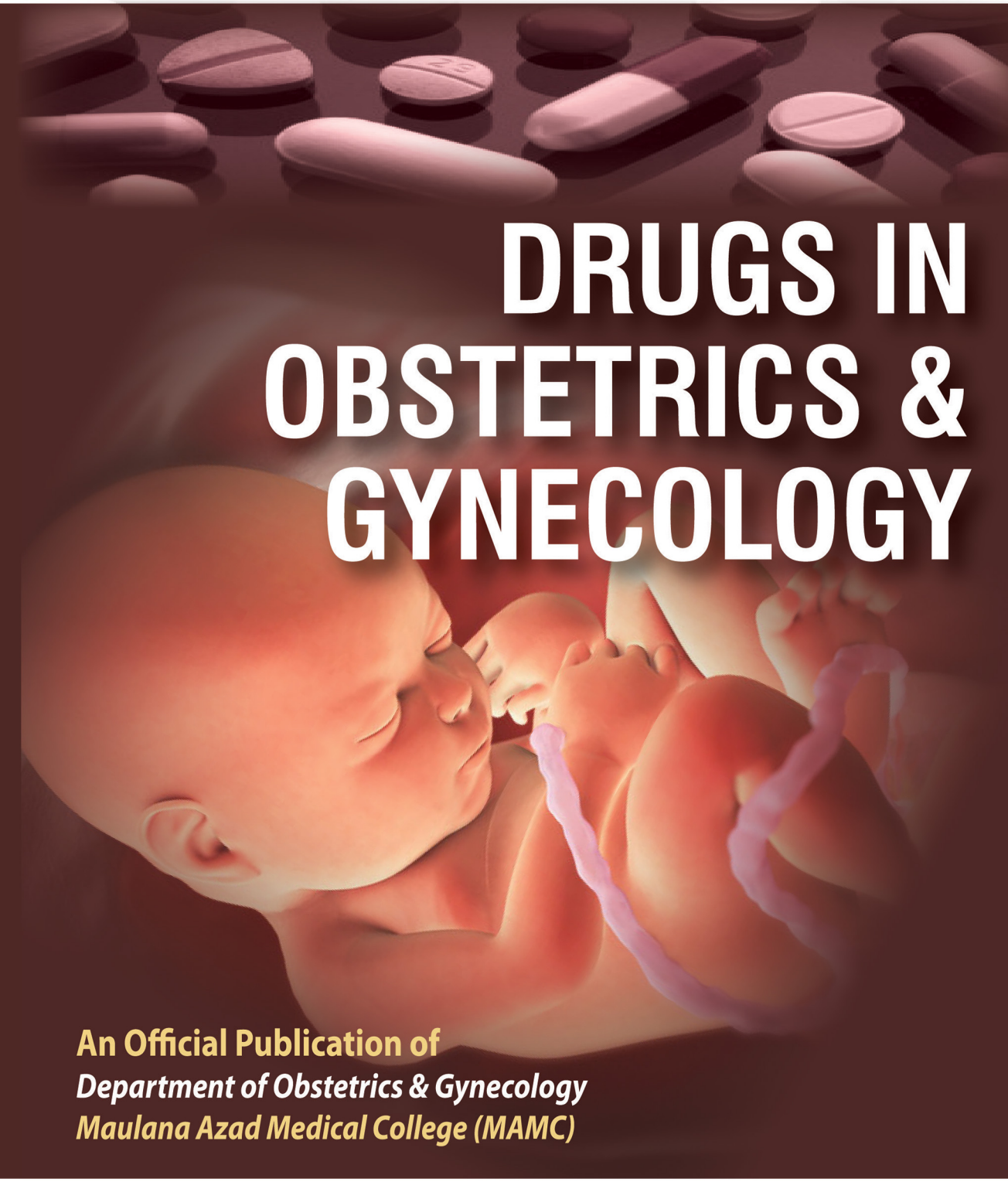
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DRUGS IN OBSTETRICS & GYNECOLOGY

An Official Publication of
Department of Obstetrics & Gynecology
Maulana Azad Medical College (MAMC)

Ashok Kumar
Krishna Agarwal
Sudha Prasad

JAYPEE

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Section II

EMERGENCY DRUGS

CHAPTER

2. Drugs Used in Medical Emergencies

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CHAPTER 2

Drugs Used in Medical Emergencies

Shakun Tyagi, Swati Kumari

INTRODUCTION

Most of the obstetric and gynecological emergencies require a combination of medical and surgical management. Medical emergencies such as shock, congestive heart failure, convulsions, electrolyte imbalance, hypocalcemia, bradycardia and anaphylactic shock are common medical emergencies which are encountered in obstetric and gynecological practice. This chapter will describe the drugs and their usage in these medical emergencies **(Table 2.1)**.

Table 2.1: Drugs used in commonly encountered medical emergencies

Emergency	*Drug(s)*
Shock	Adrenaline, noradrenaline, dopamine, dobutamine
Convulsions	Diazepam, phenytoin, midazolam
Electrolyte imbalance, acidosis	Potassium chloride, sodium bicarbonate
Hypocalcemia	Calcium gluconate
Bradycardia	Atropine
Anaphylactic shock	Hydrocortisone, adrenaline, chlorpheniramine, pheniramine

Drugs Used in Shock

Adrenaline (Epinephrine)

Pharmacology: It is a sympathomimetic catecholamine.

Indications of use: During emergency, it is used in following conditions:

- Hypotension and bradycardia
- Anaphylaxis
- Asystole, ventricular fibrillation (VF) and pulseless electrical activity (PEA).

Contraindications: It is given in life saving emergencies.

Dosage

- Bradycardia and hypotensive states, as IV infusion at an initial rate of 2–10 μg/min and increased stepwise gradually until the desired heart rate is achieved.[1]
- *Anaphylaxis:* 0.3–0.5 mg of undiluted adrenaline (1:1000) administered intramuscularly or subcutaneously in anterolateral aspect of thigh, repeated every 5–10 minutes as necessary.[2]
- In asystole, ventricular fibrillation (VF) and pulseless electrical activity, it is used in 1:10,000 dilutions in dose of 1.0 mg IV bolus dose.

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Preparation: Adrenaline is available in 1 mL ampoule with concentration of 1 mg/mL.

Preparation of IV Infusion: Dilute 1 mg in 250 mL of 5% dextrose or NS, this will make the concentration of adrenaline as 4 μg/mL. This fluid is then infused initially at the rate of 1 μg/min (15 macrodrops or 60 micro- drops per minute) and increase to desired dose.

1:1000 adrenaline concentration is:

- One ampoule of 1:1000 adrenaline in 1 mL volume
- This equals 1 mg in 1 mL
- This equals 1000 μg/mL.

If one ampoule is diluted to 10 mL:

- This equals 0.1 mg/mL
- This equals 100 μg/mL
- This equals 1:10,000 adrenaline concentration.

Adverse drug reaction: Anxiety, apprehensiveness, tremors, palpitations, headache, arrhythmias.

Drug interaction: Monoamine oxidase inhibitors, antidepressants imipramine or triptyline group of drugs.

Monitoring: Pulse rate, blood pressure, ECG, symptomatic improvement.

Safety during pregnancy: It is used as life saving drug for the mother in case of emergency.

It is FDA Category B.

Noradrenaline (Norepinephrine)

Pharmacology: It is a sympathomimetic catecholamine. Its action on alpha-1 adrenergic receptors results in peripheral vasoconstriction and ionotropic action on heart, whereas its action on beta adrenergic receptors leads to dilatation of coronary arteries.

Indications of use: Noradrenaline is used in hypotension to preserve cardiac and cerebral blood flow along with volume replacement. During shock volume replacement and treatment of the underlying cause are the mainstay.

Contraindications: It should not be used in hypovolemia without concurrent volume replacement; it is contraindicated in cases of chronic mesenteric or peripheral vasoconstriction unless as a lifesaving procedure.

Dosage: The infusion fluid is prepared by adding 2 mg of norepinephrine to 500 mL of 5% dextrose. Each milliliter of this solution contains 4 μg of noradrenaline. Initial dose is 2–3 mL (8–12 μg) of the diluted drug per minute. The rate is adjusted to maintain 100–120 mm Hg of systolic blood pressure. Average maintenance dose ranges from 0.5 mL to 1.0 mL (2 mcg to 4 mcg) per minute.[3]

Intravenous infusion is prepared in dextrose or dextrose normal saline as dextrose solution prevents loss of potency due to oxidation. *It is never diluted in saline.*

Adverse drug reaction: Tissue hypoxia, lactic acidosis and ischemic injury may occur if norepinephrine is given without plasma volume correction.

Bradycardia as a reflex result of rise in blood pressure and arrhythmias.

Drug interaction: Monoamine oxidase inhibitors, antidepressants imipramine or triptyline group of drugs. Norepinephrine injection use is contraindicated with anesthetic drugs like halothane or with cyclopropane as it can result in ventricular tachycardia or fibrillation.

Monitoring: Pulse rate, blood pressure, ECG, symptomatic improvement.

Preparation: Norepinephrine (Generic preparation)—available as 4 mL ampoule containing 1 mg per mL.

Safety during pregnancy: It is used as lifesaving drug for the mother.

It is FDA Category C.

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Dopamine

Pharmacology: The action of dopamine differs according to the concentration at which it is used.

- It acts as strong beta-1 adrenergic when given at rate of 2–10 mcg/kg/min
- It has alpha-adrenergic and dopaminergic effects at rate of more than 10 mcg/kg/min
- It has dopaminergic effect at rate of 0.5–2 mcg/kg/min.

Indications of use

- Used as an adjunct to other measures for treatment of hypotension
- In low cardiac output and poor perfusion of vital organs
- To increase mean arterial pressure in patients with septic shock which is refractory to volume expansion.

Contraindications: Pheochromocytoma, uncorrected tachyarrhythmia, ventricular fibrillation, allergy to corn or corn products, occlusive vascular diseases, patient using monoamine oxidases.

Dosage

- To increase renal blood flow and urine output: 1–5 mcg/kg/min IV infusion.
- To increase cardiac output, heart rate, cardiac contractility: 5–15 mcg/kg/min IV
- Increase in blood pressure but with vasoconstriction, may increase risk of tachyarrhythmias: 20–50 mcg/kg/min.

Increase in dosage may be at the rate of 1–4 mcg/kg/min at 10–30 minutes interval for desired response.

Simple formula for preparing the solution for IV infusion and calculating infusion rate in mL per hour.[4]

$$\frac{\text{Ordered amount of drug (mcg/kg/min)} \times \text{patient's weight (kg)} \times 60}{\text{Drug concentration (mcg/mL)}} = \text{IV infusion rate (mL/hour)}$$

So, if ordered amount of drug = 5 mcg/kg/min IV infusion

Weight of patient = 60 kg

Drug concentration = 3200 mcg/mL prepared by dissolving 1600 mg in 500 mL normal saline

$$\frac{5 \times 60 \times 60}{3200} = 5.6 \text{ mL per hour}$$

If infusion pump is not available then it can be given by microdrip set at rate of 20–25 microdrops per minute (1 mL equals 60 microdrops).

Adverse drug reaction: It may cause ventricular arrhythmia, hypertension or angina at higher doses. It can cause gangrene of extremities if high doses are administered for prolonged periods, which can occur even at low doses in patients with occlusive vascular disease.

It may rarely cause anaphylaxis.

Drug interaction: Monoamine oxidase inhibitors.

If used with phenytoin it can cause hypotension and bradycardia.

Oxytocic agents may cause severe hypertension when given with dopamine.

Monitoring: Pulse rate, blood pressure, ECG, input/output, symptomatic improvement.

Preparation: Dopamine (Generic drug)—available as 5 mL ampoule containing 40 mg/mL.

Safety during pregnancy: It is FDA Category C.

Dobutamine

Pharmacology: It has inotropic action through direct effect on the beta adrenergic receptors on heart. It has onset of action within two minutes but peak action occurs after 10 minutes.[5]

Indications of use: It is used in patients of cardiac decompensation and low cardiac output states.

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Contraindications: Dobutamine should not be used in cases of cardiac decompensation due to mechanical obstruction of ventricular filling and/or of outflow, such as pericardial tamponade, constrictive pericarditis, hypertrophic obstructive cardiomyopathy, idiopathic hypertrophic subortic stenosis. Some patients may have hypersensitivity to this drug.[3]

Dosage

Cardiac decompensation: 0.5–1 mcg/kg/min continuous infusion initially, then 2–20 mcg/kg/min, maximum dose 40 mcg/kg/min.

Low cardiac output: 2–20 mcg/kg/min IV, not exceeding 40 mcg/kg/min (this use is off label).

For preparing solution and calculating drip rate please refer to formula described in dopamine section, page 17.

Adverse drug reaction: The common side effects are nausea, headache, hypertension, tachycardia, premature, and ventricular ectopic. Rarely can it cause hypotension.

Drug interaction: This might be ineffective when used with beta blocking drugs. Side effects may be increased when it is used with cimetidine or methyl dopa. Do not add to injection sodium bicarbonate as chemically incompatible.

Monitoring: Pulse rate, blood pressure, ECG, input/output, symptomatic improvement.

Preparation: Generic drug available as 20 mL ampoule containing 12.5 mg/mL.

Safety during pregnancy: It is FDA Category B.

Drugs Used in Treatment of Convulsions

Diazepam

Pharmacology: It belongs to benzodiazepam group of drugs and acts on limbic, thalamus and hypothalamus.

Indications of use

- For acute control of seizure
- Premedication before anesthesia.

Contraindications: Hypersensitivity, glaucoma.

Dosage

- For acute control of seizure— 5–10 mg IV slowly over 2 minutes.
- Premedication before anesthesia—10 mg IM.

Adverse drug reaction: Drowsiness, confusion or depression, respiratory depression.

Drug interaction: Phenothiazines, narcotics, barbiturates, monoamine oxidase (MAO) inhibitors.

Monitoring: Patient should be monitored for cardiorespiratory depression. If any evidence of respiratory depression, antidote flumazenil should be used after measures to secure the airway, ventilation and intravenous access are taken.

Preparation

Diazepam (Generic drug): Available as 10 mL ampoule containing 5 mg/mL.

Safety during pregnancy: It is FDA Category C.

Increased risk of congenital malformations with use in first trimester.

Phenytoin

Pharmacology: It acts by preventing repetitive detonation of normal brain cells during depolarization shift that occurs in epileptic patients and consists of synchronous and large depolarization over which action potentials are superimposed. Its half-life is 12–24 hours and it gets metabolized in liver by hydroxylation and glucuronide conjugation.

Indications of use

- It is used as first-line drug in cases of generalized tonic-clonic seizures (GTCS).
- It is also used in cases of simple and complex partial seizure and status epilepticus occasionally.
- As an alternative in eclampsia when magnesium sulfate is contraindicated.

Contraindications: Hypersensitivity, sinus bradycardia, sinoatrial block, second and third degree A-V block, Adams-Stokes syndrome.

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Dosage: Initially a loading dose of 10–15 mg/kg is given over two to three minutes then infusion is given by diluting the desired dose in 100–250 mL normal saline over 35 minutes. It must not be diluted in glucose solution.[3]

It should be delivered via large gauge cannula in a large vein. Line must be flushed with saline before and after administration.

The rate must not exceed 50 mg/min.

Adverse drug reaction: Extravasation of drug can cause severe thrombophlebitis. Sometimes it may cause hypotension, arrhythmias, or respiratory depression.

Drug interaction: Chloramphenicol, isoniazid, cimetidine and warfarin inhibit phenytoin metabolism and can precipitate its toxicity.

Monitoring: Heart rate, blood pressure, respiratory rate, and ECG monitoring should be done throughout when the loading dose is being given. Inspection of delivery site is important to look for any evidence of extravasation.

Preparation: Dilantin-5 mL ampoule containing 50 mg/mL.

Safety during pregnancy: Prenatal exposure to fetus increases risk of fetal malformations and other adverse developmental outcomes.

It is FDA Category D drug.

Midazolam

Pharmacology: Midazolam is a short acting benzodiazepine and act as central nervous system depressant. It primarily act by facilitating inhibitory GABAergic transmission.

After intramuscular injection, the onset of action is after 15 minutes with peak action at 30–60 minutes. It is faster acting, shorter acting and 3 times more potent than diazepam. It is used via intravenous route for induction of anesthesia.

It is metabolized in liver by hydroxylation; the metabolites get conjugated and excreted in urine.

Indications of use: Sedation, anxiolysis, amnesia during for short surgical procedures.

Preanesthetic agent for induction of anesthesia.

Contraindications: Hypersensitivity, open angle glaucoma.

Dosage

Intravenous dose: 1 mg slowly over two minutes, then response is assessed, not more than 2.5 mg is given, maintenance dose is usually 25% of the dose required to achieve adequate sedation.[3]

Adverse drug reaction: Cardiorespiratory depression, sedation, light headedness, psychomotor and cognitive impairment, vertigo.

Drug interaction: Its sedative action is accentuated by morphine, fentanyl, etc.

Caution exhibited with drugs that inhibit P450-3A4 enzyme system (erythromycin, diltiazem, verapamil, ketoconazole).

Monitoring: For IV use, response is assessed with respect to responsiveness, speech, facial expression and eyes status.

Close cardiorespiratory monitoring by measuring SpO_2, pulse rate, blood pressure and respiratory rate.

Preparation: Midazolam (Generic drug)—available as 2 mL ampoule containing 1 mg/mL.

Safety during pregnancy: Increased risk of congenital malformations.

It is FDA Category D.

Drugs Used is Electrolyte Imbalance

Potassium Chloride

Pharmacology: It directly corrects the ionic concentration and the onset of action is immediate.

Indications of use: It is used in conditions which cause hypokalemia like excessive vomiting and diarrhea, with diuretic drugs, diabetic ketoacidosis, adrenal gland disorder, etc. It is given if serum potassium levels fall below 2.5 mEq/L.

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Contraindications: Renal failure, Addison's disease, severe burns, etc.

Dosage: Potassium chloride solution is prepared in concentration 20–40 in 500 mL of NS or 5% dextrose solution. It is transfused at rate not exceeding 10 mEq/hour and in 24 hours the dose should not exceed 200 meq.

If serum potassium level is less than 2.0 mEq/L with ECG changes it can be infused at the rate of 40 mEq/hour with maximum of 400 mEq in 24 hours.

Adverse drug reaction: These are muscle weakness, limp feeling, severe stomach pain, numbness or tingling in hands, feet and mouth, cardiac arrhythmias, heart blocker even cardiac arrest may occur.

Drug interaction: Hyperkalemia can occur with potassium sparing diuretics.

Monitoring: Pulse rate, BP, ECG monitoring.

Preparation: Potassium hydrochloride—available as ampoules containing 20 mEq/50 mL.

Safety during pregnancy: Usually used in life-threatening conditions.

It is FDA Category C.

Sodium Bicarbonate

Pharmacology: It is used as intravenous bolus or infusion for correction of acid-base imbalance.[6]

Indications of use: It is used in metabolic acidosis as in circulatory insufficiency due to shock or severe dehydration, severe renal disease, uncontrolled diabetes, etc.

Contraindications: Metabolic and respiratory alkalosis, hypocalcemia, etc.

Dosage: Depends on the indication and weight of the patient according to arterial blood gas (ABG) findings.

Requirement of sodium bicarbonate (mEq) can be calculated by following formula:

- 0.2 × weight of the patient (kg) × base deficit
  Or
- 0.5 × weight (kg) × [24-serum HCO_3 (mEq/L)].

Solution for IV infusion is prepared by dissolving required amount of sodium bicarbonate in 500 L of normal saline. Initially an infusion of 2–5 mEq/kg body weight is transfused over a period of 4–8 hours. This will produce a measurable improvement in the abnormal acid-base status of the blood. Then further dose is calculated based on patient's response and base deficit on ABG.

Adverse drug reaction: Infection at site of injection, phlebitis, suppression of respiratory drive, hypernatremia resulting in.

Drug interaction: None.

Monitoring: ABG is to be repeated to know pH of blood.

Preparation: 50 mL single dose vial containing 8.4% sodium bicarbonate which is equal to 1 mEq per mL (84 mg sodium bicarbonate equal to 1 mEq sodium bicarbonate).

Safety during pregnancy: Used for life-threatening emergencies.

It is FDA Category C.

Drugs Used in Hypocalcemia

Calcium Gluconate

Pharmacology: Calcium is an important body constituent and essential for maintenance of physiology of nervous, muscular, skeletal systems, cell membranes, coagulation and capillary permeability.

Onset of action occurs in 5 minutes.

Indications of use: Hypocalcemic tetany, hypocalcemia related to hypoparathyroidism, magnesium sulfate toxicity.

Contraindications: Hypercalcemia, ventricular fibrillation, digitalis use.

Dosage: Dose depends on the requirement of the individual patient.

In case of severe hypocalcemia (ionized serum calcium less than 1 mmol per liter).

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- Without seizure or tetany—0.5 mg/kg/hour IV infusion with maximum dose of 3–4 g IV over 4 hours
- In hypocalcemic tetany—2 g calcium gluconate given IV over 5–10 minutes, followed by continuous IV infusion at 0.5 mg/kg/hour.

Infusion fluid is prepared by dissolving calcium gluconate in 500 mL of normal saline. The number of ampoules depends on the concentration required.

Adverse drug reaction: Local reaction occurs if drug gets extravasated. There is sense of warmth on intravenous injection. Rapid injection may cause vasodilatation, hypotension, bradycardia, cardiac arrhythmias, syncope and cardiac arrest.[3]

Drug interaction: It is contraindicated in digitalized patient.

Monitoring: Pulse rate, blood pressure, respiratory rate, ECG and serum calcium levels every 6 hours.

Preparation: Calcium gluconate (Generic drug)—10 mL ampoule containing 100 mg per mL of calcium gluconate.

Safety during pregnancy: It is used during possibly life-threatening disorders.

It is FDA Category C.

Drug Used in Bradycardia

Atropine

Pharmacology: Atropine acts by inhibiting the muscarinic actions of acetylcholine. This action occurs at post ganglionic parasympathetic neuro-effector sites like smooth muscles, secretory glands and CNS sites. The action is dose related. It is rapidly absorbed and the half-life is 3–4 hours. It is metabolized in liver and excreted in the urine.[5,6]

Indications of use

- Sinus bradycardia with hypotension
- As anesthetic premedication
- Organophosphorus poisoning.

Contraindications: Absolute contraindicated are narrow iridocorneal angle, myasthenia gravis, obstructive GI diseases, e.g. pyloric stenosis.

Dosage: For sinus bradycardia with hypotension—0.5–1 mg IV every five minutes not more than 3 mg.[3]

Adverse drug reaction

Anticholinergic side effects: Patient may experience dry mouth; difficulty in talking swallowing; dry, flushed and hot skin; fever; difficulty in micturition; dilated pupil, photophobia and blurring of near vision; palpitation, excitement, ataxia and delirium. Overdosage may lead to hypotention, thready pulse or cardiovascular collapse.

Drug interaction: It delays absorption of most of drugs as it slows gastric emptying. It has additive effect with antihistaminic, tricyclic antidepressants and pethidine.

Monitoring: Cardiovasular monitoring.

Preparation: Atropine sulfate (generic preparation)—10 mL vial containing 0.1 mg/mL.

Safety during pregnancy: Safe.

Category B Drug: It is used for maternal life-threatening conditions.

Drugs Used in Anaphylactic Shock

Hydrocortisone Sodium Succinate

Pharmacology: It is a short-acting synthetic steroid with both glucocorticoid and mineralocorticoid action. It increases absorption of sodium in distal convoluted tubules of loop of Henle in kidney and increase excretion of potassium and hydrogen. It has anti-inflammatory action.[7]

It has half-life of 1.5 hours. It gets metabolized primarily by hepatic microsomal enzymes reduction, hydroxylation and oxidation and then gets conjugated with glucuronic acid or sulfate. It is excreted in urine, excretion is

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complete in 12 hours therefore 4–6 hourly dose is required.

Indications of use

- Shock unresponsive to conventional therapy
- Adrenocortical insufficiency
- Status asthmaticus
- Tubercular meningitis
- Acute exacerbation of various autoimmune and allergic disorders like systemic lupus erythematosus (SLE).

Dosage

- In shock and status asthmaticus—1–2 mg/kg slow IV for 24 hours followed by maintenance dose of 0.5–1 mg/kg slow IV every 6 hourly
- Acute adrenal insufficiency—100 mg IV bolus followed by 100 mg 8 hourly IV slowly over 30 seconds.

Adverse drug reaction: It can lead to fluid retention, hypertension, hypokalemia, alkalosis, and hyperglycemia, aggravates peptic ulcers. Congestive heart failure in susceptible patient, increased intraocular pressure.

Drug interaction: Phenobarbiturates and phenytoin the induce metabolism.

Monitoring: No short-term side effects. Long-term use can cause suppression of Hypothalamo pituitary adrenal axis.

Preparation: 100 mg vial containing 100 mg hydrocortisone sodium succinate in powder form to be reconstituted by adding 2 mL of water for injection.

Safety during pregnancy: It should be given when benefit clearly outweighs the risk.

It is FDA Category C.

Chlorpheniramine Maleate and Pheniramine Maleate

Pharmacology: They are selective antagonist for H1 histaminic receptors. Onset of action is within half an hour and duration of action is 4–6 hours. It is metabolized in liver and gets excreted in urine.

Indications of use: Allergic reaction to blood or plasma products, anaphylaxis and for treatment of allergic symptoms like bronchoconstriction, urticaria, and itching.

Contraindications: Narrow angle glaucoma, hypersensitivity.

Dosage: In the above conditions, chlorpheniramine is used in dose of 10–20 mg by IV, IM, or as SC injection single dose, maximum dose is 40 mg.

Injection pheniramine given in dose of 22.75 mg IV or IM.

Adverse drug reaction: Adverse effects such as sedation, diminution in alertness and concentration, light headedness, motor incoordination, fatigue, tendency to sleep, dryness of mouth, alteration in bowel habit, urinary hesitancy and blurring of vision is due to its anticholinergic action, epigastric discomfort, acute overdose can produce central excitation tremors, hallucination, convulsions, hypotension, fever.

Drug interaction: Monoamine oxidase inhibitors, phenytoin, drugs causing sedation.

Monitoring

- Monitoring is not required for IM dose.
- Pulse rate, blood pressure, ECG for IV use.

Preparation: Chlorpheniramine maleate (generic drug)—1 mL ampoule for injection containing 10 mg/mL.

Injection avil-available as vial containing 22.75 mg/mL.

Safety during pregnancy: Nonteratogenic.

It is FDA Category B.

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