SYMPATHOMIMETIC AGENTS¾Cardiovascular Use (Parenteral-Systemic)

VA CLASSIFICATION (Primary/Secondary)
Dobutamine¾AU100/CV900
Dopamine¾AU100/
Ephedrine¾AU100/
Epinephrine¾AU100/
Isoproterenol¾AU100/
Mephentermine¾AU100/
Metaraminol¾AU100/
Methoxamine¾AU100/
Norepinephrine¾AU100/
Phenylephrine¾AU100/; CV300
Commonly used brand name(s):Adrenalin4; Aramine7; Dobutrex1; Intropin2; Isuprel5; Levophed9; Neo-Synephrine10; Revimine2; Vasoxyl8; Wyamine6.
Indications

Accepted

Bradycardia (treatment)¾Isoproterenol is indicated for the temporary control of hemodynamically significant bradycardia, such as bradycardia associated with a denervated transplanted heart or third degree heart block due to conduction system disease. 20, 60, 71 Electrical pacing is the preferred treatment for maintenance of an adequate ventricular rate and isoproterenol is used only for temporary support when electrical pacing is unavailable. 60 Isoproterenol may also be used in long QT-related arrhythmias where underlying bradycardia is common. 71

Hypotension, acute (prophylaxis and treatment) or

Shock (treatment)¾The sympathomimetic agents (except isoproterenol) are indicated for the correction of hypotension, unresponsive to adequate fluid volume replacement, as part of shock syndrome caused by myocardial infarction, trauma, bacteremia 77 , open-heart surgery, renal failure, chronic cardiac decompensation, drug overdose 65, 76 , or other major systemic illness 70.

2, 3, 6, 8, 41

The specific choice of drug must be determined by clinical assessment. 20 This assessment may include hemodynamic status, mental status, urine output, and other measures of tissue perfusion. 20 In refractory cases, the use of multiple drug therapy may be necessary for blood pressure support. 20

In septic shock, low-dose dopamine may be used in conjunction with norepinephrine to maintain renal blood flow. 21, 25, 31, 32, 33

In hypovolemic shock, the sympathomimetic agents should be used only as adjuncts to energetic fluid volume replacement to provide temporary support for maintaining coronary and cerebral artery perfusion until volume replacement therapy is completed. 6, 20 These medications must not be used as the sole therapy in hypovolemic patients. 6, 20

In acute hypotension associated with myocardial infarction, sympathomimetic agent-induced increases in myocardial oxygen demand and the work of the heart may outweigh the beneficial effect of the medication. Also, cardiac arrhythmias induced by the sympathomimetic agents may be more likely to occur in patients with myocardial infarction. 20

Although norepinephrine is indicated in the treatment of acute hypotension occurring during spinal anesthesia, vasopressors that have a longer duration of action (e.g., metaraminol or phenylephrine) are also useful 67.

Ephedrine is indicated for the correction of hypotension secondary to spinal or other types of nontypical conduction anesthesia. 4, 28 It is also used in hypotensive states following sympathectomy, or following overdose with ganglionic blocking agents, antiadrenergic agents, or other medications that lower blood pressure in the treatment of hypertension. 4

Metaraminol is indicated for the prevention and treatment of acute hypotension occurring with spinal anesthesia and in the adjunctive treatment of hypotension resulting from hemorrhage, reactions to medications, surgical complications, and shock associated with brain damage due to trauma or tumor. 5 However, metaraminol is not indicated as the sole treatment for hypotension secondary to decreased plasma volume.
Mephentermine is indicated in the treatment of hypotension secondary to ganglionic blockade and hypotension occurring with spinal anesthesia. 15

Methoxamine is indicated for supporting, restoring, or maintaining blood pressure during general anesthesia with agents that sensitize the myocardium to arrhythmias, such as halothane. 7

Dobutamine is not recommended for the adjunctive treatment of hypovolemic shock. 20

Cardiac output, low (treatment) or

Congestive heart failure (treatment)¾Dobutamine is indicated to improve cardiac function during cardiac decompensation in congestive heart failure or depressed contractility from cardiac or major vascular surgery. 20, 53

If a vasopressor is also needed, norepinephrine or dopamine is useful for short-term management. 20 However, stimulation of alpha-1 adrenergic receptors produces vasoconstriction, which is undesirable in most patients with severe heart failure. 20, 24 In certain circumstances, a vasodilating agent such as nitroprusside or nitroglycerin may be used as an adjunct to dobutamine to decrease afterload and pulmonary pressures. 20, 24

Cardiac arrest (treatment)¾Epinephrine is indicated during resuscitation of cardiac standstill or cardiac arrest. 1, 60 Epinephrine is used as an adjunct to restore cardiac rhythm in the treatment of cardiac arrest due to various causes. 1 It also has beneficial hemodynamic effects in the setting of cardiopulmonary resuscitation (CPR), improving myocardial and cerebral blood flow. Epinephrine injection may be used for resuscitation in cardiac arrest following anesthetic accidents; 1 however, it should be used with great caution in patients receiving halogenated hydrocarbon anesthetics, especially halothane, because these anesthetics sensitize the myocardium and cardiac arrhythmias may be induced.

In acute attacks of ventricular standstill, physical measures should be used prior to administration of epinephrine. However, if external cardiac compression and attempts to restore circulation by electrical defibrillation or use of a pacemaker fail, intravenous injection of epinephrine into a major vein may be effective.

Shock, anaphylactic (treatment)¾Epinephrine injection is indicated in the emergency treatment of anaphylactic shock. 20

Tachycardia, supraventricular, paroxysmal (treatment)¾Phenylephrine is indicated in the termination of some episodes of paroxysmal supraventricular tachycardia (PSVT). 7

Precautions to Consider

Cross-sensitivity and/or related problems

Dobutamine, dopamine, epinephrine, isoproterenol, metaraminol, methoxamine, norepinephrine, and phenylephrine preparations contain sulfites.

Carcinogenicity/Mutagenicity

Long-term studies have not been done. 2, 5, 6, 7, 8, 59

Pregnancy/Reproduction

Fertility¾Dobutamine: Studies in rats and rabbits have revealed no evidence of fertility impairment. 53

Dopamine: Long-term studies have not been done. 2

Isoproterenol: Studies have not been done. 59

Mephentermine: Long-term studies have not been done. 15

Metaraminol: Long-term studies have not been done. 5

Methoxamine: Long-term studies have not been done. 7

Norepinephrine: Studies have not been done. 6

Phenylephrine: Long-term studies have not been done. 8

Pregnancy¾Dobutamine¾
Adequate and well-controlled studies in humans have not been done.
Reproduction studies in rats and rabbits found no evidence of teratogenicity or harm to the fetus. 53

Dopamine¾
Adequate and well-controlled studies in humans have not been done. 2

Studies in animals have not revealed evidence of teratogenic effects. 2 However, administration of dopamine to pregnant rats resulted in a decreased survival rate of the newborn and a potential for the development of cataracts in survivors. 2

FDA Pregnancy Category C. 2

Ephedrine¾

Adequate and well-controlled studies have not be done in humans. 4

Studies have not been done in animals. 4

FDA Pregnancy Category C. 4

Epinephrine¾

Adequate and well-controlled studies in humans have not been done. 1

Studies in rats given epinephrine at doses 25 times the human dose have revealed teratogenic effects. 1

FDA Pregnancy Category C. 1

Isoproterenol¾

Adequate and well-controlled studies have not been done in humans. 59

Studies have not been done in animals. 59

FDA Pregnancy Category C. 59

Mephentermine¾

It is not known whether mephenterine crosses the placenta. 15 However, mephentermine may increase uterine contractions in pregnant women, especially during the third trimester. 15

Studies have not been done in animals. 15

FDA Pregnancy Category C. 15

Metaraminol¾

Adequate and well-controlled studies have not been done in humans. 5

Metaraminol given to pregnant ewes at a dose of 0.025 mg per kg of body weight (mg/kg) decreased uterine blood flow. 37

FDA Pregnancy Category C. 5

Methoxamine¾

Adequate and well-controlled studies in humans have not been done. 7 However, a fetal death has been reported when the mother received methoxamine concomitantly with other medications. 7 A direct causal relationship has not been established. 7

Methoxamine administered to pregnant ewes and monkeys at doses comparable to those used in humans decreased uterine blood flow and heart rate, and adversely affected fetal acid-base status, as evidenced by hypoxia, hypercarbia, and metabolic acidosis. 7 In pregnant ewes, an inverse relationship between pressor response to methoxamine and uteroplacental blood flow was shown at doses ranging from 0.025 to 0.2 mg/kg. 7, 37 A study in baboons given methoxamine at a dose of 1.3 mg/kg over 57 minutes revealed a decrease in uterine blood flow and a possible association with fetal asphyxia. 7, 38

FDA Pregnancy Category C. 7

Norepinephrine¾

Adequate and well-controlled studies have not been done in humans. 6

Studies have not been done in animals. 6

FDA Pregnancy Category C. 6

Phenylephrine¾

Adequate and well-controlled studies have not been done in humans.

Studies have not been done in animals. 8

FDA Pregnancy Category C. 8

Labor and delivery¾If vasopressor medications are used to correct hypotension or added to the local anesthetic solution during labor and delivery, some oxytocic medications (e.g., vasopressin, ergotamine, ergonovine, methylergonovine) may cause severe persistent hypertension, 3, 7, 8 and rupture of a cerebral blood vessel may occur during the postpartum period. 8

Ephedrine: Ephedrine, when used to maintain blood pressure during low or other spinal anesthesia for delivery, may accelerate fetal heart rate. 4 Use is not recommended when maternal blood pressure exceeds 130/80 mm Hg. 4

Epinephrine: Use during labor is not recommended because epinephrine may delay the second stage of labor. 1

Mephentermine: Mephentermine may cause a decrease in uterine blood flow, which may result in fetal hypoxia. 15 Transient fetal hypertension has also been reported in animals. 15

Breast-feeding

It is not known whether these medications are distributed into breast milk.

Pediatrics

Dobutamine¾Dobutamine has been studied in a limited number of pediatric patients up to 18 years of age. 54, 55, 56, 57 There do not appear to be pediatric-specific problems that would limit the usefulness of dobutamine in pediatric patients.

Dopamine¾Dopamine has been studied in a limited number of pediatric patients up to 18 years of age. 19, 34, 35, 36 Close hemodynamic monitoring is recommended since there is a lack of controlled studies investigating age-dependent dosages and the maximum dosage at which therapeutic response occurs without causing toxicity. 34 In addition, cardiac arrhythmias and gangrene due to extravasation have been reported in pediatric patients. 34

Epinephrine¾Epinephrine has been used in pediatric patients during cardiac arrest and there do not appear to be pediatrics-specific problems that would limit its usefulness in this setting. However, caution is recommended to avoid errors in concentration selection and dosing, since two different dilutions of epinephrine are necessary for the dosing regimen. 51, 52

Geriatrics

Isoproterenol¾Data seem to indicate that elderly patients may exhibit a decreased chronotropic and peripheral vascular response to isoproterenol. 73, 74

Norepinephrine¾The pressor response to norepinephrine does not appear to be altered with aging. 73, 75

Phenylephrine¾The baroreceptor reflex response to phenylephrine appears to decrease with age. 73