

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only.

Rx

Dopamine Hydrochloride Injection I.P.

AMERICAN

Dopacan

Injection

For I.V. Use Only After Dilution

COMPOSITION
Each ml contains:
Dopamine Hydrochloride I.P.40 mg
Water for Injection I.P.q.s.

DESCRIPTION
Dopamine hydrochloride injection is a clear, practically colorless, sterile, pyrogen-free, aqueous solution of dopamine HCl for intravenous infusion after dilution. Each millilitre of the 40 mg/mL preparation contains 40 mg of dopamine hydrochloride (equivalent to 32.31 mg of dopamine base).

INDICATIONS
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.

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.

DOSAGE AND ADMINISTRATION
WARNING: This is a potent drug; it must be diluted before administration to the patient.
Dopamine Hydrochloride Injection, IP 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 intravenous

solutions listed below.
5. 0.9% Sodium Chloride Injection, IP
5% Dextrose Injection, IP
5% Dextrose and 0.9% Sodium Chloride Injection, IP
5% Dextrose and 0.45% Sodium Chloride Injection, IP
5% Dextrose and Lactated Ringer's Injection

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.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE
Warning
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.

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

DRUG INTERACTION
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.

UNDESIRABLE EFFECTS
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.

FERTILITY, PREGNANCY AND LACTATION
Pregnancy
Teratogenic Effects: 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.

CLINICAL PHARMACOLOGY
Mechanism of Action
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 elicits its pharmacological action by activating dopamine D1 and D2 receptors, beta 1 receptors and alpha 1 receptors. The activation of different receptors leading to its effects are dependent on dopamine dose.

Pharmacodynamics
Dopamine's onset of action occurs within five minutes of intravenous administration and the duration of action is less than about ten minutes. Dopamine effects are dosage-dependent.
• At <5mcg/kg/minute, Dopamine HCL activates Dopamine D1 and Dopamine D2 receptors in the renal, mesenteric, and coronary vasculature causing vasodilation.
• At 5 to 10 mcg/kg/minute, dopamine HCl activates beta-1 receptors enhancing heart rate and contractility.
• At >10 mcg/kg/minute, dopamine HCl activates alpha-1 receptors causing vasoconstriction and increased blood pressure

Pharmacokinetics
Distribution
Following intravenous administration, dopamine is widely distributed in the body but does not cross the blood-brain barrier to a significant extent.

Elimination
The half-life of dopamine in adults is less than 2 minutes.

Metabolism
About 75% of dopamine is metabolized by monoamine oxidase (MAO) and catechol O-methyl transferase (COMT) in the liver, kidney, and plasma to the inactive compounds homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid, and about 25% is metabolized to norepinephrine in the adrenergic nerve terminals

Excretion
About 80% of dopamine is renally excreted as inactive metabolites within 24 hours. Dopamine is stored in vesicles or diffused back into the plasma.

Specific Populations
Pediatric Patients The reported clearance rate of dopamine in critically ill infants and pediatric patients ranged from 46 to 168 mL/kg/minute, with the higher values seen in the younger patients. The reported apparent volume of distribution in neonates was 0.6 to 4 L/kg, leading to an elimination half life of 5 to 11 minutes.

OVERDOSE
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.

STORAGE
Protected from light & moisture, at a temperature not exceeding 30°C.
Improper storage may deteriorate the product.

PRESENTATION
5 x 5ml Ampoules packed in a carton with pack insert. .

Manufactured by:

Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)
ICO: American Remedies LLC, DE, USA
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