10]
Evidence	**Efficacy** Treatment of hypotension in preterm infants: Dobutamine is less effective than dopamine at increasing blood pressure in hypotensive infants but this may not change the clinical outcome. A single study[2] reported left ventricular output increased with dobutamine compared to a decrease with dopamine (LOE I, GOR C) [3]. Treatment of low systemic blood flow: Dobutamine increased superior vena cava (SVC) flow with little change in blood pressure, whereas dopamine increased blood pressure with little change in SVC flow. There was no difference in clinical outcome (LOE II, GOR C) [4-6]. **Summary:** Dobutamine is recommended to increase cardiac output in neonates with myocardial dysfunction and unchanged or increased systemic vascular resistance (SVR). In conditions with low SVR (e.g., septic shock) dobutamine is not the appropriate first drug of choice[1]. **Safety** No evidence of an effect on the incidence of adverse neuroradiological sequelae (severe periventricular haemorrhage and/or periventricular leucomalacia), or on the incidence of tachycardia. Insufficient data confirming long term benefit and safety of dobutamine [3]. Common side effects reported were ventricular arrhythmias, tachycardia, hypotension and chest pain (children) (LOE III-2, GOR B) [7].

	Pharmacokinetics Dobutamine concentrations positively correlated with infusion dosages. Range of values vary widely between patients despite similar doses [7]. Short half-life around 2 minutes [8].
Practice points	
References	1. Noori, S. and I. Seri, Neonatal blood pressure support: the use of inotropes, lusitropes, and other vasopressor agents. Clin Perinatol, 2012. 39(1): p. 221–38. 2. Roze, J.C., et al., Response to dobutamine and dopamine in the hypotensive very preterm infant. Arch Dis Child, 1993. 69(1 Spec No): p. 59–63. 3. Subhedar, N.V. and N.J. Shaw, Dopamine versus dobutamine for hypotensive preterm infants. Cochrane Database Syst Rev, 2003(3): p. CD001242. 4. Osborn, D., N. Evans, and M. Kluckow, Randomized trial of dobutamine versus dopamine in preterm infants with low systemic blood flow. J Pediatr, 2002. 140(2): p. 183–91. 5. Osborn, D.A., N. Evans, and M. Kluckow, Left ventricular contractility in extremely premature infants in the first day and response to inotropes. Pediatr Res, 2007. 61(3): p. 335–40. 6. Osborn, D.A., et al., Low superior vena cava flow and effect of inotropes on neurodevelopment to 3 years in preterm infants. Pediatrics, 2007. 120(2): p. 372–80. 7. Mahoney, L., et al., A Literature Review of the Pharmacokinetics and Pharmacodynamics of Dobutamine in Neonates. Pediatr Cardiol, 2015 Sep 7. [Epub ahead of print]. 8. Schwartz, P.H., M.K. Eldadah, and C.J. Newth, The pharmacokinetics of dobutamine in pediatric intensive care unit patients. Drug Metab Dispos, 1991. 19(3): p. 614–9. 9. MIMSOnline Accessed via CIAP on 29 June 2021. 10. Micromedex® online. Accessed on 29 June 2021. 11. Australian Injectable Drugs Handbook, Accessed on 29 June 2021. 12. Kirschenbaum HL, Aronoff W, Piltz GW, Perentesis GP, Cutie AJ. Compatibility and stability of dobutamine hydrochloride with large-volume parenterals and selected additives. American journal of hospital pharmacy. 1983 Oct 1;40(10):1690-1.

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