

**DOPamine HYDROCHLORIDE
AND 5% DEXTROSE INJECTION, USP
AQUEOUS SOLUTIONS FOR ACUTE CORRECTION OF
HEMODYNAMICS IN SHOCK STATES**

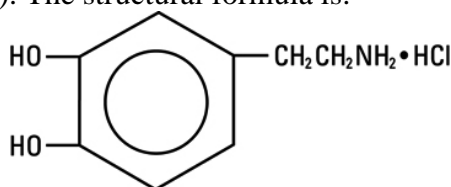
Large Volume Glass Container

R_x only

DESCRIPTION

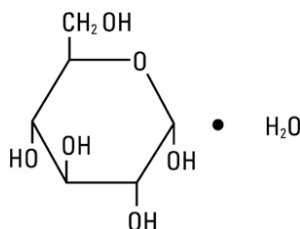
Dopamine Hydrochloride and 5% Dextrose Injection, USP is a sterile, nonpyrogenic, prediluted solution of dopamine hydrochloride in 5% dextrose injection. It is administered by intravenous infusion.

Dopamine, a sympathomimetic amine vasopressor, is the naturally occurring immediate precursor of norepinephrine. Dopamine hydrochloride is a white to off-white, crystalline powder, which may have a slight odor of hydrochloric acid. It is freely soluble in water and soluble in alcohol. Dopamine HCl is sensitive to alkalis, iron salts, and oxidizing agents. Chemically it is designated as 4-(2-aminoethyl)pyrocatechol hydrochloride, and its molecular formula is C₈H₁₁NO₂ • HCl (mol. wt. 189.64). The structural formula is:



Dopamine hydrochloride injection is a clear, practically colorless, sterile, pyrogen-free, aqueous solution of dopamine HCl for intravenous infusion after dilution.

Dextrose, USP is chemically designated D-glucose monohydrate (C₆H₁₂O₆ • H₂O) mol. wt. 198.17, a hexose sugar freely soluble in water. It has the following structural formula:



Water for Injection, USP is chemically designated H₂O.

Each 100 mL contains dopamine hydrochloride 80 mg (equivalent to 64.6 mg dopamine base), 160 mg (equivalent to 129.2 mg dopamine base) or 320 mg (equivalent to 258.4 mg dopamine base) and dextrose, hydrous 5 g in water for injection, with sodium metabisulfite 50 mg added as an antioxidant; osmolar concentration, respectively 269, 277 or 294 mOsmol/liter (calc.). pH 3.6 (2.5 to 4.5). May contain hydrochloric acid and/or sodium hydroxide for pH adjustment. Dopamine Hydrochloride and 5% Dextrose Injection, USP is oxygen sensitive. The solution contains no bacteriostat, antimicrobial agent or added buffer (except for pH adjustment), and is intended only for use as a single-dose injection. When smaller doses are required the unused portion should be discarded.

CLINICAL PHARMACOLOGY

Dopamine is a natural catecholamine formed by the decarboxylation of 3,4-dihydroxyphenylalanine (DOPA). It is a precursor to norepinephrine in noradrenergic nerves and is

also a neurotransmitter in certain areas of the central nervous system, especially in the nigrostriatal tract, and in a few peripheral sympathetic nerves.

Dopamine produces positive chronotropic and inotropic effects on the myocardium, resulting in increased heart rate and cardiac contractility. This is accomplished directly by exerting an agonist action on beta-adrenoceptors and indirectly by causing release of norepinephrine from storage sites in sympathetic nerve endings.

Dopamine's onset of action occurs within five minutes of intravenous administration, and with dopamine's plasma half-life of about two minutes, the duration of action is less than ten minutes. However, if monoamine oxidase (MAO) inhibitors are present, the duration may increase to one hour. The drug is widely distributed in the body but does not cross the blood-brain barrier to a significant extent. Dopamine is metabolized in the liver, kidney, and plasma by MAO and catechol-O-methyltransferase to the inactive compounds homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid. About 25% of the dose is taken up into specialized neurosecretory vesicles (the adrenergic nerve terminals), where it is hydroxylated to form norepinephrine. It has been reported that about 80% of the drug is excreted in the urine within 24 hours, primarily as HVA and its sulfate and glucuronide conjugates and as 3,4-dihydroxyphenylacetic acid. A very small portion is excreted unchanged.

The predominant effects of dopamine are dose-related, although it should be noted that actual response of an individual patient will largely depend on the clinical status of the patient at the time the drug is administered. At low rates of infusion (0.5–2 mcg/kg/min) dopamine causes vasodilation that is presumed to be due to a specific agonist action on dopamine receptors (distinct from alpha- and beta-adrenoceptors) in the renal, mesenteric, coronary, and intracerebral vascular beds. At these dopamine receptors, haloperidol is an antagonist. The vasodilation in these vascular beds is accompanied by increased glomerular filtration rate, renal blood flow, sodium excretion, and urine flow. Hypotension sometimes occurs. An increase in urinary output produced by dopamine is usually not associated with a decrease in osmolality of the urine.

At intermediate rates of infusion (2–10 mcg/kg/min) dopamine acts to stimulate the beta₁-adrenoceptors, resulting in improved myocardial contractility, increased SA rate and enhanced impulse conduction in the heart. There is little, if any, stimulation of the beta₂-adrenoceptors (peripheral vasodilation). Dopamine causes less increase in myocardial oxygen consumption than isoproterenol, and its use is not usually associated with a tachyarrhythmia. Clinical studies indicate that it usually increases systolic and pulse pressure with either no effect or a slight increase in diastolic pressure. Blood flow to the peripheral vascular beds may decrease while mesenteric flow increases due to increased cardiac output. Total peripheral resistance (alpha effects) at low and intermediate doses is usually unchanged.

At higher rates of infusion (10–20 mcg/kg/min) there is some effect on alpha-adrenoceptors, with consequent vasoconstrictor effects and a rise in blood pressure. The vasoconstrictor effects are first seen in the skeletal muscle vascular beds, but with increasing doses, they are also evident in the renal and mesenteric vessels. At very high rates of infusion (above 20 mcg/kg/min), stimulation of alpha-adrenoceptors predominates and vasoconstriction may compromise the circulation of the limbs and override the dopaminergic effects of dopamine, reversing renal dilation and naturesis.

Solutions containing carbohydrate in the form of dextrose restore blood glucose levels and provide calories. Carbohydrate in the form of dextrose may aid in minimizing liver glycogen depletion and exerts a protein-sparing action. Dextrose injected parenterally undergoes oxidation to carbon dioxide and water.

Water is an essential constituent of all body tissues and accounts for approximately 70% of total body weight. Average normal adult daily requirement ranges from two to three liters (1.0 – 1.5 liters each for insensible water loss due to perspiration and urine production).

Water balance is maintained by various regulatory mechanisms. Water distribution depends primarily on the concentration of electrolytes and sodium (Na⁺) plays a major role in maintaining physiologic equilibrium.

INDICATIONS AND USAGE

Dopamine Hydrochloride and 5% Dextrose Injection, USP is indicated for the correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarction, trauma, endotoxic septicemia, open-heart surgery, renal failure and chronic cardiac decompensation as in congestive failure.

Patients most likely to respond adequately to dopamine HCl are those in whom physiological parameters, such as urine flow, myocardial function, and blood pressure, have not undergone profound deterioration. Multiclinic trials indicate that the shorter the time interval between onset of signs and symptoms and initiation of therapy with blood volume correction and dopamine HCl, the better the prognosis. Where appropriate, blood volume restoration with a suitable plasma expander or whole blood should be accomplished prior to administration of dopamine HCl.

Poor Perfusion of Vital Organs — Urine flow appears to be one of the better diagnostic signs by which adequacy of vital organ perfusion can be monitored. Nevertheless, the physician should also observe the patient for signs of reversal of confusion or reversal of comatose condition. Loss of pallor, increase in toe temperature, and/or adequacy of nail bed capillary filling may also be used as indices of adequate dosage. Clinical studies have shown that when dopamine HCl is administered before urine flow has diminished to levels of approximately 0.3 mL/minute, prognosis is more favorable. Nevertheless, in a number of oliguric or anuric patients, administration of dopamine HCl has resulted in an increase in urine flow, which in some cases reached normal levels. Dopamine HCl may also increase urine flow in patients whose output is within normal limits and thus may be of value in reducing the degree of preexisting fluid accumulation. It should be noted that at doses above those optimal for the individual patient, urine flow may decrease, necessitating reduction of dosage.

Low Cardiac Output — Increased cardiac output is related to dopamine's direct inotropic effect on the myocardium. Increased cardiac output at low or moderate doses appears to be related to a favorable prognosis. Increase in cardiac output has been associated with either static or decreased systemic vascular resistance (SVR). Static or decreased SVR associated with low or moderate movements in cardiac output is believed to be a reflection of differential effects on specific vascular beds with increased resistance in peripheral beds (e.g., femoral) and concomitant decreases in mesenteric and renal vascular beds.

Redistribution of blood flow parallels these changes so that an increase in cardiac output is accompanied by an increase in mesenteric and renal blood flow. In many instances the renal fraction of the total cardiac output has been found to increase. Increase in cardiac output produced by dopamine is not associated with substantial decreases in systemic vascular resistance as may occur with isoproterenol.

Hypotension — Hypotension due to inadequate cardiac output can be managed by administration of low to moderate doses of dopamine HCl which have little effect on SVR. At high therapeutic doses, dopamine's alpha-adrenergic activity becomes more prominent and thus may correct hypotension due to diminished SVR. As in the case of other circulatory decompensation states, prognosis is better in patients whose blood pressure and urine flow have not undergone profound

deterioration. Therefore, it is suggested that the physician administer dopamine HCl as soon as a definite trend toward decreased systolic and diastolic pressure becomes evident.

CONTRAINDICATIONS

Dopamine HCl should not be used in patients with pheochromocytoma.

Dopamine HCl should not be administered to patients with uncorrected tachyarrhythmias or ventricular fibrillation.

Dextrose solutions without electrolytes should not be administered simultaneously with blood through the same infusion set because of the possibility that pseudoagglutination of red cells may occur.

WARNINGS

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Do NOT add any alkalinizing substance, since dopamine is inactivated in alkaline solution.

Patients who have been receiving MAO inhibitors prior to the administration of dopamine HCl will require substantially reduced dosage. See Drug Interactions below.

PRECAUTIONS

General

- 1. Monitoring** — Careful monitoring of the following indices is necessary during dopamine HCl infusion, as with any adrenergic agent: blood pressure, urine flow, and, when possible, cardiac output and pulmonary wedge pressure.
- 2. Hypovolemia** — Prior to treatment with dopamine HCl, hypovolemia should be fully corrected, if possible, with either whole blood or plasma as indicated. Monitoring of central venous pressure or left ventricular filling pressure may be helpful in detecting and treating hypovolemia.
- 3. Hypoxia, Hypercapnia, Acidosis** — These conditions, which may also reduce the effectiveness and/or increase the incidence of adverse effects of dopamine, must be identified and corrected prior to, or concurrently with, administration of dopamine HCl.
- 4. Decreased Pulse Pressure** — If a disproportionate increase in diastolic blood pressure and a marked decrease in pulse pressure are observed in patients receiving dopamine HCl, the rate of infusion should be decreased and the patient observed carefully for further evidence of predominant vasoconstrictor activity, unless such effect is desired.
- 5. Ventricular Arrhythmias** — If an increased number of ectopic beats are observed, the dose should be reduced if possible.
- 6. Hypotension** — At lower infusion rates, if hypotension occurs, the infusion rate should be rapidly increased until adequate blood pressure is obtained. If hypotension persists, dopamine HCl should be discontinued and a more potent vasoconstrictor agent such as norepinephrine should be administered.
- 7. Extravasation** — Dopamine Hydrochloride and 5% Dextrose Injection, USP should be infused into a large vein whenever possible to prevent the possibility of extravasation into tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of surrounding tissue. Large veins of the antecubital fossa are preferred to veins in the dorsum of the hand or ankle. Less suitable infusion sites should be used only if the patient's condition requires

immediate attention. The physician should switch to more suitable sites as rapidly as possible. The infusion site should be continuously monitored for free flow.

- 8. Occlusive Vascular Disease** — Patients with a history of occlusive vascular disease (for example, atherosclerosis, arterial embolism, Raynaud's disease, cold injury, diabetic endarteritis, and Buerger's disease) should be closely monitored for any changes in color or temperature of the skin in the extremities. If a change in skin color or temperature occurs and is thought to be the result of compromised circulation in the extremities, the benefits of continued dopamine HCl infusion should be weighed against the risk of possible necrosis. The condition may be reversed by either decreasing the rate or discontinuing the infusion.

IMPORTANT — Antidote for Peripheral Ischemia:

To prevent sloughing and necrosis in ischemic areas, the area should be infiltrated as soon as possible with 10 to 15 mL of saline solution containing from 5 to 10 mg of phentolamine mesylate, an adrenergic blocking agent. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

- 9. Weaning** — When discontinuing the infusion, it may be necessary to gradually decrease the dose of dopamine HCl while expanding blood volume with I.V. fluids, since sudden cessation may result in marked hypotension.

Drug Interactions

1. Because dopamine is metabolized by monoamine oxidase (MAO), inhibition of this enzyme prolongs and potentiates the effect of dopamine. Patients who have been treated with MAO inhibitors within two to three weeks prior to the administration of dopamine HCl should receive initial doses of dopamine HCl no greater than one tenth (1/10) of the usual dose.
2. Concurrent administration of dopamine HCl and diuretic agents may produce an additive or potentiating effect on urine flow.
3. Tricyclic antidepressants may potentiate the pressor response to adrenergic agents.
4. Cardiac effects of dopamine are antagonized by beta-adrenergic blocking agents, such as propranolol and metoprolol. The peripheral vasoconstriction caused by high doses of dopamine HCl is antagonized by alpha-adrenergic blocking agents. Dopamine-induced renal and mesenteric vasodilation is not antagonized by either alpha- or beta-adrenergic blocking agents.
5. Haloperidol appears to have strong central antidopaminergic properties. Haloperidol and haloperidol-like drugs suppress the dopaminergic renal and mesenteric vasodilation induced at low rates of dopamine infusion.
6. Cyclopropane or halogenated hydrocarbon anesthetics increase cardiac autonomic irritability and may sensitize the myocardium to the action of certain intravenously administered catecholamines, such as dopamine. This interaction appears to be related both to pressor activity and to beta-adrenergic stimulating properties of these catecholamines and may produce ventricular arrhythmias and hypertension. Therefore, **EXTREME CAUTION** should be exercised when administering dopamine HCl to patients receiving cyclopropane or halogenated hydrocarbon anesthetics. It has been reported that results of studies in animals indicate that dopamine-induced ventricular arrhythmias during anesthesia can be reversed by propranolol.
7. The concomitant use of vasopressors and some oxytocic drugs may result in severe persistent hypertension. See Labor and Delivery below.

8. Administration of phenytoin to patients receiving dopamine HCl has been reported to lead to hypotension and bradycardia. It is suggested that in patients receiving dopamine HCl, alternatives to phenytoin should be used if anticonvulsant therapy is needed.

Pregnancy: Teratogenic Effects: *Pregnancy Category C* — Animal studies have revealed no evidence of teratogenic effects due to dopamine. However, in one study, administration of dopamine HCl to pregnant rats resulted in a decreased survival rate of the newborn and a potential for cataract formation in the survivors. There are no adequate and well-controlled studies in pregnant women and it is not known if dopamine crosses the placental barrier. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if, in the judgment of the physician, the potential benefit justifies the potential risk to the fetus.

Labor and Delivery — In obstetrics, if vasopressor drugs are used to correct hypotension or are added to a local anesthetic solution, some oxytocic drugs may cause severe persistent hypertension and may even cause rupture of a cerebral blood vessel to occur during the postpartum period.

Nursing Mothers — It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when dopamine HCl is administered to a nursing woman.

Pediatric Use — Safety and effectiveness in children have not been established. Dopamine HCl has been used in a limited number of pediatric patients, but such use has been inadequate to fully define proper dosage and limitations for use.

ADVERSE REACTIONS

The following adverse reactions have been observed, but there are not enough data to support an estimate of their frequency.

Cardiovascular System: Ventricular arrhythmia, atrial fibrillation, ectopic beats, tachycardia, anginal pain, palpitation, cardiac conduction abnormalities, widened QRS complex, bradycardia, hypotension, hypertension and vasoconstriction.

Respiratory System: Dyspnea.

Gastrointestinal System: Nausea and vomiting.

Metabolic/Nutritional System: Azotemia.

Central Nervous System: Headache and anxiety.

Dermatological System: Piloerection.

Other: Gangrene of the extremities has occurred when high doses were administered for prolonged periods or in patients with occlusive vascular disease receiving low doses of dopamine HCl.

OVERDOSAGE

In the case of accidental overdosage, as evidenced by excessive blood pressure elevation, reduce rate of infusion, or temporarily discontinue administration of the drug until patient's condition stabilizes. Since dopamine's duration of action is quite short, no additional remedial measures are usually necessary. If these measures fail to stabilize the patient's condition, use of the short-acting alpha adrenergic blocking agent, phentolamine, should be considered.

DOSAGE AND ADMINISTRATION

Do NOT add sodium bicarbonate or other alkalinizing substance, since dopamine is inactivated in alkaline solution.

Dopamine Hydrochloride and 5% Dextrose Injection, USP is administered only intravenously via a suitable I.V. catheter or needle infusion.

The less concentrated 800 mcg/mL solution may be preferred when fluid expansion is not a problem. The more concentrated 1600 mcg/mL or 3200 mcg/mL solutions, may be preferred in patients with fluid retention or when a slower rate of infusion is desired.

Rate of Administration — When administering dopamine (or any potent medication) by continuous intravenous infusion, it is advisable to use a precision volume control I.V. set. Each patient must be individually titrated to the desired hemodynamic or renal response to dopamine.

In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus necessitating a reduction in rate after the hemodynamic condition is stabilized.

Administration at rates greater than 50 mcg/kg/min have safely been used in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

Suggested Regimen:

1. When appropriate, increase blood volume with whole blood or plasma until central venous pressure is 10 to 15 cm H₂O or pulmonary wedge pressure is 14 to 18 mm Hg.
2. Begin infusion of dopamine hydrochloride solution at doses of 2 to 5 mcg/kg/min in patients who are likely to respond to modest increments of heart force and renal perfusion.

In more seriously ill patients, begin infusion of dopamine hydrochloride at doses of 5 mcg/kg/min and increase gradually using 5 to 10 mcg/kg/min increments up to a rate of 20 to 50 mcg/kg/min as needed. If doses in excess of 50 mcg/kg/min are required, it is advisable to check urine output frequently. Should urinary flow begin to decrease in the absence of hypotension, reduction of dopamine dosage should be considered. Multiclinic trials have shown that more than 50% of patients have been satisfactorily maintained on doses less than 20 mcg/kg/min.

In patients who do not respond to these doses with adequate arterial pressures of urine flow, additional increments of dopamine may be given in an effort to produce an appropriate arterial pressure and central perfusion.

3. Treatment of all patients requires constant evaluation of therapy in terms of blood volume, augmentation of cardiac contractility, and distribution of peripheral perfusion.

Dosage of dopamine should be adjusted according to the patient's response, with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indices for decreasing or temporarily suspending the dosage.

4. As with all potent intravenously administered drugs, care should be taken to control the rate of administration to avoid inadvertent administration of a bolus of the drug.

Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

Do not use if the injection is darker than slightly yellow or discolored in any other way.

HOW SUPPLIED

Dopamine Hydrochloride and 5% Dextrose Injection, USP is supplied in 250 mL and 500 mL glass containers as follows:

List No. 4141-02 — 200 mg Dopamine HCl and
5% Dextrose Injection, USP 250 mL

List No. 4141-03 — 400 mg Dopamine HCl and
5% Dextrose Injection, USP 500 mL

List No. 4142-02 — 400 mg Dopamine HCl and
5% Dextrose Injection, USP 250 mL

Avoid contact with alkalis (including sodium bicarbonate), oxidizing agents or iron salts.
Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

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Printed in USA

DOPamine HYDROCHLORIDE

Injection, USP

Fliptop Vial

R_x only

Pintop Vial

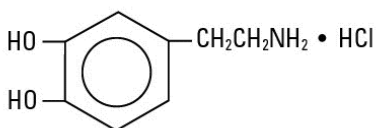
LifeShield[®] Fliptop Vial

MUST BE DILUTED PRIOR TO ADMINISTRATION

DESCRIPTION

Dopamine, a sympathomimetic amine vasopressor, is the naturally occurring immediate precursor of norepinephrine. Dopamine hydrochloride is a white to off-white crystalline powder, which may have a slight odor of hydrochloric acid. It is freely soluble in water and soluble in alcohol. Dopamine HCl is sensitive to alkalis, iron salts, and oxidizing agents. Chemically it is designated as 4-(2-aminoethyl) pyrocatechol hydrochloride, and its molecular formula is C₈H₁₁NO₂ • HCl.

The structural formula is:



and the molecular weight is 189.64.

Dopamine hydrochloride injection is a clear, practically colorless, sterile, pyrogen-free, aqueous solution of dopamine HCl for intravenous infusion after dilution. Each milliliter of the 40 mg/mL preparation contains 40 mg of dopamine hydrochloride (equivalent to 32.31 mg of dopamine base). Each milliliter of the 80 mg/mL preparation contains 80 mg of dopamine hydrochloride (equivalent to 64.62 mg of dopamine base). Each milliliter of both preparations contains the following: Sodium metabisulfite 9 mg added as an antioxidant; citric acid, anhydrous 10 mg; and sodium citrate, dihydrate 5 mg added as a buffer. May contain additional citric acid and/or sodium citrate for pH adjustment. pH is 3.3 (2.5 to 5.0).

Dopamine must be diluted in an appropriate sterile parenteral solution before intravenous administration. (See DOSAGE AND ADMINISTRATION)

CLINICAL PHARMACOLOGY

Dopamine is a natural catecholamine formed by the decarboxylation of 3,4-dihydroxyphenylalanine (DOPA). It is a precursor to norepinephrine in noradrenergic nerves and is also a neurotransmitter in certain areas of the central nervous system, especially in the nigrostriatal tract, and in a few peripheral sympathetic nerves.

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The predominant effects of dopamine are dose-related, although it should be noted that actual response of an individual patient will largely depend on the clinical status of the patient at the time the drug is administered. At low rates of infusion (0.5 – 2 mcg/kg/min) dopamine causes vasodilation that is presumed to be due to a specific agonist action on dopamine receptors (distinct from alpha- and beta-adrenoceptors) in the renal, mesenteric, coronary, and intracerebral vascular beds. At these dopamine receptors, haloperidol is an antagonist. The vasodilation in these vascular beds is accompanied by increased glomerular filtration rate, renal blood flow, sodium excretion, and urine flow. Hypotension sometimes occurs. An increase in urinary output produced by dopamine is usually not associated with a decrease in osmolality of the urine.

At intermediate rates of infusion (2 – 10 mcg/kg/min) dopamine acts to stimulate the beta₁-adrenoceptors, resulting in improved myocardial contractility, increased SA rate and enhanced impulse conduction in the heart. There is little, if any, stimulation of the beta₂-adrenoceptors (peripheral vasodilation). Dopamine causes less increase in myocardial oxygen consumption than isoproterenol, and its use is not usually associated with a tachyarrhythmia. Clinical studies indicate that it usually increases systolic and pulse pressure with either no effect or a slight increase in diastolic pressure. Blood flow to the peripheral vascular beds may decrease while mesenteric flow increases due to increased cardiac output. Total peripheral resistance (alpha effects) at low and intermediate doses is usually unchanged.

At higher rates of infusion (10 – 20 mcg/kg/min) there is some effect on alpha-adrenoceptors, with consequent vasoconstrictor effects and a rise in blood pressure. The vasoconstrictor effects are first seen in the skeletal muscle vascular beds, but with increasing doses, they are also evident in the renal and mesenteric vessels. At very high rates of infusion (above 20 mcg/kg/min), stimulation of alpha-adrenoceptors predominates and vasoconstriction may compromise the circulation of the limbs and override the dopaminergic effects of dopamine, reversing renal dilation and naturesis.

INDICATIONS AND USAGE

Dopamine HCl is indicated for the correction of hemodynamic imbalances present in the shock syndrome due to myocardial infarction, trauma, endotoxic septicemia, open-heart surgery, renal failure, and chronic cardiac decompensation as in congestive failure.

Patients most likely to respond adequately to dopamine HCl are those in whom physiological parameters, such as urine flow, myocardial function, and blood pressure, have not undergone profound deterioration. Multiclinic trials indicate that the shorter the time interval between onset of signs and symptoms and initiation of therapy with blood volume correction and dopamine HCl, the better the prognosis. Where appropriate, blood volume restoration with a suitable plasma expander or whole blood should be accomplished prior to administration of dopamine HCl.

Poor Perfusion of Vital Organs – Urine flow appears to be one of the better diagnostic signs by which adequacy of vital organ perfusion can be monitored. Nevertheless, the physician should also observe the patient for signs of reversal of confusion or reversal of comatose condition. Loss of pallor, increase in toe temperature, and/or adequacy of nail bed capillary filling may also be used as

indices of adequate dosage. Clinical studies have shown that when dopamine HCl is administered before urine flow has diminished to levels of approximately 0.3 mL/minute, prognosis is more favorable. Nevertheless, in a number of oliguric or anuric patients, administration of dopamine HCl has resulted in an increase in urine flow, which in some cases reached normal levels. Dopamine HCl may also increase urine flow in patients whose output is within normal limits and thus may be of value in reducing the degree of pre-existing fluid accumulation. It should be noted that at doses above those optimal for the individual patient, urine flow may decrease, necessitating reduction of dosage.

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Redistribution of blood flow parallels these changes so that an increase in cardiac output is accompanied by an increase in mesenteric and renal blood flow. In many instances the renal fraction of the total cardiac output has been found to increase. Increase in cardiac output produced by dopamine is not associated with substantial decreases in systemic vascular resistance as may occur with isoproterenol.

Hypotension – Hypotension due to inadequate cardiac output can be managed by administration of low to moderate doses of dopamine HCl which have little effect on SVR. At high therapeutic doses, dopamine’s alpha-adrenergic activity becomes more prominent and thus may correct hypotension due to diminished SVR. As in the case of other circulatory decompensation states, prognosis is better in patients whose blood pressure and urine flow have not undergone profound deterioration. Therefore, it is suggested that the physician administer dopamine HCl as soon as a definite trend toward decreased systolic and diastolic pressure becomes evident.

CONTRAINDICATIONS

Dopamine HCl should not be used in patients with pheochromocytoma.

Dopamine HCl should not be administered to patients with uncorrected tachyarrhythmias or ventricular fibrillation.

WARNINGS

Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Do NOT add dopamine HCl to any alkaline diluent solution since the drug is inactivated in alkaline solution.

Patients who have been receiving MAO inhibitors prior to the administration of dopamine HCl will require substantially reduced dosage. See **Drug Interactions** below.

PRECAUTIONS

General

- 1. Monitoring** – Careful monitoring of the following indices is necessary during dopamine HCl infusion, as with any adrenergic agent: blood pressure, urine flow, and, when possible, cardiac output and pulmonary wedge pressure.

2. **Hypovolemia** – Prior to treatment with dopamine HCl, hypovolemia should be fully corrected, if possible, with either whole blood or plasma as indicated. Monitoring of central venous pressure or left ventricular filling pressure may be helpful in detecting and treating hypovolemia.
3. **Hypoxia, Hypercapnia, Acidosis** – These conditions, which may also reduce the effectiveness and/or increase the incidence of adverse effects of dopamine, must be identified and corrected prior to, or concurrently with, administration of dopamine HCl.
4. **Decreased Pulse Pressure** – If a disproportionate increase in diastolic blood pressure and a marked decrease in pulse pressure are observed in patients receiving dopamine HCl, the rate of infusion should be decreased and the patient observed carefully for further evidence of predominant vasoconstrictor activity, unless such effect is desired.
5. **Ventricular Arrhythmias** – If an increased number of ectopic beats are observed, the dose should be reduced if possible.
6. **Hypotension** – At lower infusion rates, if hypotension occurs, the infusion rate should be rapidly increased until adequate blood pressure is obtained. If hypotension persists, dopamine HCl should be discontinued and a more potent vasoconstrictor agent such as norepinephrine should be administered.
7. **Extravasation** – Dopamine HCl should be infused into a large vein whenever possible to prevent the possibility of extravasation into tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of surrounding tissue. Large veins of the antecubital fossa are preferred to veins in the dorsum of the hand or ankle. Less suitable infusion sites should be used only if the patient's condition requires immediate attention. The physician should switch to more suitable sites as rapidly as possible. The infusion site should be continuously monitored for free flow.
8. **Occlusive Vascular Disease** – Patients with a history of occlusive vascular disease (for example, atherosclerosis, arterial embolism, Raynaud's disease, cold injury, diabetic endarteritis, and Buerger's disease) should be closely monitored for any changes in color or temperature of the skin in the extremities. If a change in skin color or temperature occurs and is thought to be the result of compromised circulation in the extremities, the benefits of continued dopamine HCl infusion should be weighed against the risk of possible necrosis. This condition may be reversed by either decreasing the rate or discontinuing the infusion.

IMPORTANT

Antidote for Peripheral Ischemia: To prevent sloughing and necrosis in ischemic areas, the area should be infiltrated as soon as possible with 10 to 15 mL of saline solution containing from 5 to 10 mg of phentolamine mesylate, an adrenergic blocking agent. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

9. **Weaning** – When discontinuing the infusion, it may be necessary to gradually decrease the dose of dopamine HCl while expanding blood volume with I.V. fluids, since sudden cessation may result in marked hypotension.

Drug Interactions

1. Because dopamine is metabolized by monoamine oxidase (MAO), inhibition of this enzyme prolongs and potentiates the effect of dopamine. Patients who have been treated with **MAO inhibitors** within two to three weeks prior to the administration of dopamine HCl should receive initial doses of dopamine HCl no greater than one-tenth (1/10) of the usual dose.
2. Concurrent administration of dopamine HCl and **diuretic agents** may produce an additive or potentiating effect on urine flow.
3. **Tricyclic antidepressants** may potentiate the pressor response to adrenergic agents.
4. Cardiac effects of dopamine are antagonized by **beta-adrenergic blocking agents**, such as propranolol and metoprolol. The peripheral vasoconstriction caused by high doses of dopamine HCl is antagonized by **alpha-adrenergic blocking agents**. Dopamine-induced renal and mesenteric vasodilation is not antagonized by either alpha- or beta-adrenergic blocking agents.
5. **Haloperidol** appears to have strong central antidopaminergic properties. Haloperidol and haloperidol-like drugs suppress the dopaminergic renal and mesenteric vasodilation induced at low rates of dopamine infusion.
6. **Cyclopropane or halogenated hydrocarbon anesthetics** increase cardiac autonomic irritability and may sensitize the myocardium to the action of certain intravenously administered catecholamines, such as dopamine. This interaction appears to be related both to pressor activity and to beta-adrenergic stimulating properties of these catecholamines and may produce ventricular arrhythmias and hypertension. Therefore, EXTREME CAUTION should be exercised when administering dopamine HCl to patients receiving cyclopropane or halogenated hydrocarbon anesthetics. It has been reported that results of studies in animals indicate that dopamine-induced ventricular arrhythmias during anesthesia can be reversed by propranolol.
7. The concomitant use of vasopressors and some **oxytocic drugs** may result in severe persistent hypertension. See **Labor and Delivery** below.
8. Administration of **phenytoin** to patients receiving dopamine HCl has been reported to lead to hypotension and bradycardia. It is suggested that in patients receiving dopamine HCl, alternatives to phenytoin should be used if anticonvulsant therapy is needed.

Pregnancy: Teratogenic Effects: *Pregnancy Category C* Animal studies have revealed no evidence of teratogenic effects due to dopamine. However, in one study, administration of dopamine HCl to pregnant rats resulted in a decreased survival rate of the newborn and a potential for cataract formation in the survivors. There are no adequate and well-controlled studies in pregnant women and it is not known if dopamine crosses the placental barrier. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if, in the judgment of the physician, the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

In obstetrics, if vasopressor drugs are used to correct hypotension or are added to a local anesthetic solution, some oxytocic drugs may cause severe persistent hypertension and may even cause rupture of a cerebral blood vessel to occur during the postpartum period.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when dopamine HCl is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in children have not been established. Dopamine HCl has been used in a limited number of pediatric patients, but such use has been inadequate to fully define proper dosage and limitations for use.

ADVERSE REACTIONS

The following adverse reactions have been observed, but there are not enough data to support an estimate of their frequency.

Cardiovascular System:

- ventricular arrhythmia
- atrial fibrillation
- ectopic beats
- tachycardia
- anginal pain
- palpitation
- cardiac conduction abnormalities
- widened QRS complex
- bradycardia
- hypotension
- hypertension
- vasoconstriction

Respiratory System:

- dyspnea

Gastrointestinal System:

- nausea
- vomiting

Metabolic/Nutritional System:

- azotemia

Central Nervous System:

- headache
- anxiety

Dermatological System:

- piloerection

Other:

Gangrene of the extremities has occurred when high doses were administered for prolonged periods or in patients with occlusive vascular disease receiving low doses of dopamine HCl.

OVERDOSAGE

In the case of accidental overdosage, as evidenced by excessive elevation of blood pressure, reduce rate of administration or temporarily discontinue dopamine HCl until patient's condition stabilizes. Since dopamine's duration of action is quite short, no additional remedial measures are usually necessary. If these measures fail to stabilize the patient's condition, use of the short-acting alpha-adrenergic blocking agent phentolamine should be considered.

DOSAGE AND ADMINISTRATION

WARNING: This is a potent drug; it must be diluted before administration to the patient.

Dopamine Hydrochloride Injection, USP is administered (only after dilution) by intravenous infusion.

Suggested Dilution – For the 40 mg/mL preparation, transfer by aseptic technique the contents containing either 5 mL, 200 mg or 10 mL, 400 mg of Dopamine Hydrochloride to either a 250 mL or 500 mL bottle of one of the sterile I.V. solutions listed below. For the 80 mg/mL preparation, transfer by aseptic technique the contents containing 10 mL, 800 mg of Dopamine Hydrochloride to a 250 mL, 500 mL or 1000 mL bottle of one of the following sterile I.V. solutions:

- 0.9% Sodium Chloride Injection, USP
- 5% Dextrose Injection, USP
- 5% Dextrose and 0.9% Sodium Chloride Injection, USP
- 5% Dextrose and 0.45% Sodium Chloride Injection, USP
- 5% Dextrose and Lactated Ringer's Injection
- Sodium Lactate Injection, USP 1/6 Molar
- Lactated Ringer's Injection, USP

The resultant dilutions are summarized in the following chart:

Concentration of Dopamine Hydrochloride	40 mg/mL	80 mg/mL
Volume of Dopamine Hydrochloride Injection, USP		
250 mL Bottle of I.V. Solution	5 mL	10 mL
500 mL Bottle of I.V. Solution	10 mL	10 mL
1000 mL Bottle of I.V. Solution	20 mL	10 mL
250 mL Bottle of I.V. Solution	800 mcg/mL	1600 mcg/mL
500 mL Bottle of I.V. Solution	400 mcg/mL	800 mcg/mL
1000 mL Bottle of I.V. Solution	200 mcg/mL	400 mcg/mL

Dopamine Hydrochloride Injection, USP has been found to be stable for a minimum of 24 hours after dilution in the foregoing I.V. solutions. However, as with all I.V. admixtures, dilution should be made just prior to administration.

Do NOT add Dopamine Hydrochloride to Sodium Bicarbonate Injection, USP or other alkaline I.V. solutions, since the drug is inactivated in alkaline solution.

Rate of Administration – Dopamine Hydrochloride Injection, USP after dilution, is administered intravenously by infusion via a suitable I.V. catheter or needle. When administering Dopamine Hydrochloride (or any potent medication) by continuous intravenous infusion, it is advisable to use a precision volume control I.V. set. Each patient must be individually titrated to the desired hemodynamic or renal response to dopamine.

In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus necessitating a reduction in rate after the hemodynamic condition is stabilized.

Administration at rates greater than 50 mcg/kg/min have safely been used in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

Suggested Regimen:

1. When appropriate, increase blood volume with whole blood or plasma until central venous pressure is 10 to 15 cm H₂O or pulmonary wedge pressure is 14 to 18 mm Hg.
2. Begin infusion of diluted solution at doses of 2 – 5 mcg/kg/min of Dopamine Hydrochloride in patients who are likely to respond to modest increments of heart force and renal perfusion.

In more seriously ill patients, begin infusion of diluted solution at doses of 5 mcg/kg/min of Dopamine Hydrochloride and increase gradually using 5 to 10 mcg/kg/min increments up to a rate of 20 to 50 mcg/kg/min as needed. If doses in excess of 50 mcg/kg/min are required, it is advisable to check urine output frequently. Should urinary flow begin to decrease in the absence of hypotension, reduction of dopamine dosage should be considered. Multiclinic trials

have shown that more than 50 percent of patients have been satisfactorily maintained on doses less than 20 mcg/kg/min.

In patients who do not respond to these doses with adequate arterial pressures or urine flow, additional increments of dopamine may be given in an effort to produce an appropriate arterial pressure and central perfusion.

3. Treatment of all patients requires constant evaluation of therapy in terms of blood volume, augmentation of cardiac contractility, and distribution of peripheral perfusion.

Dosage of dopamine should be adjusted according to the patient's response, with particular attention to diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias as indices for decreasing or temporarily suspending the dosage.

4. As with all potent intravenously administered drugs, care should be taken to control the rate of administration to avoid inadvertent administration of a bolus of the drug.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED

Dopamine Hydrochloride Injection, USP is supplied as follows (40 mg/mL and 80 mg/mL):

5 mL Fliptop Vial (200 mg)	List No. 5820
5 mL LifeShield [®] Fliptop Vial*	List No. 5820
10 mL Fliptop Vial (400 mg)	List No. 9104
10 mL LifeShield [®] Fliptop Vial*	List No. 9104
10 mL Fliptop Vial (800 mg)	List No. 4265

*For use with LifeShield[®] blunt cannula.

Avoid contact with alkalies (including sodium bicarbonate), oxidizing agents or iron salts.

Do not use the injection if it is darker than slightly yellow or discolored in any other way.

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.]

Revised: May 2014

HOSPIRA, INC., LAKE FOREST, IL 60045 USA

DOPamine HYDROCHLORIDE in 5% Dextrose Injection, USP

Aqueous Solutions for Acute Correction of Hemodynamics in Shock States
Flexible Plastic Container

R_x Only

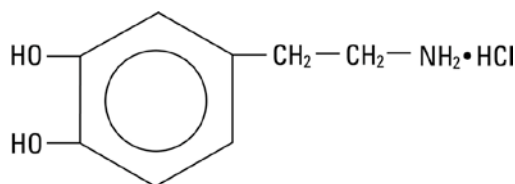
DESCRIPTION

Dopamine Hydrochloride in 5% Dextrose Injection, USP is a sterile, nonpyrogenic, prediluted solution of dopamine hydrochloride in 5% dextrose injection. It is administered by intravenous infusion.

Each 100 mL contains dopamine hydrochloride 80 mg (0.8 mg/mL), 160 mg (1.6 mg/mL) or 320 mg (3.2 mg/mL) and dextrose, hydrous 5 g in water for injection, with sodium metabisulfite added 50 mg as a stabilizer; osmolar concentration, respectively 261, 269, or 286 mOsmol/liter (calc.), pH 3.8 (2.5 to 4.5). May contain hydrochloric acid and/or sodium hydroxide for pH adjustment.

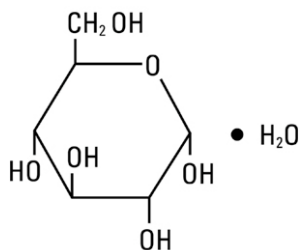
Dopamine administered intravenously is a myocardial inotropic agent, which also may increase mesenteric and renal blood flow plus urinary output.

Dopamine Hydrochloride is chemically designated 3, 4-dihydroxyphenethylamine hydrochloride (C₈H₁₁NO₂ • HCl), a white crystalline powder freely soluble in water. It has the following structural formula:



Dopamine (also referred to as 3-hydroxytyramine) is a naturally occurring endogenous catecholamine precursor of norepinephrine.

Dextrose, USP is chemically designated D-glucose monohydrate (C₆H₁₂O₆ • H₂O), a hexose sugar freely soluble in water. It has the following structural formula:



Water for Injection, USP is chemically designated H₂O.

The flexible plastic container is fabricated from a specially formulated CR3 plastic material. Water can permeate from inside the container into the overwrap but not in amounts sufficient to affect the solution significantly. Solutions in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing

was supportive of the safety of the plastic container materials. Exposure to temperatures above 25°C/77°F during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period.

CLINICAL PHARMACOLOGY

Dopamine exhibits an inotropic action on the myocardium, resulting in increased cardiac output. It causes less increase in myocardial oxygen consumption than isoproterenol and the effect of dopamine usually is not associated with tachyarrhythmia. Reported clinical studies have revealed that the drug usually increases systolic and pulse pressure without any or only a minor elevating effect on diastolic pressure. Total peripheral resistance at low and intermediate doses is usually unchanged. Blood flow to peripheral vascular beds may decrease while mesenteric blood flow is increased. The drug also has been reported to produce dilation of the renal vasculature which is accompanied by increases in glomerular filtration rate, renal blood flow and sodium excretion. Increased urinary output produced by dopamine is usually not associated with decreased urine osmolality.

Solutions containing carbohydrate in the form of dextrose restore blood glucose levels and provide calories. Carbohydrate in the form of dextrose may aid in minimizing liver glycogen depletion and exerts a protein-sparing action. Dextrose injected parenterally undergoes oxidation to carbon dioxide and water.

Water is an essential constituent of all body tissues and accounts for approximately 70% of total body weight. Average normal adult daily requirement ranges from two to three liters (1.0 to 1.5 liters each for insensible water loss due to perspiration and urine production).

Water balance is maintained by various regulatory mechanisms. Water distribution depends primarily on the concentration of electrolytes and sodium (Na⁺) plays a major role in maintaining physiologic equilibrium.

The reported clearance rate of dopamine in critically ill infants and children has ranged from 46 to 168 mL/kg/min, with the higher values seen in the younger patients. The apparent volume of distribution in neonates is reported as 0.6 to 4 L/kg, leading to an elimination half-life of 5 to 11 minutes.

INDICATIONS AND USAGE

Dopamine Hydrochloride in 5% Dextrose Injection, USP is indicated for the correction of hemodynamic imbalances present in shock due to myocardial infarction, trauma, endotoxic septicemia, open heart surgery, renal failure and chronic cardiac decompensation as in refractory congestive failure.

When indicated, restoration of circulatory volume should be instituted or completed with a suitable plasma expander or whole blood, prior to administration of dopamine hydrochloride.

Patients most likely to respond to dopamine are those whose physiological parameters (such as urine flow, myocardial function and blood pressure) have not undergone extreme deterioration. Reports indicate that the shorter the time between onset of signs and symptoms and initiation of therapy with volume restoration and dopamine, the better the prognosis.

Poor Perfusion of Vital Organs: Although urine flow is apparently one of the better diagnostic signs for monitoring vital organ perfusion, the physician also should observe the patient for signs of reversal of mental confusion or coma. Loss of pallor, increase in toe temperature or adequacy of nail bed capillary filling also may be observed as indices of adequate dosage. Reported studies indicate that when dopamine is administered before urine flow has decreased to approximately 0.3 mL/minute prognosis is more favorable.

However, it has been observed that in some oliguric or anuric patients, administration of the drug has produced an increase in urine flow which may reach normal levels. The drug also may increase urine flow in patients whose output is within normal limits and thus may help in reducing the degree of pre-existing fluid accumulation. Conversely, at higher than optimal doses for a given patient, urinary flow may decrease, requiring a reduction of dosage. Concomitant administration of dopamine and diuretic agents may produce an additive or potentiating effect.

Low Cardiac Output: Dopamine's direct inotropic effect on the myocardium which increases cardiac output at low or moderate doses is related to a favorable prognosis. Increased output has been associated with unchanged or decreased systemic vascular resistance (SVR). The association of static or decreased SVR with low or moderate increases in cardiac output is regarded as a reflection of differential effects on specific vascular beds, with increased resistance in peripheral beds (e.g., femoral), and concurrent decreases in mesenteric and renal vascular beds. Redistribution of blood flow parallels these changes so that an increase in cardiac output is accompanied by an increase in mesenteric and renal blood flow. In many instances the renal fraction of the total cardiac output has been found to increase. Increase in cardiac output produced by dopamine is not associated with substantial decreases in systemic vascular resistance as may occur with isoproterenol.

Hypotension: Low to moderate doses of dopamine, which have little effect on SVR, can be used to manage hypotension due to inadequate cardiac output. At high therapeutic doses, dopamine's α -adrenergic action becomes more prominent and thus may correct hypotension due to diminished SVR. As in other circulatory decompensation states, prognosis is better in patients whose blood pressure and urine flow have not undergone extreme deterioration. Therefore, it is suggested the physician administer dopamine as soon as a definite trend toward decreased systolic and diastolic pressure becomes apparent.

CONTRAINDICATIONS

Dopamine hydrochloride should not be used in patients with pheochromocytoma.

Dopamine should not be administered in the presence of uncorrected tachyarrhythmias or ventricular fibrillation.

WARNINGS

Do NOT add any alkalinizing substance, since dopamine is inactivated in alkaline solution.

Patients who have been treated with monoamine oxidase (MAO) inhibitors prior to administration of dopamine should receive substantially reduced dosage of the latter. See **PRECAUTIONS, Drug Interactions**, below.

Additive medications should not be delivered via this solution.

Dopamine Hydrochloride in 5% Dextrose Injection, USP contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

General:

Solutions containing dextrose should be used with caution in patients with known subclinical or overt diabetes mellitus.

Fluid and Electrolyte Balance: Excess administration of potassium-free solutions may result in significant hypokalemia.

The intravenous administration of these solutions can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states or pulmonary edema.

Careful Monitoring Required: Close monitoring of the following indices — urine flow, cardiac output and blood pressure — during dopamine infusion is necessary as in the case of any adrenergic agent.

Hypoxia, Hypercapnia, Acidosis: These conditions, which may also reduce the effectiveness and/or increase the incidence of adverse effects of dopamine, must be identified and corrected prior to, or concurrently with, administration of dopamine HCl.

Ventricular Arrhythmias: If an increased number of ectopic beats are observed the dose should be reduced if possible.

Hypotension: At lower infusion rates, if hypotension occurs, the infusion rate should be rapidly increased until adequate blood pressure is obtained. If hypotension persists, dopamine HCl should be discontinued and a more potent vasoconstrictor agent such as norepinephrine should be administered.

Occlusive Vascular Disease: Patients with a history of occlusive vascular disease (e.g., arteriosclerosis, arterial embolism, Raynaud's disease, cold injury such as frostbite, diabetic endarteritis, and Buerger's disease) should be closely monitored for any changes in color or temperature of the skin of the extremities. If a change in skin color or temperature occurs and is thought to be the result of compromised circulation to the extremities, the benefits of continued dopamine infusion should be weighed against the risk of possible necrosis. These changes may be reversed by decreasing the rate or discontinuing the infusion entirely.

Extravasation: Dopamine Hydrochloride in 5% Dextrose Injection, USP should be infused into a large vein whenever possible to prevent the possibility of infiltration of perivascular tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of surrounding tissue. Large veins of the antecubital fossa are preferred to veins of the dorsum of the hand or ankle. Administration into an umbilical arterial catheter is not recommended. Less suitable infusion sites should be used only when larger veins are unavailable and the patient's condition requires immediate attention. The physician should switch to a more suitable site as soon as possible and the infusion site in use should be continuously monitored for free flow.

IMPORTANT — Antidote for Peripheral Ischemia: To prevent sloughing and necrosis in ischemic areas, the area should be infiltrated as soon as possible with 10 to 15 mL of 0.9% Sodium Chloride Injection, USP, containing from 5 to 10 mg of Regitine[®] (brand of phentolamine) an adrenergic blocking agent. Pediatric dosage of Regitine[®] should be 0.1 — 0.2 mg/kg up to a maximum of 10 mg per dose. A syringe with a fine hypodermic needle should be used, and the solution liberally infiltrated throughout the ischemic area. Sympathetic blockade with phentolamine causes immediate and conspicuous local hyperemic changes if the area is infiltrated within 12 hours. Therefore, phentolamine should be given as soon as possible after the extravasation is noted.

Laboratory Tests: Infusion of dopamine suppresses pituitary secretion of thyroid-stimulating hormone, growth hormone, and prolactin.

Weaning: When discontinuing the infusion, it may be necessary to gradually decrease the dose of dopamine HCl while expanding blood volume with IV fluids. Sudden cessation may result in marked hypotension.

Drug Interactions: Cyclopropane or halogenated hydrocarbon anesthetics increase cardiac autonomic irritability and may sensitize the myocardium to the action of certain intravenously administered catecholamines, such as dopamine. This interaction appears to be related both to pressor activity and to the β -adrenergic stimulating properties of these catecholamines, and may produce ventricular arrhythmias and hypertension. Therefore, EXTREME CAUTION should be exercised when administering dopamine HCl to patients receiving cyclopropane or halogenated hydrocarbon anesthetics. Results of studies in animals indicate that dopamine-induced ventricular arrhythmias during anesthesia can be reversed by propranolol.

Because dopamine is metabolized by monoamine oxidase (MAO), inhibition of this enzyme prolongs and potentiates the effect of dopamine. Patients who have been treated with MAO inhibitors within two to three weeks prior to the administration of dopamine should receive initial doses of dopamine hydrochloride no greater than one-tenth (1/10) of the usual dose.

Concurrent administration of low-dose dopamine HCl and diuretic agents may produce an additive or potentiating effect on urine flow.

Tricyclic antidepressants may potentiate the cardiovascular effects of adrenergic agents.

Cardiac effects of dopamine are antagonized by β -adrenergic blocking agents, such as propranolol and metoprolol. The peripheral vasoconstriction caused by high doses of dopamine HCl is antagonized by α -adrenergic blocking agents. Dopamine-induced renal and mesenteric vasodilation is not antagonized by either α - or β -adrenergic blocking agents.

Butyrophenones (such as haloperidol) and phenothiazines can suppress the dopaminergic renal and mesenteric vasodilation induced with low-dose dopamine infusion.

The concomitant use of vasopressors, vasoconstricting agents (such as ergonovine) and some oxytocic drugs may result in severe hypertension.

Administration of phenytoin to patients receiving dopamine HCl has been reported to lead to hypotension and bradycardia. It is suggested that in patients receiving dopamine HCl, alternatives to phenytoin should be considered if anticonvulsant therapy is needed.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term animal studies have not been performed to evaluate the carcinogenic potential of dopamine HCl.

Dopamine HCl at doses approaching maximal solubility showed no clear genotoxic potential in the Ames test. Although there was a reproducible dose-dependent increase in the number of revertant colonies with strains TA100 and TA98, both with and without metabolic activation, the small increase was considered inconclusive evidence of mutagenicity. In the L5178Y TK^{+/−} mouse lymphoma assay, dopamine HCl at the highest concentrations used of 750 $\mu\text{g}/\text{mL}$ without metabolic activation, and 3000 $\mu\text{g}/\text{mL}$ with activation, was toxic and associated with increases in mutant frequencies when compared to untreated and solvent controls; at the lower concentrations no increases over controls were noted.

No clear evidence of clastogenic potential was reported in the *in vivo* mouse or male rat bone marrow micronucleus test when the animals were treated intravenously with up to 224 mg/kg and 30 mg/kg of dopamine HCl, respectively.

Pregnancy: Pregnancy Category C: Teratogenic Effects: Teratogenicity studies in rats and rabbits at dopamine HCl dosages up to 6 mg/kg/day intravenously during organogenesis produced no detectable teratogenic or embryotoxic effects, although maternal toxicity consisting of mortalities, decreased body weight gain, and pharmacotoxic signs were observed in rats. In a published study,

dopamine HCl administered at 10 mg/kg subcutaneously for 30 days, markedly prolonged metestrus and increased mean pituitary and ovary weights in female rats. Similar administration to pregnant rats throughout gestation or for 5 days starting on gestation day 10 or 15 resulted in decreased body weight gains, increased mortalities and slight increases in cataract formation among the offspring. There are no adequate and well-controlled studies in pregnant women, and it is not known if dopamine HCl crosses the placental barrier. Dopamine HCl should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery: In obstetrics, if vasopressor drugs are used to correct hypotension or are added to a local anesthetic solution the interaction with some oxytocic drugs may cause severe hypertension.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when dopamine HCl is administered to a nursing mother.

Pediatric Use: Dopamine infusions have been used in patients of every age from birth onwards. There are scattered reports of infusion rates in neonates up to 125 mcg/kg/min, but most reports in pediatric patients describe dosing that is similar (on a mcg/kg/min basis) to that used in adults. Except for vasoconstrictive effects caused by inadvertent infusion of dopamine into the umbilical artery, adverse effects unique to the pediatric population have not been identified, nor have adverse effects identified in adults been found to be more common in pediatric patients.

Geriatric Use: Clinical studies of dopamine injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

The following adverse reactions have been observed, but there are not enough data to support an estimate of their frequency.

Cardiovascular System

- ventricular arrhythmia
- atrial fibrillation
- ectopic beats
- tachycardia
- anginal pain
- palpitation
- cardiac conduction abnormalities
- widened QRS complex
- bradycardia
- hypotension
- hypertension
- vasoconstriction

Respiratory System

- dyspnea

Gastrointestinal System

- nausea
- vomiting

Metabolic/Nutritional System

azotemia

Central Nervous System

headache

anxiety

Dermatological System

piloerection

Other

Gangrene of the extremities has occurred when high doses were administered for prolonged periods or in patients with occlusive vascular disease receiving low doses of dopamine HCl.

OVERDOSAGE

In the case of accidental overdosage, as evidenced by excessive blood pressure elevation, reduce rate of infusion, or temporarily discontinue administration of the drug until patient's condition stabilizes. Since dopamine's duration of action is quite short, no additional remedial measures are usually necessary. If these measures fail to stabilize the patient's condition, consider using an alpha-adrenergic blocking agent (e.g., phentolamine).

DOSAGE AND ADMINISTRATION

Do NOT administer if solution is darker than slightly yellow or discolored in any other way. Do NOT administer unless solution is clear and container is undamaged. Discard unused portion.

Dextrose solutions without electrolytes should not be administered simultaneously with blood through the same infusion set because of the possibility that pseudoagglutination of red cells may occur.

Do NOT add sodium bicarbonate or other alkalinizing substance, since dopamine is inactivated in alkaline solution.

Dopamine Hydrochloride in 5% Dextrose Injection should be infused into a large vein whenever possible to prevent the infiltration of perivascular tissue adjacent to the infusion site. Extravasation may cause necrosis and sloughing of the surrounding tissue. Large veins of the antecubital fossa are preferred to veins of the dorsum of the hand or ankle. Less suitable infusion sites should be used only when larger veins are unavailable and the patient's condition requires immediate attention. The physician should switch to a more suitable site as soon as possible and the infusion site in use should be continuously monitored for free flow.

The less concentrated 800 mcg/mL solution may be preferred when fluid expansion is not a problem. The more concentrated 1600 mcg/mL or 3200 mcg/mL solutions, may be preferred in patients with fluid retention or when a slower rate of infusion is desired.

Rate of Administration: Administration into an umbilical artery catheter is not recommended.

Dopamine in 5% Dextrose Injection should not be infused through ordinary I.V. apparatus, regulated only by gravity and mechanical clamps. Only an infusion pump, preferably a volumetric pump, should be used.

Each patient must be individually titrated to the desired hemodynamic or renal response to dopamine.

In titrating to the desired increase in systolic blood pressure, the optimum dosage rate for renal response may be exceeded, thus necessitating a reduction in rate after the hemodynamic condition is stabilized.

If a disproportionate rise in diastolic pressure (i.e., a marked decrease in pulse pressure) is observed in patients receiving dopamine, the infusion rate should be decreased and the patient

observed carefully for further evidence of predominant vasoconstrictor activity, unless such an effect is desired.

Administration rates greater than 50 mcg/kg/min have safely been used in adults in advanced circulatory decompensation states. If unnecessary fluid expansion is of concern, adjustment of drug concentration may be preferred over increasing the flow rate of a less concentrated dilution.

When discontinuing the infusion, it may be necessary to gradually decrease the dose of dopamine HCl while expanding the blood volume with I.V. fluids to prevent the development of marked hypotension.

Suggested Regimen:

1. When appropriate, increase blood volume with whole blood or plasma until central venous pressure is 10 to 15 cm H₂O or pulmonary wedge pressure is 14 to 18 mm Hg.
2. Begin infusion of dopamine hydrochloride solution at doses of 2 to 5 mcg/kg/min in adult or pediatric patients who are likely to respond to modest increments of heart force and renal perfusion.

In more seriously ill patients, begin infusion of dopamine hydrochloride at doses of 5 mcg/kg/min and increase gradually, using 5 to 10 mcg/kg/min increments, up to a rate of 20 to 50 mcg/kg/min as needed. If doses in excess of 50 mcg/kg/min are required, check urine output frequently. Should urinary flow begin to decrease in the absence of hypotension, reduction of dopamine dosage should be considered. More than 50% of adult patients have been satisfactorily maintained on doses less than 20 mcg/kg/min.

In patients who do not respond to these doses with adequate arterial pressures or urine flow, additional increments of dopamine may be given in an effort to produce an appropriate arterial pressure and central perfusion.

3. Treatment of all patients requires constant evaluation of therapy in terms of blood volume, augmentation of cardiac contractility, urine flow, cardiac output, blood pressure, and distribution of peripheral perfusion.

Dosage of dopamine should be adjusted according to the patient's response. Diminution of established urine flow rate, increasing tachycardia or development of new dysrhythmias are reasons to consider decreasing or temporarily suspending the dosage.

4. As with all potent intravenously administered drugs, care should be taken to control the rate of infusion so as to avoid inadvertent administration of a bolus of the drug.

800 mcg/mL Dosing Chart for Dopamine (mL/hr) Infusion Rate

Infusion rate (mcg/kg/min)	Patient Body Weight (kg)									
	10	20	30	40	50	60	70	80	90	100
2.5	1.9	3.8	5.6	7.5	9.4	11.3	13.1	15	16.9	18.8
5	3.8	7.5	11.3	15	18.8	22.5	26.3	30	33.8	37.5
10	7.5	15	22.5	30	37.5	45	52.5	60	67.5	75
15	11.3	22.5	33.8	45	56.3	67.5	78.8	90	101.3	112.5
20	15	30	45	60	75	90	105	120	135	150
25	18.8	37.5	56.3	75	93.8	112.5	131.3	150	168.8	187.5
30	22.5	45	67.5	90	112.5	135	157.5	180	202.5	225
35	26.3	52.5	78.8	105	131.3	157.5	183.8	210	236.3	262.5
40	30	60	90	120	150	180	210	240	270	300
45	33.8	67.5	101.3	135	168.8	202.5	236.3	270	303.8	337.5
50	37.5	75	112.5	150	187.5	225	262.5	300	337.5	375

1600 mcg/mL Dosing Chart for Dopamine (mL/hr) Infusion Rate

Infusion rate (mcg/kg/min)	Patient Body Weight (kg)									
	10	20	30	40	50	60	70	80	90	100
2.5	0.9	1.9	2.8	3.8	4.7	5.6	6.6	7.5	8.4	9.4
5	1.9	3.8	5.6	7.5	9.4	11.3	13.1	15	16.9	18.8
10	3.8	7.5	11.3	15	18.8	22.5	26.3	30	33.8	37.5
15	5.6	11.3	16.9	22.5	28.1	33.8	39.4	45	50.6	56.3
20	7.5	15	22.5	30	37.5	45	52.5	60	67.5	75
25	9.4	18.8	28.1	37.5	46.9	56.3	65.6	75	84.4	93.8
30	11.3	22.5	33.8	45	56.3	67.5	78.8	90	101.3	112.5
35	13.1	26.3	39.4	52.5	65.6	78.8	91.9	105	118.1	131.3
40	15	30	45	60	75	90	105	120	135	150
45	16.9	33.8	50.6	67.5	84.4	101.3	118.1	135	151.9	168.8
50	18.8	37.5	56.3	75	93.8	112.5	131.3	150	168.8	187.5

3200 mcg/mL Dosing Chart for Dopamine (mL/hr) Infusion Rate

Infusion rate (mcg/kg/min)	Patient Body Weight (kg)									
	10	20	30	40	50	60	70	80	90	100
2.5	0.5	0.9	1.4	1.9	2.3	2.8	3.3	3.8	4.2	4.7
5	0.9	1.9	2.8	3.8	4.7	5.6	6.6	7.5	8.4	9.4
10	1.9	3.8	5.6	7.5	9.4	11.3	13.1	15	16.9	18.8
15	2.8	5.6	8.4	11.3	14.1	16.9	19.7	22.5	25.3	28.1
20	3.8	7.5	11.3	15	18.8	22.5	26.3	30	33.8	37.5
25	4.7	9.4	14.1	18.8	23.4	28.1	32.8	37.5	42.2	46.9
30	5.6	11.3	16.9	22.5	28.1	33.8	39.4	45	50.6	56.3
35	6.6	13.1	19.7	26.3	32.8	39.4	45.9	52.5	59.1	65.6
40	7.5	15	22.5	30	37.5	45	52.5	60	67.5	75
45	8.4	16.9	25.3	33.8	42.2	50.6	59.1	67.5	75.9	84.4
50	9.4	18.8	28.1	37.5	46.9	56.3	65.6	75	84.4	93.8

Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration, whenever solution and container permit.

INSTRUCTIONS FOR USE

To Open

Tear outer wrap at notch and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually.

Preparation for Administration

(Use aseptic technique)

1. Close flow control clamp of administration set.
2. Remove cover from outlet port at bottom of container.
3. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated. **NOTE:** See full directions on administration set carton.
4. Suspend container from hanger.

5. Squeeze and release drip chamber to establish proper fluid level in chamber.
6. Open flow control clamp and clear air from set. Close clamp.
7. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.
8. Regulate rate of administration with an infusion pump, preferably a volumetric pump.

WARNING: Do not use flexible container in series connections.

HOW SUPPLIED

Dopamine Hydrochloride in 5% Dextrose Injection, USP is supplied in 250 and 500 mL LifeCare flexible containers as follows:

NDC No. 0409-7808-22 — 200 mg Dopamine HCl in 5% Dextrose Injection, USP
250 mL (800 mcg/mL)

NDC No. 0409-7808-24 — 400 mg Dopamine HCl in 5% Dextrose Injection, USP
500 mL (800 mcg/mL)

NDC No. 0409-7809-22 — 400 mg Dopamine HCl in 5% Dextrose Injection, USP
250 mL (1600 mcg/mL)

NDC No. 0409-7809-24 — 800 mg Dopamine HCl in 5% Dextrose Injection, USP
500 mL (1600 mcg/mL)

NDC No. 0409-7810-22 — 800 mg Dopamine HCl in 5% Dextrose Injection, USP
250 mL (3200 mcg/mL)

Store at 20 to 25°C (68 to 77°F). [See USP Controlled Room Temperature.] Protect from freezing.

Avoid contact with alkalies (including sodium bicarbonate), oxidizing agents or iron salts.

NOTE — Do not use the injection if it is darker than slightly yellow or discolored in any other way.

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